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REGULAR ARTICLE

A persistently high body mass index increases the risk of atopic asthma at school age

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ABSTRACT

Aim: Being overweight has been associated with the risk of developing childhood asthma, but studies have produced conflicting results, for example with regard to possible links to allergic diseases. This study aimed to explore the relationship between body mass index (BMI) and school-age asthma.

Methods: Data were obtained from a prospective, longitudinal study of 5044 children born in western Sweden. The parents answered questionnaires at six months and one, four-and-a-half and eight years of age. The response rate to the final questionnaire at the age of eight was just over 80%. BMI was adjusted for age and gender, and a high BMI was defined as the 85th percentile and above.

Results: A multivariate analysis showed an independently increased risk of doctor-diagnosed asthma among children with a persistently high BMI, both in infancy and at school age, with an adjusted odds ratio (aOR) of 2.9 and a 95% confidence interval (CI) of 1.3–6.4. In addition, persistently high BMI was associated with an increased risk of atopic asthma (aOR 4.7, 95% CI 2.0–11.0).

Conclusion: A persistently high BMI during childhood increased the risk of doctor-diagnosed asthma at school age. The increased risk of atopic asthma suggests an effect mediated via the immune system.

INTRODUCTION

Being overweight during childhood has been associated with the risk of developing asthma, and several prospective studies have supported the link between overweight and asthma (1–4). These include a large meta-analysis that reported that being overweight and childhood wheezing disorders were associated (5). However, the association appears to be complex and the results are conflicting, for example when it comes to possible links to allergic disease.

Furthermore, it is unclear whether childhood asthma is associated with early or current overweight and how the changes in overweight status during childhood affect the risk of asthma. Some studies only report an association between current overweight and asthma (6–8). Other studies have reported that early overweight (9) or rapid growth during the first two years of life (10) is associated with an increased risk of later wheeze or asthma.

The inconsistent results from previous studies may be related to different definitions of asthma, different confounding factors and the different age distributions of the study populations. Further longitudinal studies evaluating the relationship between the changes in overweight status during childhood and asthma, and the relationship with atopic status, could increase the understanding of the association between overweight and asthma.

The aim of this longitudinal study was to explore the relationship between changes in BMI from infancy to school age and asthma at school age. We also wanted to explore the association between BMI and atopic asthma.

METHODS

Participants

Data were obtained from a prospective, longitudinal cohort study of children born in western Sweden in 2003. The region comprises urban and rural areas and has approxi-

Key Notes

- Being overweight has been associated with the risk of developing childhood asthma, but studies have produced conflicting results.
- Our study of the relationship between body mass index (BMI) and school-age asthma used data from 5044 children in western Sweden, with parents answering questionnaires at four time points between six months and eight years of age.
- We found that persistently high BMI during childhood increased the risk of doctor-diagnosed asthma at school age.

mately 1.5 million inhabitants, which is one-sixth of the total Swedish population. The random sample comprised 8176 families – 50% of births in 2003 – and 5654 families agreed to take part in the study.

Procedures

After providing written informed consent, the parents answered questionnaires when their child was aged six months and one, four-and-a-half and eight years of age. The questionnaires were based on the Swedish version of the International Study of Asthma and Allergies in Childhood and the Swedish Barn Allergi Miljö Stockholm Epidemiologi study. Details relating to the questionnaires and response rates have been published previously (11–14). The final questionnaire was distributed when the children were eight years of age, and it was given to all the families involved in the study (n = 5654), except for the 610 who no longer wished to participate. The response rate was 80.3% (4051/5044), which equated to 71.6% of the families that entered the study.

Information regarding pregnancy and post-natal factors was collected at six months of age. Supplementary data were obtained from the Swedish Medical Birth Register and provided information on gender, gestational age, Caesarean section and small or large for gestational age. Information regarding the duration of breastfeeding and the introduction of different foods was collected at 12 months of age. Specific information regarding these questions has been published previously (13).

Information on height and weight during childhood was obtained from the questionnaires. Weight and height measurements from children aged 10–13 months (median 12 months) and 7–9 years (median 8.3 years) were included. Erroneous data were not included. Swedish infants and children are weighed and measured by trained nurses at child healthcare centres and in schools. In our study, we asked the parents to use the information in these records and, if it was not available, to weigh and measure the child at home to obtain their current weight and height.

BMI was calculated as body weight in kilograms divided by height in metres squared (kg/m^2). A high BMI was defined as the 85th percentile and above, based on the children in our study, and was adjusted for gender and age. An early high BMI was defined as a high BMI at one year of age, but a normal BMI at eight years of age. A late high BMI was defined as a high BMI at eight years of age, but a normal BMI at one year of age. A persistently high BMI was defined as a high BMI at both ages, and a normal BMI was defined as a normal BMI at both ages.

The diagnosis of asthma at eight years of age was based on the answers to the following questions:

Q1. 'Has your child been diagnosed with asthma by a physician?'
Q2. 'Has your child received medication for asthma during the last 12 months?'
Q3. 'Has your child had problems with wheezing or symptoms of wheezing during the last 12 months?'

Doctor-diagnosed asthma at eight years of age was defined as a positive answer to question Q1 (reported diagnosis) and to either question Q2 (current asthma medication) and/or to question Q3 (current wheezing).

Atopic asthma at eight years of age was defined as doctor-diagnosed asthma and reported allergic sensitisation and, or, current doctor-diagnosed food allergy, rhinitis or eczema. Nonatopic asthma at eight years of age was defined as doctor-diagnosed asthma and not having allergic sensitisation or doctor-diagnosed food allergy, rhinitis or eczema.

Doctor-diagnosed rhinitis and eczema were defined as a reported diagnosis and either medication and, or, symptoms during the last 12 months. Doctor-diagnosed food allergy was defined as a reported diagnosis and current food allergy. Allergic sensitisation was defined as a parentally reported positive allergy test, skin prick test or specific immunoglobulin E in blood. Allergic sensitisation in terms of a positive allergy test was reported in 84% of the subjects with atopic asthma. Specific information regarding these questions has been published previously (14).

Statistical analyses

In the statistical analysis, the chi-square test and binary logistic regression were used. Odds ratios (ORs) were estimated with 95% confidence intervals. p values of <0.05 were considered statistically significant.

The outcome variables were doctor-diagnosed asthma at eight years of age, as well as atopic and nonatopic doctor-diagnosed asthma. The associations of asthma with an early, late and persistently high BMI compared with a normal BMI were analysed.

In the final multivariate model, we adjusted for potential confounders and known risk factors for asthma and obesity: atopic heredity, male gender, maternal medication during pregnancy, gestational age <37 weeks, Caesarean section, small for gestational age, large for gestational age, treatment with antibiotics during the first week, doctor-diagnosed food allergy during the first year, eczema during the first year, recurrent wheeze in infancy, introduction of fish before nine months of age, fish once a month or more at one year of age, outdoor time, father's employment at six months, rural living at six months, breastfeeding for four months or more, smoking during pregnancy, parental education and maternal obesity. Adjustments were made for all factors simultaneously. We also adjusted for birthweight and weight gain during the first year, but these factors had no significant influence on the analyses and were not included in the final model.

We also analysed the effect of an increase in BMI of more than two standard deviations (SD), as well as continuously.

All potential confounders were tested for multiplicative interaction with a persistently high BMI.

The IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical calculations.

Ethical approval

The study was approved by the ethics committee at the University of Gothenburg. All parents provided written informed consent.

RESULTS

Descriptives

The prevalence of children with normal BMI at one and eight years of age was 74.5%, early high BMI was 11.1%, late high BMI was 10.3%, and persistently high BMI was 4.1%. The characteristics of the study population are presented in Table S1.

The mean BMI value at one year of age was 17.4 (SD 1.4, range 12.52–31.22) for all children, 17.16 (SD 1.4) for girls and 17.56 (SD 1.4) for boys. At eight years of age, the mean BMI value was 16.6 (SD 2.2, range 11.11–33) for all children, 16.59 (SD 2.2) for girls and 16.67 (SD 2.2) for boys.

The age-adjusted and gender-adjusted values for a high BMI (85th percentile) at one and eight years of age are presented in Table S2.

In the study population, 65% of the children with asthma at eight years of age had atopic asthma (n = 150) and 35% had nonatopic asthma (n = 81).

Analysis of BMI increase

An increase in BMI of >2SD showed no association with asthma at school age. The same results were found when analysing the BMI increase as a continuous variable (data not shown).

Univariate analyses

In the univariate analyses, we found an increased risk of doctor-diagnosed asthma among children with persistently high BMI, with an odds ratio (OR) of 2.0 and a 95% confidence interval (CI) of 1.1–3.6. In addition, a persistently high BMI was associated with a significantly increased risk of atopic asthma (OR 2.9, 95% CI 1.5–5.5), but not of nonatopic asthma (OR 0.4, 95% CI 0.1–3.1). The results of the univariate analyses are presented in Table 1.

Multivariate analyses

In the multivariate analyses, a persistently high BMI increased the risk of doctor-diagnosed asthma at eight years of age (adjusted OR 2.9, 95% CI 1.3–6.4). An early or late high BMI on its own did not increase the risk of school-age asthma. In addition, a persistently high BMI was associated with a significantly increased risk of atopic asthma (aOR 4.7, 95% CI 2.0–11.0). However, due to the small numbers we could not calculate the OR for nonatopic asthma (Table 2).

Table 1 Univariate analyses of early, late and persistently high BMI with current doctor-diagnosed asthma, atopic and nonatopic asthma, respectively

	Current asthma OR (95% CI)	Atopic asthma OR (95% CI)	Nonatopic asthma OR (95% CI)
Normal BMI	1 ref.	1 ref.	1 ref.
Early high BMI	0.6 (0.4–1.2)	0.8 (0.4–1.5)	0.4 (0.1–1.4)
Late high BMI	0.9 (0.5–1.6)	1.1 (0.6–2.1)	0.6 (0.2–1.8)
Persistently high BMI	**2.0 (1.1–3.6)**	**2.9 (1.5–5.5)**	0.4 (0.1–3.1)

Significant ($p < 0.05$) factors are in bold.

The prevalence of atopic asthma at eight years of age at different time patterns of BMI was 3.6% among children with normal BMI, 2.7% among children with early high BMI, 3.9% among children with late high BMI and 9.7% among children with persistently high BMI.

Interaction and stratified analyses

All potential confounders in the multivariate analyses were tested for multiplicative interaction with a persistently high BMI. We did not find any interaction between a persistently high BMI and male gender, atopic heredity or allergic manifestations in infancy. However, there was an interaction between gestational age and a persistently high BMI ($p = 0.049$). Term infants with a persistently high BMI had a risk of 2.3 (1.1–4.7) for atopic asthma, and preterm infants had a considerably higher risk of 13.6 (3.3–55.2).

Birthweight and weight gain during the first year did not influence the association between a persistently high BMI and atopic asthma.

DISCUSSION

The main result of this prospective study was the finding of an increased risk of school-age asthma among children with a persistently high BMI, while only an early or late high BMI did not increase the risk of school-age asthma. Another major result was that the association was significant for atopic asthma, suggesting a link mediated through immunological mechanisms.

Several prospective studies support a link between a high BMI and asthma or wheeze in children (1–4,6,7,9,15). Asthma development may be related to how long a child has been overweight. It is not fully understood how changes in the overweight status during childhood affect the risk of asthma. We found that only an early or late high BMI did not increase the risk of school-age asthma, but a persistently high BMI from infancy to school age increased the risk. However, some studies have reported an association between asthma and only current overweight (6–8). Other studies have found associations between overweight in early childhood and subsequent asthma. Rhezak et al. investigated how the development of BMI during childhood is associated with asthma in eight European birth cohort studies. They found that children with rapid growth during the first two years of life had an increased risk of asthma up to six years compared with children with a less pronounced weight gain in early childhood (10).

Different mechanisms have been suggested as underlying the link between being overweight and asthma. In a review of the mechanisms, the proposed pathways include mechanical effects of obesity, an inflammatory pathway driven by obesity-related cytokines and environmental and lifestyle changes resulting in asthma in predisposed individuals (16).

In this study, the increased risk of atopic asthma among children with a persistently high BMI suggests an

Table 2 Multivariate analyses for current doctor-diagnosed asthma, atopic and nonatopic asthma at 8 years of age

Risk factor	Current asthma aOR (95% CI)	Atopic Asthma aOR (95% CI)	Nonatopic asthma aOR (95% CI)
Normal BMI	1 ref.	1 ref.	1.ref
Early high BMI	0.7 (0.3–1.5)	0.8 (0.3–2.1)	0.4 (0.1–1.8)
Late high BMI	1.1 (0.5–2.2)	1.1 (0.4–2.5)	1.5 (0.5–4.6)
Persistently high BMI	**2.9 (1.3–6.4)**	**4.7 (2.0–11.0)**	*
Atopic heredity (mother or father with asthma, eczema or rhinitis)	1.5 (0.9–2.5)	1.2 (0.7–2.2)	**2.5 (1.01–6.4)**
Male gender	1.4 (0.9–2.2)	1.7 (0.9–3.0)	1.1 (0.5–2.4)
Maternal medication during pregnancy	1.4 (0.9–2.2)	1.3 (0.8–2.2)	1.8 (0.9–3.9)
Gestational age <37 weeks	1.0 (0.4–2.7)	1.1 (0.3–3.6)	1.9 (0.5–7.9)
Caesarean section	1.3 (0.7–2.3)	1.3 (0.6–2.6)	1.2 (0.4–3.1)
Small for gestational age	2.6 (0.9–8.2)	**4.2 (1.3–14.2)**	0.8 (0.06–11.2)
Large for gestational age	0.2 (0.03–1.6)	0.3 (0.04–2.4)	*
Treatment with antibiotics during the first week	**2.8 (1.4–5.9)**	**3.5 (1.5–8.0)**	2.2 (0.6–9.0)
Doctor-diagnosed food allergy during the first year	**5.6 (2.9–10.9)**	**8.0 (3.9–16.3)**	1.0 (0.1–8.3)
Eczema during the first year	1.5 (0.9–2.4)	**2.2 (1.3–3.8)**	0.6 (0.2–1.6)
Recurrent wheeze during the first year	**4.4 (2.4–8.0)**	**2.7 (1.2–6.0)**	**10.8 (4.6–25.8)**
Introduction of fish before 9 months of age	**0.6 (0.4–0.97)**	**0.5 (0.3–0.96)**	0.7 (0.3–1.9)
Fish once a month or more at one year of age	0.9 (0.4–1.9)	0.6 (0.3–1.4)	*
Maternal obesity	1.3 (0.7–2.6)	1.5 (0.7–3.2)	0.8 (0.2–3.7)
Daily outdoor activity at 12 months			
Less than one hour	1 ref.	1 ref	1 ref.
One to three hours	2.4 (0.7–7.9)	4.7 (0.6–35.4)	1.4 (0.3–6.2)
More than three hours	1.3 (0.3–5.0)	2.0 (0.3–17.5)	1.3 (0.2–7.6)
Rural living at 6 months	0.9 (0.6–1.6)	0.9 (0.5–1.8)	0.8 (0.3–2.1)
Breastfeeding for 4 months or more	0.8 (0.5–1.3)	0.7 (0.4–1.4)	1.0 (0.4–2.7)
Smoking during pregnancy	1.3 (0.6–2.8)	1.5 (0.7–3.6)	0.5 (0.06–4.0)
Parental educational level (>12 years) at 6 months	1.2 (0.7–1.9)	0.9 (0.5–1.7)	1.8 (0.7–4.3)

Independent risk factors for current doctor-diagnosed asthma are in bold, as well as the independently significant aORs.
*No OR is given due to too few subjects in this analysis with nonatopic asthma.

effect mediated via the immune system. The results are of significant clinical importance because children with atopic asthma tend to have more persistent asthma (17,18).

Overweight may affect the development of atopic asthma by its effects on the immune response. Obesity alters the innate and adaptive immune system and changes the production of adiponectin and leptin. These effects may be important in the pathogenesis of allergic asthma (19).

Some studies have found that the association between obesity and asthma was stronger among nonatopic children (20). However, Forno et al. reported a link between obesity and asthma and found that atopy mediated the association (21). There are also some studies that have explored the relationship between obesity and allergy, but the results have been conflicting. Some studies report a positive association between overweight and allergy (7,22), while other studies have found no association (6,23).

It has been suggested that the mechanisms in the link between obesity and asthma differ with regard to gender and age so that, after puberty, this association tends to be stronger in girls than in boys (24). Other studies have confirmed the stronger association in girls than in boys (1,3), but the effect of gender on the link has been inconsistent. In this study, we did not find any gender difference in the risk of asthma development at eight years of age among children with a persistently high BMI.

It has been suggested that premature birth, low birthweight and high childhood BMI are independent risk factors for allergic respiratory symptoms in children (25). Wang et al. explored the combined effects of birthweight, gestational age and childhood BMI and found that children with a currently high BMI could have a larger respiratory burden if they also had a history of low birthweight or who were born premature or small for gestational age. Another study reported that children born premature with high infant weight gain had an increased risk of school-age asthma. Premature birth was associated with asthma, independent of birthweight (26).

Strengths and weaknesses

The strengths of the study are the large size of the birth cohort, access to perinatal data and the high response rate. Another strength is that the asthma diagnosis was based on a doctor's diagnosis of asthma and, in addition, asthma medication and, or, asthma symptoms. Also, the longitudinal design was of great value in judging temporal relationships between BMI and asthma.

To improve the validity of answers, we used questions based on well-known, validated questionnaires. As reported

earlier, the material appeared to be largely representative of the population (11). However, as is often seen in questionnaire studies, the responders were somewhat more health conscious and educated than the nonresponders (14).

We used parentally reported height and weight and calculated BMI from these measures. Measures reported by parents should be used with reservations, and measuring height and weight by trained professionals remains the gold standard. As that option was not available, we asked the parents to use the records from child healthcare centre and schools and weigh and measure their child if these were not available. A Belgian study of children aged seven to nine years of age found that parentally reported measures of weight and length were strongly correlated with measured values, although parents tended to underreport weight (27).

It can be argued that BMI may not the best method for determining whether infants are overweight. However, defining high BMI as the 85th percentile and above based on the children in our study allowed us to compare our results with the well-known Swedish Barn Allergi Miljö Stockholm Epidemiologi study that also used this methodology (7). Furthermore, the values of a high BMI at eight years of age in our study were similar to the isoBMI 25 value for overweight suggested by the International Obesity Task Force, using the international standard definition by Cole et al. (28). The mean values for BMI at one and eight years of age in our study were also similar to the descriptive values in the Swedish population reported by Werner and Bodin (29).

In our study, we defined atopic asthma at eight years of age as doctor-diagnosed asthma with reported allergic sensitisation and, or, current doctor-diagnosed food allergy, rhinitis or eczema. This meant that 65% of the children with asthma at eight years of age were classified as having atopic asthma and 35% as having nonatopic asthma (14). In a study, on children aged seven to eight years of age from northern Sweden (30), 64.9% of the participants with asthma had allergic sensitisation based on a skin prick test. The results of these skin prick tests, carried out on 1700 children in 2006, showed the same proportion of allergic and nonallergic asthma as our study. Therefore, we think that we have used a reasonable definition of atopic asthma.

Regarding the validity of self-reported sensitisation, it should be noted that in Sweden, allergy testing is included in the asthma workup. Allergic sensitisation in terms of a positive allergy test was reported in 84% of the subjects with atopic asthma. Furthermore, Swedish parents are anxious to have children with asthma tested. There is also good knowledge of allergic diseases in the general population. Taken together, this makes us think that our data are valid.

CONCLUSION

In conclusion, we found that a persistently high BMI during childhood increased the risk of doctor-diagnosed asthma at school age. The increased risk of atopic asthma suggests an effect mediated via the immune system.

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References

1. 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.
2. 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.
3. Castro-Rodriguez 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.
4. Murray CS, Canoy D, Buchan I, Woodcock A, Simpson A, Custovic A. Body mass index in young children and allergic disease: gender differences in a longitudinal study. *Clin Exp Allergy* 2011; 41: 78–85.
5. Mebrahtu TF, Feltbower RG, Greenwood DC, Parslow RC. Childhood body mass index and wheezing disorders: a systematic review and meta-analysis. *Pediatr Allergy Immunol* 2015; 26: 62–72.
6. Scholtens S, Wijga AH, Seidell JC, Brunekreef B, de Jongste JC, Gehring U, et al. Overweight and changes in weight status during childhood in relation to asthma symptoms at 8 years of age. *J Allergy Clin Immunol* 2009; 123: 1312–8.
7. Magnusson JO, Kull I, Mai XM, Wickman M, Bergström A. Early childhood overweight and asthma and allergic sensitization at 8 years of age. *Pediatrics* 2012; 129: 70–6.
8. Törmänen S, Lauhkonen E, Saari A, Koponen P, Korppi M, Nuolivirta K. Excess weight in preschool children with a history of severe bronchiolitis is associated with asthma. *Pediatr Pulmonol* 2015; 50: 424–30.
9. Taveras EM, Rifas-Shiman SL, Camargo CA Jr, Gold DR, Litonjua AA, Oken E, et al. Higher adiposity in infancy associated with recurrent wheeze in a prospective cohort of children. *J Allergy Clin Immunol* 2008; 121: 1161–6.
10. Rzehak P, Wijga AH, Keil T, Eller E, Bindslev-Jensen C, Smit HA, et al. Body mass index trajectory classes and incident asthma in childhood: results from 8 European Birth Cohorts–a Global Allergy and Asthma European Network. *J Allergy Clin Immunol* 2013; 131: 1528–36.
11. Alm B, Erdes L, Möllborg P, Pettersson R, Norvenius SG, Åberg N, et al. Neonatal antibiotic treatment is a risk factor for early wheezing. *Pediatrics* 2008; 121: 697–702.
12. Alm B, Goksör E, Thengilsdottir H, Pettersson R, Möllborg P, Norvenius G, et al. Early protective and risk factors for allergic rhinitis at age 4(1/2) yr. *Pediatr Allergy Immunol* 2011; 22: 398–404.
13. Goksör E, Alm B, Thengilsdottir H, Pettersson R, Åberg N, Wennergren G. Preschool wheeze - impact of early fish introduction and neonatal antibiotics. *Acta Paediatr* 2011; 100: 1561–6.
14. Goksör E, Alm B, Pettersson R, Möllborg P, Erdes L, Åberg N, et al. Early fish introduction and neonatal antibiotics affect the risk of asthma into school age. *Pediatr Allergy Immunol* 2013; 24: 339–44.

15. Granell R, Henderson AJ, Evans DM, Smith GD, Ness AR, Lewis S, et al. Effects of BMI, fat mass, and lean mass on asthma in childhood: a Mendelian randomization study. *PLoS Med* 2014; 11: e1001669.
16. Rasmussen F, Hancox RJ. Mechanisms of obesity in asthma. *Curr Opin Allergy Clin Immunol* 2014; 14: 35–43.
17. Phelan PD, Robertson CF, Olinsky A. The Melbourne Asthma Study: 1964-1999. *J Allergy Clin Immunol* 2002; 109: 189–94.
18. Tai A, Tran H, Roberts M, Clarke N, Gibson AM, Vidmar S, et al. Outcomes of childhood asthma to the age of 50 years. *J Allergy Clin Immunol* 2014; 133: 1572–8.
19. Sideleva O, Dixon AE. The many faces of asthma in obesity. *J Cell Biochem* 2014; 115: 421–6.
20. Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Siega-Riz AM, et al. Association of childhood obesity with atopic and nonatopic asthma: results from the National Health and Nutrition Examination Survey 1999-2006. *J Asthma* 2010; 47: 822–9.
21. Forno E, Acosta-Perez E, Brehm JM, Han YY, Alvarez M, Colon-Semidey A, et al. Obesity and adiposity indicators, asthma, and atopy in Puerto Rican children. *J Allergy Clin Immunol* 2014; 133: 1308–14.
22. Schachter LM, Peat JK, Salome CM. Asthma and atopy in overweight children. *Thorax* 2003; 58: 1031–5.
23. von Mutius E, Schwartz J, Neas LM, Dockery D, Weiss ST. Relation of body mass index to asthma and atopy in children: the National Health and Nutrition Examination Study III. *Thorax* 2001; 56: 835–8.
24. Matricardi PM, Gruber C, Wahn U, Lau S. The asthma-obesity link in childhood: open questions, complex evidence, a few answers only. *Clin Exp Allergy* 2007; 37: 476–84.
25. Wang WH, Chen PC, Hsieh WS, Lee YL. Joint effects of birth outcomes and childhood body mass index on respiratory symptoms. *Eur Respir J* 2012; 39: 1213–9.
26. Sonnenschein-van der Voort AM, Jaddoe VW, Raat H, Moll HA, Hofman A, de Jongste JC, et al. Fetal and infant growth and asthma symptoms in preschool children: the Generation R Study. *Am J Respir Crit Care Med* 2012; 185: 731–7.
27. Van Cauwenberghe J, Delvaux I, Michels N, Den Hond E, Schoeters G, Nelen V, et al. Validity of parentally reported versus measured weight, length and waist in 7- to 9-year-old children for use in follow-up studies. *Eur J Pediatr* 2014; 173: 921–8.
28. 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.
29. Werner B, Bodin L. Growth from birth to age 19 for children in Sweden born in 1981: descriptive values. *Acta Paediatr* 2006; 95: 600–13.
30. Bjerg A, Hedman L, Perzanowski M, Wennergren G, Lundbäck B, Rönmark E. Decreased importance of environmental risk factors for childhood asthma from 1996 to 2006. *Clin Exp Allergy* 2015; 45: 146–53.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Characteristics of the study population.
Table S2. Age- and gender-adjusted values for a high BMI, *i.e* 85th percentile, at 1 and 8 years of age.

