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Obesity and the Risk of Newly Diagnosed Asthma in School-age Children

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To determine the relation between obesity and new-onset asthma among school-age children, the authors examined longitudinal data from 3,792 participants in the Children's Health Study (Southern California) who were asthma-free at enrollment. New cases of physician-diagnosed asthma, height, weight, lung function, and risk factors for asthma were assessed annually at five school visits between 1993 and 1998. Incidence rates were calculated, and proportional hazards regression models were fitted to estimate the adjusted relative risks of new-onset asthma associated with percentile of body mass index (weight (kg)/height $(m)^2$) and indicators of overweight (>85th body mass index percentile) and obesity (>95th body mass index percentile). The risk of new-onset asthma was higher among children who were overweight (relative risk (RR) = 1.52, 95% confidence interval (CI): 1.14, 2.03) or obese (RR = 1.60, 95% CI: 1.08, 2.36). Boys had an increased risk associated with being overweight (RR = 2.06, 95% 1.33, 3.18) in comparison with girls (RR = 1.25, 95% CI: 0.83, 1.88). The effect of being overweight was greater in nonallergic children (RR = 1.77, 95% CI: 1.26, 2.49) than in allergic children (RR = 1.16, 95% CI: 0.63, 2.15). The authors conclude that being overweight is associated with an increased risk of new-onset asthma in boys and in nonallergic children.

allergy and immunology; asthma; body mass index; body weight; child; obesity

Abbreviations: BMI, body mass index; CI, confidence interval; ETS, environmental tobacco smoke; RR, relative risk.

Asthma is a large and growing threat to children's health and well-being (1). In some communities, the prevalence of asthma among school-age children exceeds 25 percent, and prevalence has been rapidly rising in many regions of the developed world (2–6). Although asthma is the subject of intense research efforts, the etiology of asthma and the reason for the increase in prevalence have yet to be firmly established (1, 7–10).

Much of the focus of childhood asthma research has been on atopy and the development of allergic responses to common indoor allergens; however, atopic pathways do not appear to contribute to a substantial portion of cases, and other etiologic pathways that involve nonallergic mechanisms are likely to be involved (7, 8, 11–14). Exposures of interest whose effects may be partly mediated by nonallergic pathways include in-utero and postnatal tobacco smoke exposure, ozone, infant feeding practices, and viral infections (9, 12, 13, 15–21). An emerging body of evidence suggests that obesity may play a role in the development of childhood asthma through nonallergic pathways (1, 14, 22–28).

It has long been recognized that obesity is more common among children with asthma, and associations between asthma and high body mass index (BMI) (weight (kg)/height $(m)^2$) have been observed in cross-sectional studies of adults and children (1, 14, 22, 29). These associations have been explained as evidence that asthma causes obesity due to a lack of physical activity among children with asthma; however, this interpretation has been challenged by the results of recent longitudinal studies. In adults, obesity is associated with an increased risk of asthma in prospective studies, especially among women (23, 26, 27). In girls, becoming overweight or obese between the ages of 6 and 11 years has been found to increase the risk of developing new asthma and to increase bronchial responsiveness during adolescence (25). Additional longitudinal studies of children are needed to define the temporality of the association between asthma and obesity and to determine whether the

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association with obesity is restricted to girls or to nonallergic children (30).

The Children's Health Study, a longitudinal study of respiratory health among school-age children in 12 Southern California communities, provided us with an opportunity to investigate whether being overweight or obese is an antecedent condition associated with increased risk of newly diagnosed asthma and whether any risk associated with being overweight or obese varies by sex or allergy status (3). We examined the association of new cases of physician-diagnosed asthma and the development of obesity using data collected at yearly assessments between 1993 and 1998 from a cohort of 3,792 children who were asthma-free at study enrollment.

MATERIALS AND METHODS

The Children's Health Study is a prospective study of the determinants of children's respiratory health (3). Children were recruited in 1993 from fourth-, seventh-, and 10th-grade classes in public schools in 12 Southern California communities. A second cohort of fourth graders was recruited in 1996. At study entry, the parents or guardians of each participating student provided written informed consent and completed written questionnaires that provided information on sociodemographic factors, history of respiratory and allergic illnesses and their associated risk factors, exposures, including smoking by household members, and household characteristics. Children with any lifetime history of asthma at study entry were considered to not be at risk and were excluded from the analysis. This resulted in a cohort of 3,792 children (1,993 girls and 1,799 boys). Wheezing was defined as any lifetime history of wheezing at study entry. Children with a history of wheezing but no diagnosis of asthma were considered to be at risk for a new diagnosis of asthma and were included in the study.

Children were assessed annually during school visits until high school graduation. The analyses described here included data collected at five visits between 1993 and 1998 for fourth and seventh graders who entered the study in 1993 and data collected at three visits for 10th graders between 1993 and 1995 and the second cohort of fourth graders between 1996 and 1998. During each annual assessment visit to schools, children completed an update questionnaire and interview that included items on physician diagnoses of asthma, other respiratory symptoms, and recent exposure history. An incident asthma case was defined as a new physician diagnosis of asthma during the time between follow-up assessments. Date of diagnosis for incident asthma cases was assigned as the midpoint of the period between follow-up assessments.

Height, weight, and lung function were measured annually using standard protocols. Because the relation between BMI and obesity changes with age and varies by sex, we categorized BMI into age- and sex-specific percentiles based on the Centers for Disease Control and Prevention BMI growth charts using 1-month age intervals (31). Overweight was defined as BMI greater than the age- and sex-specific 85th percentile and obesity as BMI greater than the 95th percentile. Lung function was measured as previously described (32). Age- and sex-specific percent predicted values for forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow rate between 25 percent and 75 percent of forced vital capacity were calculated on the basis of lung function-height relations in the study population.

Potential cofounders or effect modifiers were identified by review of the literature and preliminary analyses and included age, sex, race/ethnicity, health insurance, community of residence, parental history of asthma and allergies, birth weight, humidifier use, history of wheezing, history of allergy, participation in team sports, personal smoking, household environmental tobacco smoke (ETS) exposure, household pets and pests, puberty, and lung function level. Wheezing with exercise was defined as a parental report of wheezing with exercise, and personal and parental family histories of allergy were based on self-reported physician diagnoses of allergies on the baseline questionnaire, including eczema, hay fever, and symptoms of allergy to pets and dust. Allergic rhinitis was defined by parental report of hay fever or nasal allergy. Age of puberty was defined as the age of peak height velocity and was assigned as the midpoint of the interval between annual examinations where maximum growth occurred. Recent inhaled medication use and personal smoking habits were ascertained annually by private interview by field team members.

Statistical methods

Incidence rates for new cases of physician-diagnosed asthma were calculated using the number of new cases divided by the person-years at risk over a 4-year period of follow-up. Stratified rates were calculated for boys and girls, as well as age- and sex-specific BMI percentile categories at study entry. The numbers of new cases and person-years at risk within each stratum were determined and summed over the follow-up period. For cases, the number of person-years at risk was fixed at 0.5 for the year in which asthma was diagnosed.

To further investigate the relations between BMI and new physician diagnoses of asthma with adjustment for the effects of confounding variables, we fitted Cox proportional hazards regression models. We used stratified baseline hazards allowing for sex and age strata in the analysis of the entire cohort and in analyses stratified by allergy status, and we used baseline hazards stratified on age in the analyses of subgroups defined by sex. We investigated associations of new-onset asthma with obesity by including BMI percentiles and overweight and obesity status in the models as time-dependent variables using a 1-year lag period. For sensitivity analyses, we used 2-year lag periods for BMI, overweight, and obesity, as well as fixed BMI and obesity categories at study entry. Additional time-varying covariates included puberty status and ETS exposure variables. In the final regression models, the association between asthma and BMI was adjusted for age, community, race/ethnicity, wheezing, and sex-specific effects of allergy. We found little evidence for confounding (<10 percent change in BMI estimates) by other covariates, including lung function level (forced expiratory volume in 1 second percent predicted). We assessed the heterogeneity of associations among subgroups by fitting

TABLE 1. Selected characteristics of participants with no history of physician-diagnosed asthma at study entry, Children's Health Study, 1993–1998

Characteristic	Girls (n = 1,993)		Boys (n = 1,799)	
	No.	%	No.	%
Race/ethnicity				
White	1,132	56.8	1,070	59.5
Hispanic	574	28.8	503	28.0
Asian	108	5.4	105	5.8
Black	112	5.6	69	3.8
Other	67	3.4	52	2.9
Age (years) at study entry				
7–9	1,045	52.4	894	49.7
10–11	292	14.7	367	20.4
12–14	365	18.3	277	15.4
15–18	291	14.6	261	14.5
Postpubertal at study entry				
Yes	298	15.2	248	14.0
No	1,663	84.8	1,519	86.0
Health insurance				
Yes	1,595	82.5	1,482	85.3
No	338	17.5	256	14.7
Family history of asthma				
Yes	278	15.3	247	14.9
No	1,544	84.7	1,414	85.1
History of allergy in mother				
Yes	537	28.6	496	29.0
No	1,338	71.4	1,215	71.0
History of allergy in father				
Yes	429	23.8	383	23.5
No	1,371	76.2	1,246	76.5
History of allergy				
Yes	418	22.1	403	23.6
No	1,470	77.9	1,306	76.4
History of wheezing				
Yes	404	21.5	404	24.0
No	1,471	78.5	1,281	76.0
History of allergic rhinitis				
Yes	431	22.4	345	19.8
No	1,491	77.6	1,397	80.2
Wheezing with exercise				
Yes	70	3.8	64	3.8
No	1,793	96.2	1,618	96.2
Personal smoking				
Yes	59	3.0	60	3.3
No	1,934	97.0	1,739	96.7
Household ETS* exposure				
Yes	351	18.1	308	17.7
No	1,587	81.9	1,436	82.3
Humidifier use				
Yes	486	26.0	462	27.0
No	1,384	74.0	1,251	73.0
Yearly parental income				
Low (<$15,000)	241	15.8	241	15.8
Middle ($15,000–<$50,000)	673	41.9	652	42.6
High (≥$50,000)	660	41.1	637	41.6
Weight status†				
Obese				
Yes	176	8.8	216	12.0
No	1,816	91.2	1,578	88.0
Overweight				
Yes	456	22.9	461	25.7
No	1,536	77.1	1,333	74.3

* ETS, environmental tobacco smoke.

† Cutpoints were based on age- and sex-specific body mass index (weight (kg)/height $(m)^2$) categories from the Centers for Disease Control and Prevention body mass index growth charts (31). Obesity was defined as a body mass index greater than the 95th percentile and overweight as a body mass index greater than the 85th percentile.

separate models in each subgroup and by including interaction terms in regression models applied to the entire cohort; the statistical significance of differences was tested by likelihood ratio test. We conducted sensitivity analyses by limiting the case definition to children who reported inhaled medication use and by restricting the cohort to children without a history of wheezing at study entry. All analyses were carried out using SAS software (SAS Institute, Inc., Cary, North Carolina). Unless otherwise noted, all hypothesis testing was conducted assuming a 0.05 significance level and a two-sided alternative hypothesis.

RESULTS

At study entry, participants ranged in age from 7 years to 18 years (table 1). The majority of children were non-Hispanic White or Hispanic White. Approximately 20 percent of the children had a history of physician-diagnosed allergic rhinitis. A lifetime history of any wheezing was reported for 24 percent of boys and 21 percent of girls. Few children smoked, but approximately 18 percent had a lifetime history of ETS exposure. More boys than girls were overweight or obese at study entry.

Risk factors for a new physician diagnosis of asthma varied by sex (table 2). Among girls, a history of allergy in the mother and a history of wheezing or exercise-induced wheezing were risk factors for new-onset asthma. Among boys, risk factors for new-onset asthma included other race/

TABLE 2. Relative risk of new-onset physician-diagnosed asthma, Children's Health Study, 1993–1998*

	Girls (n = 1,993)		Boys (n = 1,799)		p value for test of sex difference in RRs†,‡
	RR	95% CI†	RR	95% CI	
Race/ethnicity					
White	1.00		1.00		0.31
Asian	0.95	0.44, 2.03	0.66	0.23, 1.93	
Black	1.53	0.77, 3.02	2.15	0.95, 4.88	
Hispanic	1.05	0.70, 1.57	1.29	0.83, 2.03	
Other	1.07	0.33, 3.46	3.62	1.40, 9.32	
Postpubertal vs. prepubertal	1.43	0.92, 2.21	3.07	1.89, 4.97	0.03
Health insurance	1.55	0.94, 2.56	1.16	0.66, 2.02	0.36
Family history of asthma	1.14	0.74, 1.76	2.21	1.43, 3.43	0.03
Allergy history in mother	1.58	1.13, 2.21	1.38	0.93, 2.04	0.55
History of allergy	1.17	0.79, 1.74	2.23	1.51, 3.29	0.05
History of allergic rhinitis	1.23	0.85, 1.79	2.81	1.89, 4.16	0.01
History of wheezing	1.92	1.35, 2.73	3.15	2.12, 4.69	0.04
Exercise-induced wheezing	4.23	2.50, 7.17	6.22	3.45, 11.23	0.74
Household ETS† exposure	0.84	0.59, 1.19	1.53	1.03, 2.26	0.03
Humidifier use	1.05	0.73, 1.52	1.54	1.04, 2.26	0.15

* All effect estimates are from models that included one factor adjusted for community and ethnicity using baseline hazards stratified by age group.

† RR, relative risk; CI, confidence interval; ETS, environmental tobacco smoke.

‡ p value for the difference in the association between asthma and the risk factor by sex (likelihood ratio test).

ethnicity, puberty, family history of asthma, history of allergy or allergic rhinitis, history of wheezing or wheezing with exercise, household ETS exposure, and household humidifier use. The effects of puberty, wheezing status, family history of asthma, allergy and allergic rhinitis history, and ETS exposure differed significantly in boys compared with girls. Health insurance, history of allergy in the father, household pets and pests, participation in team sports, parental income, and education were not significant risk factors in this analysis.

Over the 4-year period of follow-up, 288 new cases of asthma were diagnosed. The overall crude incidence rate was 24.6 per 1,000 person-years at risk. Girls had a higher incidence rate than boys (table 3). Crude rates of new-onset physician-diagnosed asthma were higher in overweight and obese children than in children of normal weight. Although the elevated rates were apparent in both overweight and obese boys and girls, the patterns of rates varied by sex. Incidence rates of asthma were generally higher for normal-weight girls than for normal-weight boys. In contrast, obese boys had higher rates of asthma than obese girls. As a result of this pattern of rates, boys had a larger difference between the obese and normal-weight groups than did girls. Among girls, the rates in the overweight group at study entry were higher than the rates in the obese group. Rates in the lowest percentiles of BMI were not substantially different from those among normal-weight children.

Results from the multivariable models showed that the relative risk for new physician-diagnosed asthma was increased in the upper BMI percentiles (table 4). Overweight and obesity were both associated with increased risk of a new diagnosis of asthma (relative risk (RR) = 1.52 (95 percent confidence interval (CI): 1.14, 2.03) and RR = 1.60 (95 percent CI: 1.08, 2.36), respectively).

As is suggested by the patterns of crude incidence rates for BMI percentiles, we saw some evidence that the adjusted relative risks comparing overweight or obese children with normal-BMI children were larger in boys than in girls (p = 0.09). Obese boys had an adjusted relative risk of 2.29 (95 percent CI: 1.35, 3.88) compared with nonobese boys. Among girls, the relative risk associated with obesity (RR = 1.10, 95 percent CI: 0.60, 2.05) was smaller than that among boys, and none of the relative risk estimates for BMI percentile were statistically significant. To assess the potential for misclassification of new-onset asthma, we conducted a sensitivity analysis that used a case definition that required a report of inhaled medication use in addition to a new diagnosis of asthma. When we restricted cases to children who had used inhalers recently, the risk estimates changed little. For example, in the analysis restricted to those who had recently used inhalers, the relative risk for obese children compared with nonobese children was 2.31 (95 percent CI: 1.22, 4.37) for boys and 1.10 (95 percent CI: 0.49, 2.47) for girls. The associations with being overweight followed the same patterns and were of approximately equal magnitude as those for obesity. In further sensitivity analyses that restricted the cohort to children without a history of wheezing, the risk estimates did not change substantially in

TABLE 3. Numbers of new asthma cases, person-years at risk, and crude rates of asthma incidence by percentile of body mass index at study entry and weight status, Children's Health Study, 1993–1998

Factor and percentile	All children (*n* = 3,792)			Girls (*n* = 1,993)			Boys (*n* = 1,799)		
	No. of cases	Person-years at risk	Incidence rate (per 1,000 person-years)	No. of cases	Person-years at risk	Incidence rate (per 1,000 person-years)	No. of cases	Person-years at risk	Incidence rate (per 1,000 person-years)
Body mass index*									
≤25	52	2,132.6	24.4	29	1,113.2	26.1	23	1,019.4	22.6
25.1–50	50	2,405.0	20.8	31	1,191.0	26.0	19	1,214.0	15.7
50.1–75	74	3,064.6	24.1	45	1,718.2	26.2	29	1,346.4	21.5
75.1–85	27	1,310.0	20.6	15	736.0	20.4	12	574.1	20.9
85.1–95	49	1,624.2	30.2	30	870.2	34.5	19	754.0	25.2
>95	36	1,147.8	31.4	14	546.7	25.6	22	601.1	36.6
Weight status†									
Overweight									
≤85	203	8,912.1	22.8	120	4,758.3	25.2	83	4,153.8	20.0
>85	85	2,772.0	30.7	44	1,417.0	31.1	41	1,355.0	30.3
Obese									
≤95	252	10,536.3	23.9	150	5,628.5	26.6	102	4,907.8	20.8
>95	36	1,147.8	31.4	14	546.7	25.6	22	601.1	36.6
Total cohort‡	288	11,684.1	24.6	164	6,175.3	26.6	124	5,508.9	22.6

* Weight (kg)/height $(m)^2$. Body mass index percentiles were calculated using 1-month age intervals (31).

† Cutpoints were based on age- and sex-specific body mass index categories from the Centers for Disease Control and Prevention body mass index growth charts (31). Obesity was defined as a body mass index greater than the 95th percentile and overweight as a body mass index greater than the 85th percentile.

‡ Total numbers of cases and person-years at study entry.

comparison with the estimates from the analyses that included all children.

The associations of overweight with new-onset asthma were significant and were larger in nonallergic children (RR = 1.77, 95 percent CI: 1.26, 2.49) than in allergic children (RR = 1.16, 95 percent CI: 0.63, 2.15) ($p = 0.03$) (table 5). There was little evidence for an effect of overweight in allergic children. The asthma risk associated with being overweight was larger and statistically significant in nonallergic boys.

We found that the effects of being overweight were larger among boys than among girls in models that assessed interactive effects of obesity and sex in children with different allergy statuses ($p < 0.03$) (data not shown). The relative risk for overweight in boys was 1.93 (95 percent CI: 1.05, 3.59) times higher than that in girls ($p = 0.03$). In addition, the effect of being overweight was approximately half (RR = 0.47, 95 percent CI: 0.23, 0.94) that in allergic children compared with nonallergic children ($p = 0.01$). We found little evidence for differences in the relative risks for being overweight or obese by age, puberty status, early onset of puberty, family history of asthma or allergy, wheezing status, race/ethnicity, participation in team sports, and household ETS exposure.

In sensitivity analyses, adjustment for health insurance, parent/guardian educational attainment, parental income, parental history of asthma and allergies, birth weight, humidifier use, history of exercise-induced wheezing, history of allergy, participation in team sports, personal smoking, household ETS exposure, household pets and pests, puberty status, and lung function level did not substantially change any of the risk estimates for BMI percentiles in either boys or girls. We attempted to assess the effects of change in obesity over the follow-up period by modeling the annual change in obesity status; however, too few nonobese children became obese in the subsequent year for an informative analysis. The associations with new-onset asthma were slightly reduced in magnitude when fixed BMI and obesity categories at study entry or 2-year lagged BMI categories were used in the models instead of the 1-year lagged time-varying BMI percentiles.

DISCUSSION

Understanding the relation between obesity and asthma in children may be an important step in clarifying the etiology of childhood asthma. Our findings support the hypothesis that being overweight or obese is associated with increased risk of new-onset asthma in children. A growing body of evidence supports the possibility that obesity increases the risk of new-onset asthma (1, 22, 23, 25–28). Because the vast majority of studies on the relation between asthma and obesity have been cross-sectional, the temporal relation between obesity and asthma onset is not clear. Three recent

TABLE 4. Adjusted relative risk of new-onset asthma by percentile of body mass index and weight status, Children's Health Study, 1993–1998*

Factor and percentile	All children (n = 3,792)		Girls (n = 1,993)		Boys (n = 1,799)		p value for test of sex difference in RRs†
	RR‡	95% CI†	RR‡	95% CI	RR‡	95% CI	
Body mass index§							
≤25	1.00		1.00		1.00		0.55
25.1–50	1.12	0.71, 1.76	1.08	0.59, 1.95	1.28	0.63, 2.63	
50.1–75	0.98	0.62, 1.54	0.99	0.56, 1.77	1.05	0.49, 2.28	
75.1–85	1.06	0.62, 1.83	1.08	0.54, 2.17	1.02	0.42, 2.49	
85.1–95	1.45	0.92, 2.31	1.33	0.71, 2.51	1.87	0.93, 3.78	
>95	1.78	1.07, 2.94	1.20	0.57, 2.54	2.87	1.39, 5.92	
Weight status¶							
Overweight							
≤85	1.00		1.00		1.00		0.09
>85	1.52	1.14, 2.03	1.25	0.83, 1.88	2.06	1.33, 3.18	
Obese							
≤95	1.00		1.00		1.00		0.09
>95	1.60	1.08, 2.36	1.10	0.60, 2.05	2.29	1.35, 3.88	

* Relative risks and 95% confidence intervals for body mass index percentiles lagged by 1 year, calculated from Cox proportional hazards models using stratified baseline hazards for age in models for boys and girls and stratified baseline hazards for age and sex in the model for all subjects.

† RR, relative risk; CI, confidence interval.

‡ Adjusted for race/ethnicity, community, sex-specific effects of allergy, and history of wheezing.

§ Weight (kg)/height $(m)^2$. Body mass index percentiles were calculated using 1-month age intervals (31).

¶ Cutpoints were based on age- and sex-specific body mass index categories from the Centers for Disease Control and Prevention body mass index growth charts (31). Obesity was defined as a body mass index greater than the 95th percentile and overweight as a body mass index greater than the 85th percentile.

longitudinal studies in adults have suggested that obesity precedes asthma and is associated with an increased risk in adults that has been more consistently observed in women and appears to be larger in women than in men (23, 26, 27). In the Nurses' Health Study cohort, obese women and women who gained weight after 18 years of age were at significantly increased risk of developing asthma during the 4-year follow-up period (23). Among participants in the two Canadian National Population Health Surveys, asthma incidence was associated with BMI in females but not in males (33). In the Coronary Artery Risk Development in Young Adults Study, gain in BMI predisposed women to new asthma diagnosis, and decreased physical activity did not explain the association of weight gain with asthma (26). To date, one prospective study has examined the association between obesity and new-onset asthma in children (25). In girls, becoming overweight or obese between 6 and 11 years of age increased the risk of developing new asthma and increased bronchial responsiveness during adolescence (25). Obesity was not associated with asthma incidence in boys.

Our findings are consistent with an increased risk of asthma among overweight and obese children; however, we found evidence that the risk was largely restricted to boys. We lacked data to explore the inconsistency in results for boys and girls between studies; however, chance, differences in study populations, the age distribution of participants, or unrecognized confounding or effect modification may have contributed. After we accounted for sex differences in the effects of allergy and differences in the effects of BMI percentile by allergy status, the relative risks for overweight and obesity were larger in boys than in girls (p = 0.03). Differences in allergy status and in the age distribution of our population, which was slightly older than the cohort examined by Castro-Rodriguez et al. (25), might explain the discrepant results, particularly if the sex differences in the relation of obesity with asthma reverse in late adolescence. Because obese women appear to be at higher risk than men, a reversal of the sex difference in late adolescence is not a likely explanation. In addition, we found no variation in the effect of obesity over the age range in our study. Risk factors for asthma varied by sex in our cohort, suggesting that different patterns of confounding or effect modification may have occurred, especially in relation to allergy status. We assessed a wide spectrum of potential confounders in both boys and girls, including lung function level, physical activity, ETS exposure, and puberty status, and found that adjustments did not substantially change the sex-specific relative risks. Unrecognized bias or differences in exposures or doses that interact with obesity to affect asthma risk could also play a role in explaining the inconsistent results in boys and girls.

TABLE 5. Adjusted relative risk of new-onset asthma by allergy status and overweight status, Children's Health Study, 1993–1998*

Allergy status and overweight† status	All children (*n* = 3,792)		Girls (*n* = 1,993)		Boys (*n* = 1,799)	
	RR‡,§	95% CI‡	RR§	95% CI	RR§	95% CI
Nonallergic						
Normal weight	1.00		1.00		1.00	
Overweight	1.77	1.26, 2.49	1.53	0.97, 2.40	2.77	1.56, 4.90
Allergic						
Normal weight	1.00		1.00		1.00	
Overweight	1.16	0.63, 2.15	0.54	0.14, 2.02	1.35	0.62, 2.92
p for interaction¶	0.03		0.04		0.12	

* Relative risks and 95% confidence intervals were calculated from Cox proportional hazards models using stratified baseline hazards for age in models for boys and girls and stratified baseline hazards for age and sex in the model for all subjects.

† Cutpoints were based on age- and sex-specific body mass index (weight (kg)/height $(m)^2$) categories from the Centers for Disease Control and Prevention body mass index growth charts (31). Overweight was defined as a body mass index greater than the 85th percentile.

‡ RR, relative risk; CI, confidence interval.

§ Adjusted for age, race/ethnicity, community, sex-specific effects of allergy, and history of wheezing.

¶ Test of the difference between relative risks for overweight in nonallergic and allergic children.

A better understanding of the mechanisms for the effects of BMI on asthma risk may contribute to interpretation of the results from epidemiologic studies. It has been suggested that the association between obesity and asthma results from mutual correlation of obesity and asthma with common etiologic factors (10, 34, 35). Change in lifestyle may explain the association, as well as the co-occurrence of increasing prevalence for these conditions. Obesity is associated with a lack of physical exercise and a diet high in calories, and activity levels and dietary habits may be related to the onset of childhood asthma (10, 24, 34, 35). Thus, some aspect of the lifestyle associated with obesity, such as more time spent indoors, may be the etiologically important factor for new-onset asthma in some communities.

Obesity is associated with a large number of changes in physiology that may mediate the relation of obesity with asthma (24). Obese persons show systemic inflammation that appears to play a role in the etiology of nonatopic conditions, including cardiovascular disease, diabetes, and potentially asthma. Adipose tissue is a source of proinflammatory cytokines and chemokines such as interleukin-6, leptin, interleukin-18, and tumor necrosis factor-α. An increase in circulating levels or local concentrations of proinflammatory cytokines has the potential to enhance pulmonary inflammation, which is a key component of asthma pathophysiology. Because obesity is not clearly associated with allergy, obesity may enhance noneosinophilic inflammatory pathways that increase the risk of nonatopic asthma. The effects of obesity may also be mediated by changes in airway function, since obesity and weight change have been prospectively associated with increased bronchial hyperresponsiveness in asthmatic children as well as in nonasthmatic children. The combined effect of increased bronchial hyperresponsiveness and the proinflammatory milieu in obese subjects may set the stage for the onset of asthma (36–40).

In the present study, the incidence rate of physician-diagnosed asthma was higher than incidence rates of childhood asthma reported in earlier decades (41–43). Incidence rates for young adults during recent periods have been reported to be in the range of 3–7 cases per 1,000 person-years, with higher rates in women than in men (26, 44, 45). While incidence rates for children have been reported to be lower in earlier birth cohorts than in Children's Health Study children (41–43), incidence rates in more recent cohorts are comparable to those in the present study. In a cohort of children in Tucson, Arizona, the cumulative incidence of newly diagnosed asthma was 12.0 percent, which is approximately equal to the cumulative incidence in the present study (46). In the British 1958 birth cohort, the average annual incidence of new cases was 26 per 1,000 person-years, 11 cases per 1,000 person-years, 7.1 cases per 1,000 person-years, and 7.6 cases per 1,000 person-years, respectively, over the four age periods examined (0–7 years, 8–11 years, 12–16 years, and 17–23 years) (47, 48). Among 7- and 8-year-old children residing in northern Sweden during 1996 and 1997, the incidence of physician-diagnosed asthma was nine cases per 1,000 person-years (49). Among eighth grade students residing in northern Sweden, the asthma incidence rate was 11 per 1,000 person-years in 1991 (50). In a third study conducted in Sweden between 1990 and 1993, the yearly incidence of asthma in 16- to 19-year-olds was 13 per 1,000 person-years (51). The yearly incidence of asthma in 15 European countries increased more than twofold between

the 1946–1950 birth cohort and the 1966–1971 birth cohort (52).

Our cohort entry criteria and ascertainment of new cases of asthma were based on self-reports of physician diagnosis, a process that might have affected incidence rates and relative risk estimates. Physician assessment of asthma has been recommended and has been widely used as a method of classifying asthma status in epidemiologic studies (4, 53). Differences in access to care and differences in practice among physicians have the potential to influence asthma diagnoses (54). Misclassification of asthma status at study entry did not appear to bias our results. We based this conclusion on the fact that exclusion of cases diagnosed in the first year, a period when unrecognized prevalent cases are likely to be diagnosed, did not substantially change the point estimates for obesity and overweight. We found that adjustment for factors that mediate access to care, including parental income, education, and medical insurance, did not explain our results. This indicates that differential access to care in obese and nonobese children did not substantially bias our results. To investigate the role of a past history of wheezing on physician diagnosis of asthma, we examined the risk of a new diagnosis in children with and without a history of wheezing and found that BMI associations showed little variation between groups. This indicates that any bias from initial symptoms was likely to have been small.

On the basis of the assumption that variation in practice patterns is likely to be larger between communities than within a community, we indirectly assessed the role of physician variation between communities by accounting for differences in community of residence; we found little change in the associations with BMI. To further investigate the potential for bias from variations in medical practice, we conducted analyses restricting cases to children who had recently used inhaled medication; we found little change in the risk associated with obesity. Because the associations with BMI were apparent in the group of cases for which the diagnosis was most certain, our results are unlikely to be explained by variation in diagnosis. Furthermore, underdiagnosis of asthma in overweight and obese children may occur, since physicians may inaccurately attribute a child's post-exercise wheezing or shortness of breath to a general lack of physical fitness related to the child's weight. However, this practice would result in a bias toward the null and therefore would not explain our findings. Because we did not follow the cohort from birth, we could not determine whether a new diagnosis represented an incident occurrence of asthma or a second occurrence of asthma that had first occurred during infancy. We also used parental reports of physician-diagnosed allergy to classify children's atopic status. Because this approach is likely to underestimate the occurrence of atopy compared with skin testing, the associations of overweight with asthma are likely to have been overestimated in the allergic group of children, lessening the difference in risk between allergic and nonallergic children.

Our findings may have public health significance, since the increasing prevalence of overweight and obesity among children may be an important contributor to the increasing incidence and prevalence of asthma. The prevalence of overweight and obesity among children has been rapidly increasing over the past 20 years—the same period in which the epidemic increase in asthma prevalence has occurred. In the 10 years between the Second and Third National Health and Nutrition Examination Surveys, the prevalence of overweight in the United States increased by 40 percent (55). If obesity contributes to the incidence of asthma, then the rising prevalence of childhood obesity may contribute to the ongoing asthma epidemic, and we may need to target obesity prevention in our efforts to control the epidemic. Further longitudinal epidemiologic and mechanistic studies are needed to identify the causes of the childhood asthma epidemic.

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