High body mass index, asthma and allergy in Swedish schoolchildren participating in the International Study of Asthma and Allergies in Childhood: Phase II

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Aim: To assess the relationship between high body mass index (BMI) and asthma and atopic manifestations in 12-y-old children.

Methods: The relationship between high BMI and asthma symptoms was studied in 457 sixth-grade children, with (n = 161) and without (n = 296) current wheeze. High BMI was defined as ≥75th percentile of gender-specific BMI reference values for Swedish children at 12 y of age; overweight as a subgroup of high BMI was defined as ≥95th percentile. Children with a BMI <75th percentile served as controls. Questionnaires were used to assess asthmatic and allergic symptoms, and bronchial hyperresponsiveness was assessed by hypertonic saline provocation tests.

Results: Current wheeze was associated with high BMI after adjustment for confounding factors (adjusted OR 1.7, 95% CI 1.0–2.5) and overweight had an even more pronounced effect (adjusted OR 1.9, 95% CI 1.0–3.6). In addition, asthma severity was associated with high BMI, as evaluated by the number of wheezing episodes during the previous 12 mo among the wheezing children (adjusted OR 1.9, 95% CI 1.0–4.0). There was also an association between high BMI and the presence of eczema in wheezing children (adjusted OR 2.2, 95% CI 1.0–4.6). However, high BMI was not significantly associated with hay fever, positive skin prick tests or bronchial hyperresponsiveness.

Conclusion: The study confirms and extends a previously observed relationship between BMI and the presence of wheezing and asthma.

Key words: Asthma, body mass index, bronchial hyperreactivity, eczema, overweight

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The increasing prevalence of asthma in Western countries (1) has coincided with an increase in the number of people who are overweight, both children and adults (2, 3). An increased body mass index (BMI) has been reported to be associated with an increased prevalence of asthma (4–9). Furthermore, high BMI appears to be a risk factor for the development of asthma rather than a consequence, as indicated by several prospective studies (10–13). A gender-specific relationship has been shown consistently in female but not in male adults (4–6, 11–13), whereas the findings are inconsistent in children (7–10). The association of BMI with other allergic diseases and bronchial hyperresponsiveness has been less extensively studied, although a high prevalence of positive skin-prick tests was observed in teenage Taiwanese girls (14) and young Finnish adults (15) with high BMI. In another study, however, there was no relationship between BMI and skin-prick-test positivity, nor serum eosinophil counts (9). Exercise-induced bronchospasm, but not bronchial hyper-responsiveness to histamine (16), is more common in obese children than in children of normal weight (17). These contradictory reports prompted us to analyse the relationship between high BMI and asthma symptoms as well as other allergic diseases, skin-prick tests and bronchial hyperresponsiveness in 12-y-old children.

Materials and Methods

Data collection

The study was part of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase II (18) and
High BMI, asthma and allergy in children

Skin-prick tests

Skin-prick tests were performed in duplicate on the forearms using extracts of birch pollen, grass pollen, dander of cat, dog and horse, *D. pteronyssinus*, *D. farinae* and *Alternaria* (ALK, Hørsholm, Denmark) according to the ISAAC module (18). Histamine 10 mg/ml and 50% glycerine were used as positive and negative controls, respectively. The size of a wheal was recorded as the mean of the greatest diameter and the diameter perpendicular to its mid-point. A mean diameter of 3 mm or more of the duplicate wheals was regarded as positive.

Hypertonic saline provocation tests

Hypertonic saline provocation tests were performed according to the ISAAC protocol (18). The method has been validated in a previous study (21). In brief, two reproducible measurements (within 5%) of FEV\(_1\) (forced expiratory volume in 1 s) were performed using a MasterScope spirometer (Jaeger), and the highest measurement was recorded as the baseline FEV\(_1\). Hypertonic saline (4.5%) was nebulized via a Devilbiss Ultraneb 2000 connected to a 60-cm tube (Devilbiss No. 8885) and a two-way valve (Laerdal valve No. 560 200/850 500, Devilbiss, manufactured by Dahlhausen, Cologne, Germany). The child was encouraged to maintain tidal breathing. The exposure time was progressively increased from 30 s to 1, 2, 4 and 8 min each and the maximum total inhalation period was 15.5 min. After each exposure, two reproducible measurements of FEV\(_1\) were made. The exposure time was doubled if the fall in FEV\(_1\) was less than 10%. The same dose was repeated if the fall was between 10 and 15%. The challenge test was stopped and considered to be positive when the decline in FEV\(_1\) was more than 15%.

Statistical analyses

The Epi Info 2000 program (Centres for Disease Control and Prevention, Epidemiology Program Office and WHO) was used to calculate \(\chi^2\) for a trend of increased BMI for current wheeze. Since controls were random samples in this case-control study, unconditional logistic regression (22) was used with Stat View 5.0 for Macintosh (Abacus Concepts Inc., Berkeley, California, USA) to obtain crude and adjusted ORs (95% CI) of high BMI and overweight as a subgroup in relation to current wheeze. When the 95% CI excludes unity, the result is referred to as statistically significant. The possible association between high BMI and episodes of wheezing during the previous 12 mo, current exercise-induced wheeze, ever asthma, hay fever or eczema, positive skin-prick tests and bronchial hyperresponsiveness was analysed separately in children with current wheezing and children without current wheezing.

Ethical aspects

The study was approved by the Human Research Ethics Committee of the Medical Faculty at Linköping University. Parents of the participating children gave their informed consent.

Results

Current wheeze was associated with increased BMI (Table 1). Furthermore, current wheeze was associated with high BMI after adjustment for potential confounding factors (parental history of allergy, maternal
smoking during pregnancy, environmental tobacco smoke, gender, number of siblings and place of residence) (adjusted OR 1.7, 95% CI 1.0–2.5). This was even more pronounced in the subgroup of overweight children (BMI ≥95th percentile) (Table 2).

There was a significant relationship between overweight and current wheeze among boys, but it was not significant among girls. However, the formal test of interaction did not show any significant difference in the association between boys and girls.

Among children with current wheeze, children with high BMI were more likely to have four or more episodes of wheezing during the previous 12 mo compared with the controls (OR 1.9, 95% CI 1.0–3.8) (Table 3). The positive relationship remained after adjustment for confounding factors (adjusted OR 2.0, 95% CI 1.0–4.0). High BMI tended to be associated with ever eczema in children both with and without current wheeze (p = 0.06 and p = 0.09, respectively). However, the relationship between high BMI and eczema persisted only among children with current wheeze after adjustment for confounding factors (adjusted OR 2.2, 95% CI 1.0–4.6), and not among children without current wheeze (adjusted OR 1.6, 95% CI 0.9–2.7). High BMI was not significantly associated with hay fever, positive skin-prick tests or bronchial hyperresponsiveness in either of the groups (Table 3).

### Discussion

In this case-control analysis of 12-y-old children, current wheeze was associated with high BMI (BMI ≥75th percentile) and this was particularly obvious in the subgroup of overweight children (BMI ≥95th percentile). Furthermore, asthma severity was associated with high BMI, as evaluated by the number of wheezing episodes during the previous 12 mo among the wheezing children. There was also an association between high BMI and presence of eczema in wheezing children.

A relationship between increased BMI and asthma has been shown consistently only in female adults (4–6, 11–13). However, gender differences have not been seen consistently in children (7–10), nor did we find a gender-specific association in the present study. The significant relationship between high BMI and presence of eczema in wheezing children.

### Table 1. Increased body mass index in relation to current wheeze.

<table>
<thead>
<tr>
<th></th>
<th>Current wheeze (n = 161; Boys: 86)</th>
<th>No current wheeze (n = 296; Boys: 150)</th>
<th>χ² for trend, p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;75th percentile</td>
<td>84</td>
<td>52</td>
<td>188</td>
</tr>
<tr>
<td>75th &lt; BMI &lt;95th</td>
<td>50</td>
<td>31</td>
<td>77</td>
</tr>
<tr>
<td>BMI ≥95th percentile</td>
<td>27</td>
<td>17</td>
<td>31</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;75th percentile</td>
<td>44</td>
<td>51</td>
<td>100</td>
</tr>
<tr>
<td>75th &lt; BMI &lt;95th</td>
<td>27</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>BMI ≥95th percentile</td>
<td>15</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;75th percentile</td>
<td>40</td>
<td>53</td>
<td>88</td>
</tr>
<tr>
<td>75th &lt; BMI &lt;95th</td>
<td>23</td>
<td>31</td>
<td>42</td>
</tr>
<tr>
<td>BMI ≥95th percentile</td>
<td>12</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

BMI: Body mass index.

Groups were classified according to BMI reference values for 12-y-old Swedish children, stratified for gender [20].

### Table 2. Crude and adjusted odds ratios and 95% confidence intervals of high body mass index and overweight for current wheeze in multivariate logistic regression.

<table>
<thead>
<tr>
<th></th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Boys</td>
</tr>
<tr>
<td>High BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>1.6 (1.0–2.4)</td>
<td>1.9 (1.1–3.3)</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.9 (1.0–3.5)</td>
<td>2.3 (1.0–5.1)</td>
</tr>
</tbody>
</table>

OR: Odds ratio; CI: confidence interval; BMI: body mass index.

High BMI: BMI ≥75th percentile of the reference value for Swedish children at 12 y of age, stratified for gender [20]. Overweight: BMI ≥95th percentile. Adjustment was made for parental history of allergy, maternal smoking during pregnancy, environmental tobacco smoke, gender, number of siblings and place of residence.
higher degree of physical activity among boys and therefore a greater likelihood of discovering their symptoms. Underdiagnosis of asthma is more prevalent among girls and is associated with low physical activity and underreporting of symptoms (23).

The association between high BMI and asthmatic symptoms could be due to a variety of factors, such as low physical activity, diet, hormonal influence, immune modification and/or mechanical factors. Low physical activity is clearly associated with being overweight (24), and the reduction in deep breathing associated with a sedentary lifestyle may lead to a latching state of airway smooth muscle, and in turn to airway obstruction and hyperreactivity (25). In their epidemiological study, Rasmussen et al. demonstrated that low physical activity in childhood was associated with the development of asthma in young adulthood (26). Whether being overweight causes asthma symptoms through low physical activity, or whether asthma symptoms result in avoidance of exercise, which then leads to weight gain, cannot be answered in a cross-sectionally based study. However, the results of prospective studies suggest that high BMI is a risk factor for asthma (10–13). In addition, airway obstruction and peak expiratory flow variability in obese asthmatics were improved after moderate weight loss, indicating a causal relationship (27). Beckett et al. found that gain in BMI predisposed young females to asthma, irrespective of physical activity (12). Therefore high BMI appears to be a risk factor for asthma, and low physical activity may not explain the relationship.

There are several other possible explanations for the association between high BMI and asthma; for example dietary factors. A low intake of antioxidants may be associated with asthmatic symptoms in children (28), and a high intake of salt with bronchial hyperresponsiveness (29). It is conceivable that there are differences in the intake of nutrients between children with high BMI and those with normal BMI. Furthermore, overweight males and females have elevated oestradiol levels (30), which has been suggested to play a causal role in the development of asthma (31). Wheezing symptoms in children with a high BMI may also be induced by a low level of systemic inflammation, which is present in overweight and obese subjects (32). Finally, asthma symptoms in children with high BMI may simply be explained by mechanical factors, i.e. the deposition of adipose tissue in the chest wall and the airways, leading to narrow airways, and/or the presence of gastro-oesophageal reflux, which is associated with both overweight and asthma (25).

In our study, bronchial hyperresponsiveness to hypertonic saline was not significantly associated with high BMI, nor was the positive histamine challenge test discussed in a report elsewhere (16). However, methacholine-induced bronchial hyperresponsiveness in adult men was recently found to be associated with high BMI (33), and exercise-induced bronchospasm is more common in obese children (17).

Eczema, but not hay fever or positive skin-prick tests, was associated with high BMI in wheezing children. As yet, there is insufficient evidence to demonstrate a relationship between overweight and atopy (9), although two previous studies have shown an association between high BMI and positive skin-prick tests (14, 15).

In conclusion, high BMI seems to be a risk factor for asthma. There are several possible underlying mechanisms for such an association, but these all remain speculative.

### Table 3. High body mass index in relation to asthmatic and allergic manifestations among children with or without current wheeze.

<table>
<thead>
<tr>
<th></th>
<th>Children with current wheeze</th>
<th></th>
<th>Children without current wheeze</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High BMI N = 77</td>
<td>Controls N = 84</td>
<td>OR 95% CI</td>
<td>High BMI N = 108</td>
</tr>
<tr>
<td>Episodes of wheeze</td>
<td>35</td>
<td>26</td>
<td>1.9</td>
<td>1.0–3.8</td>
</tr>
<tr>
<td>(≥4 times during the past year)</td>
<td></td>
<td></td>
<td>0.7–2.8</td>
<td>0.4–3.4</td>
</tr>
<tr>
<td>Current exercise-induced wheeze</td>
<td>52</td>
<td>51</td>
<td>1.4</td>
<td>0.5–2.0</td>
</tr>
<tr>
<td>Ever asthma</td>
<td>51</td>
<td>55</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Ever hay fever</td>
<td>33</td>
<td>36/78</td>
<td>0.9</td>
<td>13/104</td>
</tr>
<tr>
<td>Ever eczema</td>
<td>53</td>
<td>46</td>
<td>1.9</td>
<td>43</td>
</tr>
<tr>
<td>Positive SPT</td>
<td>42/65</td>
<td>41/71</td>
<td>1.3</td>
<td>21/103</td>
</tr>
<tr>
<td>Bronchial hyperresponsiveness</td>
<td>35/65</td>
<td>31/67</td>
<td>1.4</td>
<td>27/97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.6–2.7</td>
<td>0.6–2.7</td>
</tr>
</tbody>
</table>

High BMI: BMI ≥ 75th percentile of the reference values for Swedish children at 12 y of age, stratified for gender [20].

Controls: BMI < 75th percentile.

BMI: Body mass index; OR: odds ratio; CI: confidence interval; positive SPT: positive skin-prick test, i.e. at least one positive skin reaction to tested allergens. N is indicated if it differs from the original number.
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