

The association of obesity and asthma severity and control in children

Kenneth B. Quinto, MD, MPH,^a Bruce L. Zuraw, MD,^{a,b} Kwun-Yee T. Poon,^c Wansu Chen,^c Michael Schatz, MD, MS,^{a,d} and Sandra C. Christiansen, MD^{a,d} La Jolla, San Diego, and Pasadena, Calif

Background: The association between obesity and asthma severity and control in children is not well understood.

Objective: The objective of this study was to examine the association of childhood body mass index (BMI) percentile for age of 85% or greater with the number of β -agonist canisters dispensed, corticosteroid courses, emergency department visits, and hospitalizations for asthma.

Methods: A retrospective cohort of 32,321 children aged 5 to 17 years and given a diagnosis of asthma who received at least 1 asthma (controller or rescue) medication and were enrolled in Kaiser Permanente from 2004-2008 was identified. Outcomes from electronic medical records included β -agonist canister and nebulizer units dispensed per year, hospitalizations and emergency department visits for asthma exacerbations, and oral corticosteroid courses. Potential confounding factors known to influence asthma outcomes were also collected: demographics, parental education level, asthma controller use, gastroesophageal reflux disease diagnosis, and diabetes mellitus diagnosis. Multiple logistic regression models were used to measure the independent association of BMI status with outcomes.

Results: Even after adjusting for demographics, parental education level, asthma controller use, and gastroesophageal reflux disease and diabetes mellitus diagnoses, overweight (BMI percentile for age, 85% to 94%) and obese (BMI percentile for age, $\geq 95\%$) children were more likely to have increased β -agonists dispensed (odds ratio of 1.15 [95% CI, 1.02-1.27] and odds ratio of 1.17 [95% CI, 1.06-1.29], respectively) and increased risk for oral corticosteroids dispensed (odds ratio of 1.21 [95% CI, 1.13-1.29] and odds ratio of 1.28 [95% CI,

1.21-1.36], respectively) compared with normal-weight (BMI percentile for age, 16% to 84%) children.

Conclusions: Our findings suggest that childhood obesity is associated with an increased risk of worse asthma control and exacerbations. (J Allergy Clin Immunol 2011;■■■■:■■■-■■■.)

Key words: Asthma, childhood obesity, risk for exacerbation, asthma control, β -agonists dispensed, oral corticosteroid courses

The prevalence of obesity and asthma in the United States has increased over the past 20 to 30 years in both adults and children. In adults, the National Health and Nutrition Examination surveys show that the prevalence of obesity (body mass index [BMI] ≥ 30 kg/m²) has increased from 15.0% between 1976 and 1980 to 32.9% in 2003 to 2004.¹ Since 1980, the number of overweight children has doubled, whereas the number of overweight adolescents has more than tripled.² The number of children aged 2 to 19 years who are considered obese is currently estimated at 16%.³ During this time period, asthma has also showed a dramatic increase in prevalence in the US population. The prevalence of asthma in the United States has more than doubled, with an increase from 3.1% in 1980 to 7.1% in 2004 and increased prevalence in children (8.5%) compared with adults (6.7%).⁴

Epidemiologic studies have shown that obesity serves as a modifier for asthma risk. In one of the earlier studies, Shaheen et al⁵ found that the prevalence of asthma increased with increasing adult BMI. In a prospective study conducted by Camargo et al,⁶ the investigators found a significant relationship between BMI and the incidence of asthma using data from the Nurses' Health Study. In addition, that study also demonstrated that women with weight gain during a 4-year span experienced an increased risk of asthma in a dose-dependent manner.⁶ Overweight and obese children also displayed this increased asthma risk. Gold et al⁷ showed that boys and girls in the top quintile of annual BMI growth rates displayed increased risks of incident asthma. The increased risk for incident asthma in overweight children was also found in a study by Gilliland et al.⁸

With the association between asthma development and obesity established, the effect of obesity on asthma severity and control began to be investigated. In a study conducted by Mosen et al,⁹ obese adults were more likely to have worse quality of life, poorer asthma control, and increased risk of asthma-related hospitalizations compared with their nonobese counterparts. In another study by Taylor et al,¹⁰ adult obese asthmatic subjects experienced more continuous asthma symptoms, had increased rescue and controller medication use, and reported increased asthma-related work absenteeism. However, the effect of pediatric obesity on asthma severity and control has not been as well studied. In a study performed by Tantisira et al,¹¹

From ^athe Department of Allergy and Immunology, University of California, San Diego, La Jolla; ^bSan Diego VA Healthcare; ^cKaiser Permanente Department of Research and Evaluation, Pasadena; and ^dKaiser Permanente Medical Center Department of Allergy, San Diego.

Supported by National Institutes of Health grant T32 AI 07469 and a grant from Kaiser Permanente.

Disclosure of potential conflict of interest: B. L. Zuraw has received grants and research support from the National Institutes of Health/National Institute of Allergy and Infectious Diseases. M. Schatz is a research consultant for Merck, Amgen, and Glaxo-SmithKline and has received research support from Merck, GlaxoSmithKline, Aerocrine, and Genentech. The rest of the authors have declared that they have no conflict of interest.

Received for publication January 19, 2011; revised May 7, 2011; accepted for publication June 13, 2011.

Reprint requests: Sandra C. Christiansen, MD, Kaiser Permanente Medical Center Department of Allergy, 7060 Clairemont Mesa Blvd, San Diego, CA 92111. E-mail: Sandra.C.Christiansen@kp.org.

0091-6749/\$36.00

© 2011 American Academy of Allergy, Asthma & Immunology

doi:10.1016/j.jaci.2011.06.031

Abbreviations used

BMI: Body mass index
 DM: Diabetes mellitus
 ED: Emergency department
 GERD: Gastroesophageal reflux disease

there was no relationship found between BMI and asthma outcomes, such as corticosteroid use, emergency department (ED) care, hospitalizations, and school absenteeism. In a study conducted by Michelson et al,¹² there was an association found between BMI and asthma severity, whereas another study by Kattan et al¹³ demonstrated an association between BMI and asthma severity only in girls. To further clarify the effect of obesity on asthma severity and control in children, we sought to examine the effect of childhood obesity on asthma-related outcomes, including β -agonist canisters dispensed per year, number of corticosteroids courses for exacerbations, ED visits for asthma, and hospitalizations for asthma. We examine these relationships adjusting for selected demographic variables, asthma controller use, and gastroesophageal reflux disease (GERD) and diabetes mellitus (DM) diagnoses.

METHODS**Study subjects**

Study subjects were members of the Southern California region of Kaiser Permanente. Health plan members were eligible for the study if they were children aged 5 to 17 years given a diagnosis of asthma by a health care provider, had at least 1 asthma (controller or rescue) medication filled within the study period, and were enrolled in Kaiser Permanente from 2004 to 2008 for at least 2 years. The first 12 months the subjects were eligible for the study was considered the index year. After the index year, the following 12 months and time afterward until the end of December 2008 was defined as the follow-up period. Children given a diagnosis of immunodeficiency, cystic fibrosis, or cardiac disease were excluded from the study. A search of more than 1,000,000 electronic medical records identified 32,321 patients who met these criteria. The study was approved by the Kaiser Permanente Southern California Institutional Review Board.

Predictors and outcomes

The primary predictor variable, BMI, was analyzed both as a continuous variable and as a categorical variable. By using clinic-obtained height and weight measurements at the beginning of the index year, BMI percentile for age as a continuous variable was calculated based on Centers for Disease Control and Prevention growth charts. On the basis of Centers for Disease Control and Prevention recommendations, children with a BMI percentile for age between 16% and 85% were classified as the normal BMI group, children with a BMI percentile for age of between 85% and 94% were classified as overweight, and children with a BMI percentile for age of 95% or greater were classified as the obese group.

Secondary predictor variables included the following: age, sex, race/ethnicity, census block (based on address)-defined highest grade in school completed by parents (high school diploma or less or greater than high school diploma), census block-defined household income (less or more than the national income median \$44,512), asthma controller use, GERD, and DM. All secondary predictor variables were collected during the index year, except for the diagnoses of GERD or DM, for which any time during the study period was considered a positive response. A child who had a prescription filled for inhaled corticosteroids, montelukast, or theophylline at any time within the study period was considered to have asthma controller use.

The primary outcome was weighted β -agonist canister and nebulizer units dispensed per year. Weighted β -agonist canister and nebulizer units per year were calculated as follows:

Number of canisters of albuterol metered-dose inhalers + 0.8 * (number of 20-mL vials of 0.5% nebulizer solution) + 0.02 * (number of 3-mL vials of 0.083% albuterol nebulizer solution).

β -Agonist units were analyzed as both a continuous variable and dichotomized at 6 based on a prior study conducted by Schatz et al.¹⁴ Secondary outcomes included hospitalizations for asthma exacerbations, visits to the ED for asthma exacerbations, and oral corticosteroid dispensing linked to visits in which asthma was coded as the primary diagnosis. Because of the low number of hospitalizations and ED visits, these outcomes were combined as any asthma hospitalization or ED visit and expressed as a dichotomous (yes/no) variable. All primary and secondary outcome data were collected during the follow-up period.

Data analyses

All analyses were performed with SAS software (SAS Institute, Inc, Cary, NC). Nominal statistical significance was set at a *P* value of less than .05 for all analyses. Multiple linear or logistic regression models were constructed to analyze the independent effect of BMI status (expressed as a categorical or continuous variable, as described above) on asthma outcomes after adjustment for possible confounding factors. Each outcome measure was regressed on BMI status, adjusting for the following covariates: demographics (ie, age, sex, race/ethnicity, and parental education level), controller use, GERD, and DM. Because of high collinearity between parental education level and household income, household income was not included in the regression models.

In these models, age was analyzed as a continuous variable, whereas sex, race/ethnicity, parental education level (less than high school vs greater than high school), GERD (yes vs no), any controller medication dispensing (yes vs no), and DM (yes vs no) were analyzed as dichotomous measures. Linear regression was used for the continuous outcome variable (number of weighted β -agonist units dispensed), and logistic regression was used for dichotomous outcomes (β -agonists >6, asthma ED visit or hospitalization, and any oral corticosteroid dispensings). Interaction terms tested included BMI category with sex, race, parental educational level, and asthma controller use.

RESULTS**Sample characteristics**

As shown in Table I, study subjects were more likely to be male (56.8% male and 43.2% female) and primarily white (21.1%), African American (14.4%), or Hispanic (32.9%). There were a larger number of subjects aged 5 to 11 years (59%) compared with 12 to 17 years (41%). There were slightly more overweight and obese children in the cohort (49.3%) than normal-weight children (49.1%). The rates of overweight and obese children in this cohort are similar to those of another Kaiser Permanente study of children in the southern California area.¹⁵ Almost the entire cohort, 99.97% of subjects, used asthma controller medications.

Boys and girls showed similar rates of being overweight or obese (50.1% and 47.1% respectively). African American (51.1%) and Hispanic (56.7%) children were more likely to be overweight or obese in comparison with white children (41.5%). There were higher rates of overweight or obese status in children aged 5 to 11 years (51.6%) compared with those aged 12 to 17 years (46.0%). Children whose parents obtained less than a high school diploma had higher rates of overweight or obese status (58.0%) compared with children whose parents obtained an education beyond a high school diploma (47.9%).

Association of BMI status with outcome measures

BMI status was significantly associated with β -agonist unit dispensing and oral corticosteroid dispensing in both unadjusted

TABLE I. Demographics and characteristics of the cohort

	Total n	Weight class							
		Underweight†		Normal weight*		Overweight§		Obese‡	
		n	Percent	n	Percent	n	Percent	n	Percent
All	32,321	544	1.7	15,850	49.1	6,228	19.3	9,699	30.0
Gender									
Boys	18,361	307	1.7	8,704	47.4	3,394	18.5	5,956	32.4
Girls	13,960	237	1.7	7,146	51.1	2,834	20.3	3,743	26.8
Age (y)									
5-11	19,057	328	1.7	8,903	46.7	3,648	19.1	6,178	32.4
12-17	13,264	216	1.6	6,947	52.4	2,580	19.5	3,521	26.6
Race/ethnicity									
Caucasian	6,812	133	2.0	3,843	56.4	1,274	18.7	1,562	22.9
Hispanic	10,624	133	1.3	4,462	42.0	2,117	19.9	3,912	36.8
African American	4,653	72	1.6	2,202	47.3	933	20.1	1,446	31.1
Asian	1,707	54	3.2	943	55.2	289	16.9	421	24.7
Other	678	11	1.6	335	49.4	117	17.3	215	31.7
Unknown	7,847	141	1.8	4,065	51.8	1,498	19.1	2,143	27.3
Parental education level									
HS diploma or less	4,673	50	1.1	1,914	40.1	876	18.8	1,833	39.2
Greater than HS diploma	27,648	494	1.8	13,936	50.4	5,352	19.4	7,866	28.5
Controller use	32,310	544	1.7	15,846	49.0	6,225	19.3	9,695	30.0

CDC, Centers for Disease Control; HS, high school.

*16th-84th percentile of CDC growth chart.

†≤15th percentile of CDC growth chart.

‡≥95th percentile of CDC growth chart.

§85th-94th percentile of CDC growth chart.

TABLE II. Odds ratios for asthma outcomes based on weight classification

	Outcomes					
	≥6 β-agonist units dispensed per year		Oral corticosteroid dispensed		ED visit or hospitalization	
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
	Crude	Adjusted*	Crude	Adjusted*	Crude	Adjusted*
BMI status						
Overweight‡	1.14 (1.02-1.27)	1.15 (1.02-1.29)	1.18 (1.11-1.26)	1.21 (1.13-1.29)	1.10 (1.03-1.18)	1.07 (0.99-1.15)
Obese†	1.23 (1.12-1.35)	1.17 (1.06-1.29)	1.27 (1.20-1.34)	1.28 (1.21-1.36)	1.12 (1.06-1.19)	1.04 (0.98-1.11)

CDC, Centers for Disease Control; OR, odds ratio.

*Adjusted for age, gender, race, parental education level, asthma controller use, GERD diagnosis, DM diagnosis.

†≥95th percentile of CDC growth chart.

‡85th-94th percentile of CDC growth chart.

and multivariate analyses (Table II). BMI status was associated with hospitalizations for asthma and ED visits for asthma in the univariate analyses but not in the multivariate analysis.

Mean β-agonist units dispensed per year increased linearly with BMI status ($P < .001$, multiple linear regression; Fig 1). We performed additional analysis to discover whether there might be a dose-dependent relationship between BMI and asthma control and risk for exacerbation. Using a baseline value of 10% BMI percentile for age, we found that for every 10% increase in BMI percentile for age greater than 10%, there was a small but significant 0.3% and 0.4% increased risk of greater than 6 units/y of β-agonist dispensed and dispensing of oral corticosteroids, respectively (Table III). Using a baseline value of 20% BMI percentile for age did not change the findings (data not shown). In addition, several other covariates were associated with worse asthma control and risk for exacerbation, including female sex, older age, and asthma controller medication use, whereas other covariates, including

GERD diagnosis, DM diagnosis, and parental education level, were not associated with these outcomes (Table III). African American and Hispanic children had a 64% and 19% increased risk of an asthma hospitalization or ED visit, respectively (Table III), whereas African American children had a 44% increased risk of high (≥6) β-agonist unit dispensings per year (Table III). When evaluated, interaction terms, including BMI category with sex, race, parental educational level, and asthma controller use, were not found to be significant in the models (data not shown).

DISCUSSION

Increased BMI has been associated with an increased incidence of asthma in children,^{7,8} but the association between BMI status and asthma control and exacerbations in children has been less well defined. This study found that being overweight and obese

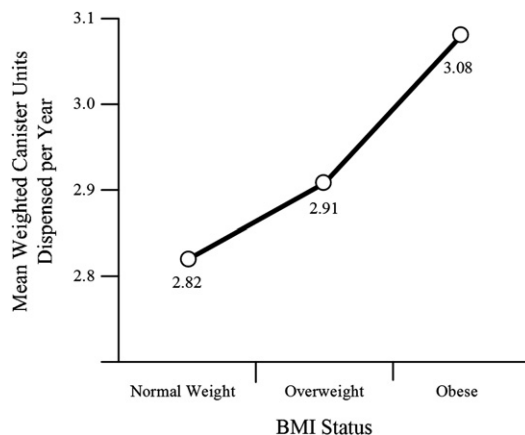


FIG 1. Mean weighted β -agonist units dispensed per year by BMI status. The difference was significant ($P < .001$). There seemed to be a linear relationship between mean weighted canister units dispensed per year and BMI category.

as a child is associated with increased risk of worse asthma control and asthma exacerbations as measured by β -agonist units dispensed per year and oral corticosteroid dispensing. We also discovered that there was a small linear association between increasing BMI status and increasing number of β -agonist units dispensed per year. Our findings are the first to show that childhood obesity is associated with worse asthma control and increased risk for exacerbation independent of sex, age, race, asthma controller use, parental education level, GERD diagnosis, and DM diagnosis. Mosen et al⁹ helped establish this relationship in adults. The evidence in children is less understood. In 2 studies published by Kattan et al¹³ and Michelson et al,¹² higher BMI in childhood was associated with increased asthma severity; however, a study conducted by Tantisira et al¹¹ in children did not find this relationship. The differences in outcomes found between our study and the Tantisira et al study might be due to the different outcome measures used; the large number of children included in our study, which increased study power; or the large proportion of our cohort who were overweight or obese (49.3%). This study is also the first to suggest that there might be a small dose-dependent association of BMI in childhood on asthma control and risk for exacerbation. Although the dose-dependent association between BMI percentile for age and increased risk of greater than 6 units/year of β -agonist dispensed and dispensing of oral corticosteroids was significant, it is unlikely to be of clinical relevance given the small increase in risk (0.3% and 0.4%, respectively). In addition, there was no association found between overweight and obese children and increased risk for ED visits and inpatient hospitalizations for exacerbations. This might be due to the low occurrence of ED visits (3546) and hospitalizations (801) for asthma exacerbations experienced by this particular cohort.

There have been various mechanisms proposed for the differences in asthma control and severity seen in obese and nonobese asthmatic subjects. A proinflammatory factor produced by adipocytes, leptin, has been shown in a murine model to significantly increase airway reactivity and total serum IgE levels,¹⁶ but in human subjects leptin has not been associated with asthma.¹⁷ Another proposed mechanism for the differences seen in obese asthmatic subjects and their nonobese counterparts is the mechanical effect of extra weight on the lungs. Pulmonary compliance is

reduced in obese subjects, which produces a subjective increase in dyspnea¹⁸ and might increase the use of their asthma medications. Boulet and Franssen¹⁹ reported that obese asthmatic subjects treated with inhaled corticosteroids were less likely to achieve asthma control when compared with nonobese asthmatic subjects. The impaired glucocorticoid sensitivity seen in obese asthmatic subjects compared with nonobese asthmatic subjects²⁰ might explain the observation that obese asthmatic subjects have increased use of asthma medications, including inhaled glucocorticoids, the mainstay of therapy for asthma. In our study nearly all patients were receiving controllers, especially inhaled corticosteroids (Table I), but we could not evaluate responsiveness to inhaled corticosteroids in this cohort.

The role of sex and its effect on asthma in those who are overweight and obese is controversial. There have been several studies that have shown a similar positive relationship between BMI and incident asthma in both men and women,^{21,22} but other studies have suggested that the increased risk for asthma is stronger in women.²³⁻²⁵ In the current study girls exhibited an increased risk for exacerbations and worse asthma control independent of BMI status. Castro-Rodriguez et al²⁶ found that the prevalence of asthma in obese girls was increased in those who underwent early menarche. Aromatase, the enzyme responsible for converting androgen into estrogen, is present in adipose tissue. It has been proposed that obesity might disrupt the production of hormones related to puberty and that these hormones lead to disruption of lung development and regulation of airway tone in pubertal girls. This hypothesis could help partially, but not fully, explain the increased risk for exacerbations and worse asthma control for girls found in this study. However, the increased asthma morbidity associated with increased BMI in this study was independent of sex.

In the current study it was found that various ethnic backgrounds demonstrated different risks for asthma control and exacerbations. In our cohort, Hispanic and African American children account for a disproportionate burden of obesity, whereas African American children seem to be more severely affected by asthma morbidity, as measured by ED visits, hospitalizations, and β -agonist units dispensed. Health care access has been thought to be a reason for health outcome disparities seen between different ethnic groups. It is interesting to note that these results remained significant despite equal member access to health care in the Kaiser Permanente system. The asthma outcomes among various ethnic groups were also not influenced by parental education level, a marker for socioeconomic status, and BMI remained an independent risk factor for asthma severity in the adjusted multivariate analyses. Although there seems to be no additive effect of different ethnic groups and obesity on asthma outcomes because no interactions were found, it is possible that there are different views between ethnic groups with regard to medical care, nutrition, obesity, and physical activity levels that might contribute to the disproportionate risks seen in these various ethnic groups.

This study does have several limitations. First, this study is retrospective in nature, thereby introducing potential bias. However, clinical and pharmaceutical information was collected at the time of each clinic and pharmacy visit, reducing recall bias. In addition, the use of an electronic database consisting of all medical and pharmaceutical information for members within the Kaiser Permanente Southern California network reduced the effect of selection bias and allowed formation of a large cohort

TABLE III. Full logistic regression model with BMI expressed as a continuous variable

	Outcomes		
	≥ 6 β -agonist units dispensed per year	Oral corticosteroid dispensed	ED visit or hospitalization
	OR (95% CI)	OR (95% CI)	OR (95% CI)
BMI per 10% increases	1.003 (1.001-1.005)	1.004 (1.003-1.005)	1.00 (0.99-1.01)
Boys	0.82 (0.75-0.90)	0.86 (0.81-0.90)	1.00 (0.94-1.06)
Age	1.06 (1.05-1.08)	1.10 (1.09-1.11)	1.04 (1.03-1.05)
Hispanic	0.99 (0.87-1.12)	0.89 (0.83-0.96)	1.19 (1.10-1.28)
African American	1.43 (1.24-1.64)	0.94 (0.87-1.03)	1.64 (1.51-1.79)
Asian	1.02 (0.82-1.27)	0.79 (0.69-0.89)	0.88 (0.77-1.00)
Other	1.07 (0.78-1.46)	0.88 (0.74-1.05)	1.52 (1.28-1.82)
Unknown	0.83 (0.72-0.95)	0.74 (0.68-0.80)	0.37 (0.34-0.41)
Parental education HS diploma or less	0.99 (0.87-1.13)	0.97 (0.90-1.06)	1.08 (1.00-1.17)
GERD diagnosis	1.05 (0.87-1.28)	1.08 (0.96-1.21)	1.58 (1.41-1.77)
DM diagnosis	1.10 (0.68-1.78)	0.79 (0.58-1.07)	1.59 (1.19-2.13)
Controller use	1.06 (1.06-1.07)	1.06 (1.06-1.06)	1.03 (1.02-1.03)

HS, High school; OR, odds ratio.

followed for at least 2 years or longer. Another limitation of the observational cohort study design is that it allows for investigation of an association between childhood obesity and asthma severity but cannot prove causal mechanisms.

A second limitation of the study is that spirometric measurements that confirmed the diagnosis of asthma were not obtained. The initial association between incident asthma and obesity was primarily obtained through epidemiologic cross-sectional studies. The relationship between incident asthma and obesity has also been shown in studies that had strict definitions for asthma, including spirometric and bronchial provocation test results confirming asthma, such as the study conducted by Rönmark et al.²⁷ It has also been shown that overdiagnosis of asthma is similar in obese and nonobese adults,²⁸ reducing the likelihood of misclassification in this study. This study has the advantage that diagnosis of asthma does not depend on self-report but instead is diagnosed by a health care provider and recorded from the patient's medical record. It is also possible that multiple courses of oral corticosteroid for asthma exacerbations resulted in increased BMI percentile for age. This possibility seems less likely given that there were not enough children in the cohort who changed weight categories to perform additional analysis because most children's BMIs did not change substantially over the study period (data not shown).

Another limitation is that our findings might not be applicable to obese and overweight asthmatic children outside of the Kaiser Permanente health care system. However, a Kaiser Permanente population has been shown to be representative of the demographics within the region that it serves.²⁹

Despite these limitations, these findings have important implications for clinical practice. A recent study performed at Kaiser Permanente Southern California showed that there is a shift toward extreme body weights in children aged 2 to 19 years.¹⁴ Overweight and obese adolescents tend to maintain their nutritional status into adulthood.³⁰ It has been proposed that between 15% and 38% of asthma cases among adults could be prevented if obesity were to be controlled.³¹ An adult study that used surgical intervention for weight loss showed improved asthma symptoms, severity, and hospitalizations.³² The best time for prevention of obesity and nonsurgical weight reduction likely occurs in childhood. Improving nutritional status, preventing obesity, and stressing the importance of weight loss might improve asthma control

and exacerbation risk in children and decrease the incidence of asthma in adults. Future research should be aimed at using longitudinal data to further evaluate the possible dose-dependent relationship between obesity and asthma control and exacerbation risk, as well as evaluating whether weight loss interventions improve asthma control and decrease exacerbation risk.

Clinical implications: Overweight and obese children with asthma might benefit from weight loss and more intense monitoring and treatment to improve outcomes.

REFERENCES

1. National Center for Health Statistics. Chartbook on trends in the health of Americans, health, United States, 2006. Hyattsville (MD): Public Health Service; 2006.
2. World Health Organization. Global strategy on diet, physical activity, and health. Geneva: World Health Organization; 2007.
3. Ogden CL, Carroll MD, Flegal KM. High body mass index for age among US children and adolescents, 2003-2006. JAMA 2008;299:2401-5.
4. Moorman JE, Rudd RA, Johnson CA, King M, Minor P, Bailey C, et al. National surveillance for asthma—United States, 1980-2004. MMWR Surveill Summ 2007; 56:1-54.
5. Shaheen SO, Sterne JA, Montgomery SM, Azima H. Birth weight, body mass index and asthma in young adults. Thorax 1999;54:396-402.
6. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Arch Intern Med 1999;159:2582-8.
7. Gold DR, Damokosh AI, Dockery DW, Berkey CS. Body-mass index as a predictor of incident asthma in a prospective cohort of children. Pediatr Pulmonol 2003;36: 514-21.
8. Gilliland FD, Berhane K, Islam T, McConnell R, Gauderman WJ, Gilliland SS, et al. Obesity and the risk of newly diagnosed asthma in school-age children. Am J Epidemiol 2003;158:406-15.
9. Mosen DM, Schatz M, Magid DJ, Camargo CA Jr. The relationship between obesity and asthma severity and control in adults. J Allergy Clin Immunol 2008;122: 507-11.
10. Taylor B, Mannino D, Brown C, Crocker D, Twum-Baah N, Holguin F. Body mass index and asthma severity in the National Asthma Survey. Thorax 2008;63:14-20.
11. Tantisira KG, Litonjua AA, Weiss ST, Fuhlbrigge AL. Childhood Asthma Management Program Research Group. Association of body mass with pulmonary function in the Childhood Asthma Management Program (CAMP). Thorax 2003;58: 1036-41.
12. Michelson PH, Williams LW, Benjamin DK, Bernato AE. Obesity, inflammation, and asthma severity in childhood: data from the National Health and Nutrition Examination Survey 2001-2004. Ann Allergy Asthma Immunol 2009;135:381-5.
13. Kattan M, Kumar R, Bloomerberg GR, Mitchell HE, Gan VN, et al. Asthma control, adiposity, and adipokines among inner-city adolescents. J Allergy Clin Immunol 2010;125:583-92.

14. Schatz M, Zeiger RS, Vollmer WM, Mosen D, Apter AJ, Stibolt TB, et al. Validation of a beta-agonist long-term asthma control scale derived from computerized pharmacy data. *J Allergy Clin Immunol* 2006;117:995-1000.
15. Koebeck C, Smith N, Coleman KJ, Getahun D, Reynolds K, Quinn VP, et al. Prevalence of extreme obesity in a multiethnic cohort of children and adolescents. *J Pediatr* 2010;157:26-31.
16. Shore SA, Schwartzman IN, Mellema MS, Flynt L, Imrich A, Johnston RA. Effect of leptin on allergic airway responses in mice. *J Allergy Clin Immunol* 2005;115:103-9.
17. Sood A, Ford ES, Camargo CA Jr. Association between leptin and asthma in adults. *Thorax* 2006;61:300-5.
18. Sin DD, Jones RL, Man SF. Obesity is a risk factor for dyspnea but not for airflow obstruction. *Arch Intern Med* 2002;162:1477-81.
19. Boulet LP, Franssen E. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. *Respir Med* 2007;101:2240-7.
20. Sutherland ER, Goleva E, Strand M, Beuther DA, Leung DY. Body mass and glucocorticoid response in asthma. *Am J Respir Crit Care Med* 2008;178:682-7.
21. Ford ES, Mannino DM, Redd SC, Mokdad AH, Mott JA. Body mass index and asthma incidence among USA adults. *Eur Respir J* 2004;24:740-4.
22. Gunnbjörnsdóttir MI, Omenaas E, Gíslason T, Norrman E, Olin AC, Jögi R, et al. Obesity and nocturnal gastro-oesophageal reflux are related to onset of asthma and respiratory symptoms. *Eur Respir J* 2004;24:116-21.
23. Beckett WS, Jacobs DR Jr, Yu X, Iribarren C, Williams OD. Asthma is associated with weight gain in females but not males, independent of physical activity. *Am J Respir Crit Care Med* 2001;164:2045-50.
24. Chen Y, Dales R, Tang M, Krewski D. Obesity may increase the incidence of asthma in women but not in men: longitudinal observations from the Canadian National Population Health Surveys. *Am J Epidemiol* 2002;155:191-7.
25. Nystad W, Meyer HE, Nafstad P, Tverdal A, Engeland A. Body mass index in relation to adult asthma among 135,000 Norwegian men and women. *Am J Epidemiol* 2004;160:969-76.
26. Castro-Rodríguez JA, Holberg CJ, Morgan WJ, Wright AL, Martinez FD. Increased incidence of asthmalike symptoms in girls who become overweight or obese during the school years. *Am J Respir Crit Care Med* 2001;163:1344-9.
27. Rönmark E, Andersson C, Nyström L, Forsberg B, Järnholm B, Lundbäck B. Obesity increases the risk of incident asthma among adults. *Eur Respir J* 2005;25:282-8.
28. Aaron SD, Vandemheen KL, Boulet LP, McIvor RA, Fitzgerald JM, Hernandez P, et al. Overdiagnosis of asthma in obese and nonobese adults. *CMAJ* 2008;179:1121-31.
29. Van Den Eeden S, Tanner CM, Bernstein AL, Fross RD, Leimpeter A, Bloch DA, et al. Incidence of Parkinson's disease: variation by age, gender and race/ethnicity. *Am J Epidemiol* 2003;157:1015-22.
30. Wright CM, Parker L, Lamont D, Craft AW. Implications of childhood obesity for adult health: findings from thousand families cohort study. *BMJ* 2001;323:1280-4.
31. Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005;115:897-909.
32. Spivak H, Hewitt MF, Onn A, Half EE. Weight loss and improvement of obesity-related illness in 500 U.S. patients following laparoscopic adjustable gastric banding procedure. *Am J Surg* 2005;189:27-32.