

# Excessive body weight is associated with additional loss of quality of life in children with asthma

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**Background:** Asthma and excessive body weight frequently coexist, whereas the exact relationship between the 2 diseases is unknown.

**Objective:** To study whether asthma combined with excessive body weight has a greater effect on quality of life in children than the separate effects of asthma or excessive body weight alone.

**Methods:** In a cross-sectional design, 1758 school children (age 7-10 years) participated: 4 study groups were composed of children with asthma and with/without excessive body weight, and healthy controls with/without excessive body weight.

**Diagnosis of asthma** was defined by either a doctor's diagnosis or by core questions of the International Study of Asthma and Allergies in Childhood questionnaire in combination with either reversible airway obstruction or bronchial hyperresponsiveness. Excessive body weight was defined by using international cutoff points for body mass index. Quality of life was evaluated by the Pediatric Asthma Quality of Life Questionnaire.

**Results:** For all domains of quality of life, children with both asthma and excessive body weight had lower scores than children with either asthma alone or excessive body weight alone. Compared with healthy controls, the score was 25% lower in children with asthma and excessive body weight, 14% lower in children with asthma and normal weight, and only 1% lower in overweight controls.

**Conclusion:** Excessive body weight is associated with an additional decrease in quality of life in children with asthma.

**Clinical implications:** Clinicians should be aware of the interaction between asthma and excessive body weight and the effect on quality of life and should give extra attention to children with both conditions. (*J Allergy Clin Immunol* 2007;119:591-6.)

**Key words:** Asthma, children, quality of life, overweight, obesity, body mass index

## Abbreviations used

BHR: Bronchial hyperresponsiveness

BMI: Body mass index

FVC: Forced vital capacity

PAQLQ: Pediatric Asthma Quality of Life Questionnaire

Asthma and excessive body weight frequently coexist, but the underlying mechanism remains obscure. Recently, Hallstrand et al<sup>1</sup> reported shared genetic risks for asthma and obesity. Other potential mechanisms include obesity-related changes in lung volumes and adipocyte-derived factors that might alter airway smooth muscle function.<sup>2</sup> Moreover, it was recently hypothesized that the elementary lesion of obesity might be inflammatory in origin, making a link with asthma as an inflammatory condition more plausible.<sup>3</sup> Furthermore, the decreased activity level associated with poorly controlled asthma may predispose a child to gain excessive body weight. Although a considerable number of studies using different designs indicate that excessive body weight might increase the risk of asthma development, the topic remains controversial because of potential methodologic limitations including definitions of asthma, different anthropometric measures, directionality of causality, and residual confounding in many of these studies.<sup>4</sup>

In addition to clinical measures of airway status (such as airway caliber and markers of inflammation), quality of life provides valuable information about functional impairment (physical, emotional, and social) that is relevant to a patient's everyday life.<sup>5</sup> Children with excessive body weight are less fit and may have more symptoms of breathlessness on exertion than their healthy peers.

Because asthma and excessive body weight frequently coexist, we hypothesized that excessive body weight may be related to an additional decrease in quality of life in children with asthma. Therefore, in children with asthma, we studied the combined effect of asthma and excessive body weight on quality of life compared with the effect of asthma with normal weight alone, and also compared with healthy controls with normal weight or excessive body weight.

## METHODS

### Population and study protocol

From 2002 to 2005, we conducted a survey among primary school children age 7 to 10 years in the southern region of The Netherlands.

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The study protocol was composed of a questionnaire for parents on respiratory symptoms, demographic and household characteristics, and the child's assessment of height and weight, lung function, and assessment of airway reversibility to salbutamol. First, the ISAAC questionnaire and a consent form were distributed at participating schools to all eligible children. Lung function and assessment of airway reversibility were performed at school by experienced lung function technicians in all children who gave written consent. All eligible children with asthma symptoms (wheeze or dry cough in the past 12 months) or with proven airway reversibility to salbutamol were invited to the Máxima Medical Center in Veldhoven for bronchial challenge with hypertonic saline.

For the current study, asthma was considered if 1 of the following criteria was fulfilled: (1) a parent's report of asthma diagnosis, with or without airway reversibility or bronchial hyperresponsiveness (BHR); or (2) asthma symptoms in the past 12 months combined with airway reversibility or BHR. For each child with asthma, a healthy control was selected randomly from the same classroom. Healthy controls had no asthma diagnosis, no asthma symptoms in the last 12 months, and no airway reversibility to salbutamol. Selected healthy controls were invited for bronchial challenge as well. Quality of life was assessed in children with asthma and healthy controls after completing the bronchial challenge with hypertonic saline. Questionnaires were returned by mail. Parents received a letter with the results of the symptom questionnaire and lung function tests 2 weeks after finishing the study protocol.

Approval was obtained from both the National Committee on Research Involving Human Subjects (The Hague, The Netherlands) and the local Hospital Ethics Committee. Informed written consent was obtained from the parents of all participating children at the start of the study, when they returned the questionnaire. Apart from a small present for the children, there was no compensation for the participants.

## Body mass index

Before lung function testing, height and weight were assessed by trained research assistants. The child was stretched against the wall, and height was measured to the nearest 0.1 cm, without wearing shoes. Children were weighed on a calibrated electronic step-scale, wearing no shoes and only light indoor clothing with empty pockets. Body mass index (BMI) was calculated from height and weight measurements ( $BMI = \text{weight [kg]} / [\text{height (m)}]^2$ ). Excessive body weight was defined using international cutoff points for children with overweight and obesity stratified by sex, which are defined to match with the adult cutoff point of a BMI of 25 kg/m<sup>2</sup> (overweight) and 30 (obesity) kg/m<sup>2</sup> at 18 years of age.<sup>6</sup>

## Questionnaire

Parents completed a questionnaire that included the ISAAC core questions on symptoms of asthma, rhinitis, and eczema.<sup>7</sup> Additional data were collected on household characteristics such as parental education, passive smoking, and pet ownership. Questions asked a response of yes/no. Asthma symptoms were defined as wheeze or a dry cough at night in the past 12 months.

## Lung function testing

Maximal flow-volume curves were measured by using a hand-held spirometer (Vitalograph Ltd, Buckingham, United Kingdom) according to the European Respiratory Society guidelines.<sup>8</sup> Airway reversibility was defined as an increase of FEV<sub>1</sub> of  $\geq 10\%$  of the predicted value 10 minutes after administration of 800  $\mu\text{g}$  salbutamol using a volumatic spacer (GSK, Uxbridge, United Kingdom).<sup>9</sup>

## Hypertonic saline testing

Bronchial hyperresponsiveness was assessed by inhalation challenge with nebulized hypertonic (4.5%) saline by using an ultrasound

nebulizer (Klava 2000/4000; Klava Eltromed, Bielefeld, Germany) according to the ISAAC protocol.<sup>10</sup> All children were asked to withhold all asthma medications for at least 12 hours beforehand. Children with a baseline FEV<sub>1</sub>  $\leq 75\%$  were excluded. The children inhaled the saline for periods of increasing duration: 0.5, 1, 2, 4, and 8 minutes. FEV<sub>1</sub> was measured 1 minute after each inhalation period, and the next inhalation period started after 3 minutes. Bronchial challenge was stopped if FEV<sub>1</sub> had fallen at least 15% from baseline or if the total inhalation period of 15.5 minutes had been completed. A child was defined as having BHR if FEV<sub>1</sub> had dropped by  $\geq 15\%$  from baseline during the inhalation challenge.

## Quality of life

Quality of life was measured with the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) for children.<sup>11</sup> Children were asked to recall impairments they experienced the last week; for instance, "How much did wheezing bother you during the past week?" Scores range from 1 to 7, with 7 indicative of maximal quality of life. The PAQLQ consists of 3 domains: the emotions domain, activity domain, and symptom domain. Individual items within the PAQLQ were equally weighted. Results are expressed as the mean score per domain as well as for overall quality of life. Raat et al<sup>12</sup> showed good validation of the PAQLQ in a Dutch population.

## Statistical analysis

All data of the questionnaires were double-entered into the database by using Microsoft Access software. Data were analyzed using the statistical package SPSS version 13.0 (SPSS Inc, Chicago, Ill). To analyze potential differences in clinical characteristics (ie, asthma symptoms, lung function, and quality of life),  $\chi^2$  tests and ANOVA (with a Bonferroni post hoc test) were used. To adjust for potential confounders (eg, parental asthma, current parental smoking, and the education level of parents), multivariate regression analyses were performed. In this model, we tested the effect of all potential confounders 1 by 1. The following model was tested: quality of life =  $\alpha + \beta 1 \times \text{group} + \beta 2 \times \text{potential confounder}$ . Because the estimates were not influenced by these possible confounders, crude effect estimates were presented. To evaluate the interaction between excessive overweight and asthma, we compared the combined effect of asthma and excessive body weight with the sum of separate effects as described by Pearce.<sup>13</sup>

## RESULTS

### Participants

Of 44 eligible schools, 41 participated in the study. Reasons for nonparticipation were recent involvement in another study ( $n = 2$ ) and school policy ( $n = 1$ ). Subsequently, all 2745 children and their parents were invited for the study, of whom 1758 (64%) agreed. We excluded 144 children from further analysis because of missing questionnaire data ( $n = 60$ ) or refusal to participate in bronchial challenge testing ( $n = 31$ ). Additionally, 53 children did not complete the bronchial challenge test because of nausea or coughing ( $n = 3$ ) or were unable to meet technical conditions ( $n = 50$ ). All children with a parent's report of asthma reported asthma symptoms (wheeze or dry cough at night) in the last 12 months. For each child with asthma, a healthy control was selected from the same classroom. There were no differences in FEV<sub>1</sub> and forced vital capacity (FVC) between the selected control group and the whole nonasthmatic population: 98% predicted for FEV<sub>1</sub> and 93% for FVC. The final

**TABLE I.** Characteristics of the 4 study groups\*

	Asthma		Healthy controls	
	Normal weight	Excessive body weight	Normal weight	Excessive body weight
n (%)	171 (84)	33 (16)	174 (87)	26 (13)
Sex, n (%)				
Male	97 (57)	17 (52)	86 (49)	12 (46)
Female	74 (43)	16 (48)	88 (51)	14 (54)
Mean age ± SD (y)	9.3 (0.8)	9.5 (0.8)	9.4 (0.7)	9.6 (0.6)
Mother asthma ever, n (%)	28 (19)	6 (19)	4 (3)	0 (0)
Father asthma ever, n (%)	16 (12)	2 (8)	7 (5)	5 (24)
Mother current smoker, n (%)	24 (16)	10 (32)	36 (22)	5 (22)
Father current smoker, n (%)	34 (23)	12 (40)	40 (24)	2 (8)
Mother's education level				
Low, n (%)	24 (16)	5 (16)	24 (15)	9 (37)
Moderate, n (%)	73 (49)	15 (48)	88 (53)	6 (26)
High, n (%)	53 (35)	11 (36)	53 (32)	9 (37)
Father's education level				
Low, n (%)	24 (17)	10 (38)	29 (18)	7 (32)
Moderate, n (%)	52 (38)	9 (35)	59 (37)	6 (27)
High, n (%)	62 (45)	7 (27)	73 (45)	9 (41)

\*n, Absolute number for the weight or disease group. %, Percent of total weight or disease group; however, because of missing values, data can be lower or higher than calculated.

study population was composed of 1614 children, of whom 204 (13%) had asthma (171 [84%] with normal weight and 33 [16%] with excessive body weight), and 200 were defined as healthy controls (174 [87%] with normal weight and 26 [13%] with excessive body weight). The number of children with overweight was 24 (73%) in the asthma group and 23 (89%) in the healthy controls. The number of obese children was 9 (27%) in the asthma group and 3 (12%) in the healthy controls.

Table I presents the characteristics of children with asthma and healthy controls. The occurrence of excessive body weight was similar for both groups. Children with asthma with excessive body weight more frequently had a smoking father ( $P < .05$ ) and more frequently used inhaled corticosteroids ( $P < .05$ ).

Table II presents clinical characteristics of children with asthma and healthy controls. Wheeze or dry cough at night was equally distributed in children with asthma with normal weight or overweight. There were also no differences in symptoms on the basis of the ISAAC questionnaire. Lung function reversibility was most frequent in normal weight children with asthma (43% of children). Bronchial hyperresponsiveness was most frequent in children with asthma combined with excessive body weight (73% of children). In healthy controls with excessive body weight, bronchial hyperresponsiveness was also more frequent than in healthy controls with normal weight (respectively, 19% and 9%;  $P < .001$ ). Lung function reversibility was present in 24% of children with a parent's report of asthma. Bronchial hyperresponsiveness was present in 47% of these children.

### Quality of life

Fig 1, A to D, and Table III present data on the separate and combined effects of asthma and excessive body weight for different domains of quality of life. Children with

asthma combined with excessive body weight had the lowest quality of life compared with all other groups of children for all domains ( $P < .01$ ). For the combined domain, scores were 5.2 (95% CI, 4.5-5.9) in children with asthma and excessive body weight, 6.0 (95% CI, 5.8-6.2) in children with asthma with normal weight, 6.9 (95% CI, 6.9-7.0) in healthy controls with excessive body weight, and 7.0 (95% CI, 6.6-7.0) in healthy controls with normal weight (Fig 1, D;  $P < .05$  for all comparisons, except between healthy controls with excessive body weight and with normal weight).

Table III presents percentage differences in the quality-of-life scores among 3 of the study groups compared with healthy controls with normal weight. Compared with healthy controls with normal weight, quality-of-life scores for the combined domain were respectively 14% lower in children with asthma and normal weight and 1% lower in healthy controls with excessive body weight. On the basis of the separate effects for asthma and overweight, we expected a 15% lower score; however, the score for the combined effect in overweight children with asthma proved to be 25% lower.

### DISCUSSION

In the current study, quality of life in children with both excessive body weight and asthma was lower than expected on the basis of the sum of the separate effects of asthma alone or excessive body weight alone. Children with asthma and excessive body weight had a lower quality of life compared with children with asthma and normal weight, and compared with healthy controls irrespective of their weight.

Our results are in agreement with results in adults that showed a significant association between BMI and quality of life in adults with asthma.<sup>14,15</sup> Data on the effect of asthma in children with excessive body weight in the

TABLE II. Clinical characteristics of the 4 study groups\*

	Asthma		Healthy controls		P value
	Normal weight	Excessive body weight	Normal weight	Excessive body weight	
n (%)	171 (84)	33 (16)	174 (87)	26 (13)	
BMI (mean)	16.0	21.9	15.8	20.9	
Wheeze, n (%)	115 (67)	21 (64)	0	0	
Dry cough at night, n (%)	53 (31)	11 (33)	0	0	
Lung function parameters					
Mean baseline FEV <sub>1</sub> % predicted	95	98	100	101	.001†
Mean baseline FVC % predicted	91	95	94	94	NS
Change in FEV <sub>1</sub> after bronchodilation (%)	8.6	2.1	1.7	0.6	<.05†‡§
Reversibility ≥10%, n (%)	73 (43)	12 (36)	0	0	<.001†§  ¶
BHR, n (%)	102 (60)	24 (73)	16 (9)	5 (19)	<.001†§  ¶
FEV <sub>1</sub> <75%, n	1	0	0	0	
Medication					
Inhaled corticosteroids, n (%)	52 (30)	14 (46)	0 (0)	0 (0)	
Bronchodilator, n (%)	73 (43)	15 (45)	0 (0)	0 (0)	
Cromoglycate, n (%)	2 (1)	0 (0)	0 (0)	0 (0)	
Theophylline	0 (0)	0 (0)	0 (0)	0 (0)	
Oral steroids	0 (0)	0 (0)	0 (0)	0 (0)	

NS, Not significant.

\*n, Absolute number for the weight or disease group. %, Percent of total weight or disease group; however, because of missing values, data can be lower or higher than calculated.

†Significant difference between patients with asthma with normal weight and healthy controls with normal weight.

‡Significant difference between patients with asthma with normal weight and with excessive body weight.

§Significant difference between patients with asthma with normal weight and healthy controls with excessive body weight.

||Significant difference between patients with asthma with excessive body weight and healthy controls with excessive body weight.

¶Significant difference between patients with asthma with excessive body weight and healthy controls with normal weight.

population are scarce. Blandon et al<sup>16</sup> found a lower quality of life in children with asthma recruited from a population attending a specialized allergy and immunology clinic. In a sample of inner-city children, Belamarich et al<sup>17</sup> reported that obese children with asthma had more unscheduled emergency department visits and received more medication than nonobese children. The effect of overweight and obesity is higher with increasing BMI. For instance, among 3457 subjects in the Framingham Study, those who were overweight at age 40 years lived about 3 years less and those who were obese at age 40 years lived 6 to 7 years less than those who were not.<sup>18</sup> In the same cohort, the relative risk in obese for vascular disease was higher for obese than for overweight adults.<sup>19</sup>

In our study, children with asthma combined with excessive body weight were more often treated with inhaled corticosteroids than children with asthma without excessive body weight. Possible explanations for this phenomenon are a different perception of dyspnea by children, greater awareness of respiratory complaints by parents, or a different coping behavior with respiratory complaints in these children with excessive body weight.

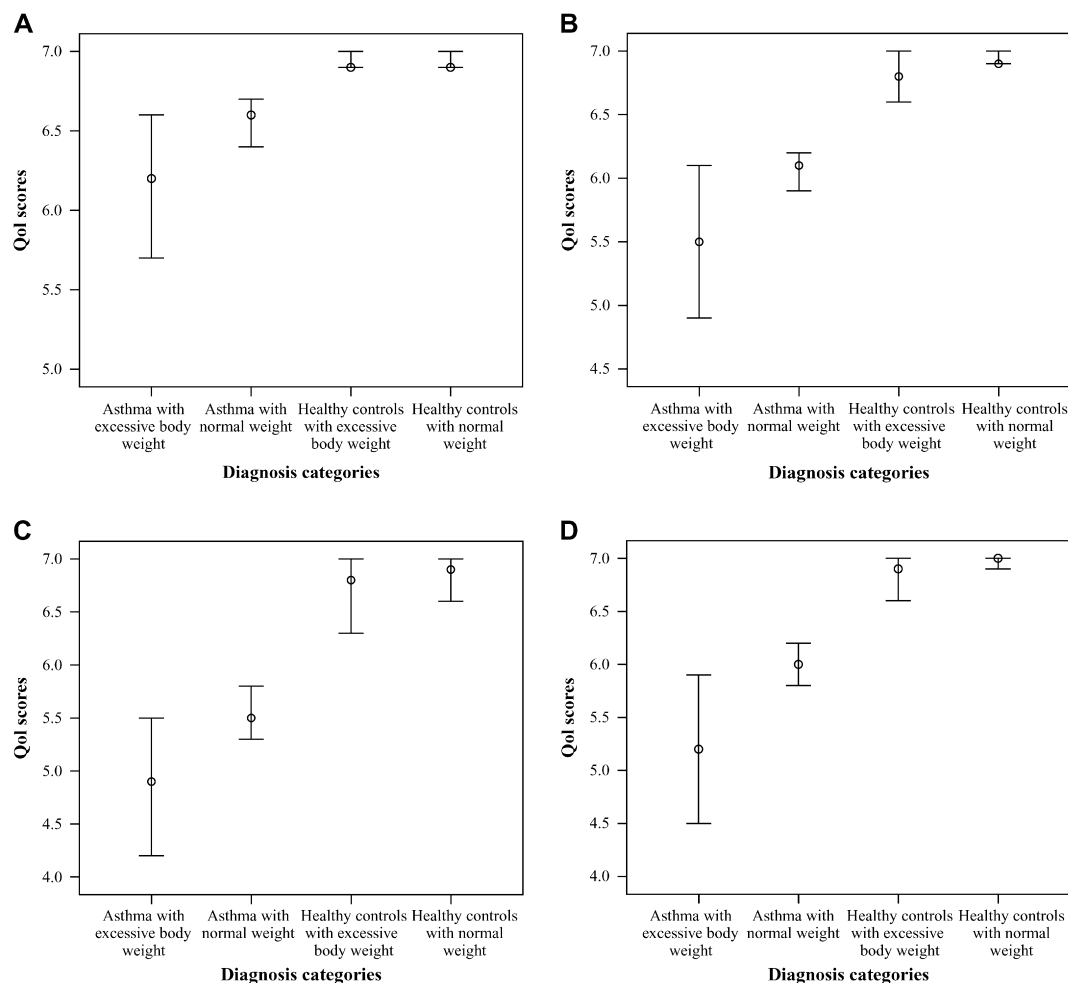
To our knowledge, this is the first community-based study in children to evaluate the relationship among excessive body weight, asthma, and quality of life measured with a disease-specific, validated, and well known quality-of-life questionnaire. Disease-specific questionnaires have a higher discriminative property and sensitivity

to detect small differences for the disease of interest.<sup>20-22</sup>

In contrast, general questionnaires on quality of life tend to be designed to assess moderate or severe effect of chronic conditions on children's quality of life, which make them less sensitive to small differences between groups.

The clinical interpretation of differences in quality of life is difficult because experience in their use is still limited. Juniper et al<sup>20</sup> proposed a difference of 0.5 or higher as being clinically relevant for the PAQLQ. Knorr et al<sup>23</sup> studied the effect of treatment in children with asthma 6 to 14 years old and observed a significant improvement in both FEV<sub>1</sub> and quality-of-life scores (with 0.4 for the emotional domain and 0.5 for the activity domain). In light of these studies, our results suggest a clinically relevant impairment of quality of life in children with asthma with excessive body weight.

Our results suggest that treatment in children should be aimed at both asthma and excessive body weight. We know from adults that the response to different asthma medications is influenced by an increasing BMI.<sup>24</sup> The effect of placebo or corticosteroid treatment on asthma symptom-free days was lower in obese patients with asthma, whereas this effect was not seen in treatment with leukotriene antagonists. Data on children with asthma combined with excessive body weight are still scarce. However, the combination of health problems makes it likely that a combined treatment for both conditions by a multidisciplinary team (including a psychologist and a dietitian) is beneficial for the quality of life in



**FIG 1.** A, Separate and joint effects of asthma and excessive body weight for the emotions domain.  $P < .05$  for all comparisons except between healthy controls with normal weight and healthy controls with excessive body weight. B, Separate and joint effects of asthma and excessive body weight for the symptom domain.  $P < .05$  for all comparisons except between healthy controls with normal weight and healthy controls with excessive body weight. C, Separate and joint effects of asthma and excessive body weight for the activity domain.  $P < .05$  for all comparisons except between healthy controls with normal weight and healthy controls with excessive body weight. D, Separate and joint effects of asthma and excessive body weight for the combined domain.  $P < .05$  for all comparisons except between healthy controls with normal weight and healthy controls with excessive body weight.

**TABLE III.** Data on quality of life scores of the study groups

	Asthma with excessive body weight		Asthma with normal weight		Healthy controls with excessive body weight		P value
	Absolute difference Mean (95% CI)	Percent difference	Absolute difference Mean (95% CI)	Percent difference	Absolute difference Mean (95% CI)	Percent difference	
Symptom domain	1.5 (0.8-2.1)	21%	0.9 (0.7-1.1)	13%	0.2 (0.0-0.4)	3%	<.01*
Emotions domain	0.7 (0.3-1.3)	10%	0.3 (0.2-0.6)	4%	0 (0-0.1)	0%	<.05*
Activity domain	2.0 (1.1-2.8)	29%	1.4 (0.8-1.7)	20%	0.1 (0.0-0.7)	1%	<.05*
Combined domain	1.8 (1.0-2.5)	25%	1.0 (0.8-1.2)	14%	0.1 (0.0-0.4)	1%	.001*

\*Significant difference in quality of life scores among all study groups except between healthy controls with excessive body weight and healthy controls with normal weight.

these children. Caloric restriction and increasing energy expenditure are hallmarks in the treatment of excessive body weight. Ford et al<sup>25</sup> suggested a need for weight control programs among adults with asthma, because they

found that many adults with asthma did not use recommended approaches of caloric restriction and adequate physical activity. Further studies are needed to establish which strategy is best in children.



Until now, no reports have been available about the influence of a reduction in excessive body weight on asthma severity in children, and there are few evidence-based guidelines for intervention regarding excessive body weight in children.<sup>26</sup> In adults, a reduction in excessive body weight by medical treatment and surgical procedures has resulted in a reduction of asthma symptoms, medication usage, and severity, and in improvement of lung function, indicating a possible causal relationship.<sup>27-29</sup>

When considering our results, some possible limitations of this study should be discussed. First, the ISAAC questionnaire used in this study depended on the recall of asthma symptoms by parents. Recall by parents can be faulty. Further, parents may not witness every asthma symptom a child experiences. Nonetheless, patient report of asthma symptoms has long been a key factor in physician's decision making, and the ISAAC questionnaire mimics the questions they pose as part of assessment. Second, misclassification of asthma is possible. However, we believe that using a combination of the well known and validated ISAAC questionnaire and objective measures such as lung function reversibility and BHR resulted in the best possible clinical definition of asthma. Third, because of the cross-sectional design of this study, we can not speculate on the causal relationship between asthma and excessive body weight and the effect on quality-of-life. Fourth, one might argue that asthma-specific quality-of-life questionnaires are inappropriate to be used in healthy controls. However, the PAQLQ also includes questions on the effect of respiratory symptoms without making reference to asthma. Therefore, we have considered them appropriate for use in children serving as healthy controls. Our observations of the highest scores in healthy controls that approximated the maximum value may be considered a confirmation.

In conclusion, excessive body weight is associated with an additional decrease in quality of life in children with asthma. Clinicians should realize that children with asthma need extra attention if they also have excessive body weight. We therefore consider that treatment by specialized multidisciplinary teams will have the largest beneficial effect in these children.

## REFERENCES

- Hallstrand TS, Fischer ME, Wurfel MM, Afari N, Buchwald D, Goldberg J. Genetic pleiotropy between asthma and obesity in a community-based sample of twins. *J Allergy Clin Immunol* 2005;116:1235-41.
- Shore SA, Fredberg JJ. Obesity, smooth muscle, and airway hyperresponsiveness. *J Allergy Clin Immunol* 2005;115:925-7.
- Sbarbati A, Osculati F, Silvagni D, Benati D, Galie M, Camoglio FS, et al. Obesity and inflammation: evidence for an elementary lesion. *Pediatrics* 2006;117:220-3.
- Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005;115:897-909.
- Juniper EF, Wisniewski ME, Cox FM, Emmett AH, Nielsen KE, O'Byrne PM. Relationship between quality of life and clinical status in asthma: a factor analysis. *Eur Respir J* 2004;23:287-91.
- Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000;320:1240-3.
- Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483-91.
- Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;16:5-40.
- Dales RE, Spitzer WO, Tousignant P, Schechter M, Suissa S. Clinical interpretation of airway response to a bronchodilator: epidemiologic considerations. *Am Rev Respir Dis* 1988;138:317-20.
- Weiland SK, Bjorksten B, Brunekreef B, Cookson WO, von Mutius E, Strachan DP. Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods. *Eur Respir J* 2004;24:406-12.
- Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res* 1996;5:35-46.
- Raat H, Bueving HJ, de Jongste JC, Grol MH, Juniper EF, van der Wouden JC. Responsiveness, longitudinal and cross-sectional construct validity of the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) in Dutch children with asthma. *Qual Life Res* 2005;14:265-72.
- Pearce N. Analytical implications of epidemiological concepts of interaction. *Int J Epidemiol* 1989;18:976-80.
- Lavoie KL, Bacon SL, Labrecque M, Cartier A, Ditto B. Higher BMI is associated with worse asthma control and quality of life but not asthma severity. *Respir Med* 2006;100:648-57.
- Ford ES, Mannino DM, Redd SC, Moriarty DG, Mokdad AH. Determinants of quality of life among people with asthma: findings from the Behavioral Risk Factor Surveillance System. *J Asthma* 2004;41:327-36.
- Blandon V, del Rio NB, Berber EA, Sienra-Monge JJ. Quality of life in pediatric patients with asthma with or without obesity: a pilot study. *Allergol Immunopathol (Madr)* 2004;32:259-64.
- Belamarich PF, Luder E, Kattan M, Mitchell H, Islam S, Lynn H, et al. Do obese inner-city children with asthma have more symptoms than nonobese children with asthma? *Pediatrics* 2000;106:1436-41.
- Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, Bonneux L. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med* 2003;138:24-32.
- Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med* 2002;162:1867-72.
- Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific Quality of Life Questionnaire. *J Clin Epidemiol* 1994;47:81-7.
- Osman L, Silverman M. Measuring quality of life for young children with asthma and their families. *Eur Respir J Suppl* 1996;21:35s-41s.
- Juniper EF. Health-related quality of life in asthma. *Curr Opin Pulm Med* 1999;5:105-10.
- Knorr B, Matz J, Bernstein JA, Nguyen H, Seidenberg BC, Reiss TF, et al. Montelukast for chronic asthma in 6-to 14-year-old children: a randomized, double-blind trial. Pediatric Montelukast Study Group. *JAMA* 1998;279:1181-6.
- Peters-Golden M, Swern A, Bird SS, Hustad CM, Grant E, Edelman JM. Influence of body mass index on the response to asthma controller agents. *Eur Respir J* 2006;27:495-503.
- Ford ES, Mannino DM, Redd SC, Mokdad AH, Galuska DA, Serdula MK. Weight-loss practices and asthma: findings from the behavioral risk factor surveillance system. *Obes Res* 2003;11:81-6.
- Summerbell CD, Ashton V, Campbell KJ, Edmunds L, Kelly S, Waters E. Interventions for treating obesity in children. *Cochrane Database Syst Rev* 2003;3:CD001872.
- Macgregor AM, Greenberg RA. Effect of surgically induced weight loss on asthma in the morbidly obese. *Obes Surg* 1993;3:15-21.
- Dixon JB, Chapman L, O'Brien P. Marked improvement in asthma after Lap-Band surgery for morbid obesity. *Obes Surg* 1999;9:385-9.
- Stenius-Aarniala B, Poussa T, Kvarnstrom J, Gronlund EL, Ylikahri M, Mustajoki P. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ* 2000;320:827-32.