

REGULAR ARTICLE

# No association between overweight and asthma or allergy in adolescence after wheezing in infancy

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## ABSTRACT

**Aims:** The aim of the study was to evaluate the association between weight status and asthma, allergy and respiratory symptoms in adolescents with bronchiolitis in infancy.

**Subjects and methods:** At age 15–18 years, a questionnaire was sent to 96 study subjects hospitalized for wheezing at age <24 months and followed up subsequently. Sixty-seven (70%) of them answered. Weight and height data for body mass index (BMI) calculation were available in 60 (63%) cases. Asthma, allergy, respiratory symptoms and the use of asthma medication were compared between overweight or obese and normal weight groups constructed by age- and sex-specific BMI standard deviation scores (BMI-SDS). Population controls matched for sex, and birth month and place, were recruited for this study phase at age 15–18 years.

**Results:** Eleven (18.3%) study subjects were overweight (BMI-SDS >0.78 in males and >1.16 in females) and only 3 (5.0%) were obese (BMI-SDS >1.70 in males and >2.10 in females) at 16.5 (median) years of age. Overweight or obesity had no significant association with doctor-diagnosed or self-reported asthma, allergy or the use of inhaled corticosteroids. The negative results were confirmed by adjusted analyses.

**Conclusion:** Weight status had no association with asthma or allergy in adolescence after wheezing in infancy.

## INTRODUCTION

Epidemiological studies have shown that overweight and obesity have increased concomitantly with the increase of asthma and allergy in industrialized countries (1). Excessive weight gain has been associated with respiratory symptoms, asthma diagnoses and decreased lung function but not necessarily with bronchial hyper-reactivity (2,3). In young adults, there was increasing asthma prevalence by increasing body mass index (BMI) (4), and some authors have identified obese asthma as a new, separate asthma phenotype (5). A recent meta-analysis and epidemiological study found evidence for an association between emerging overweight and subsequent onset of asthma in children (2,6).

The association between weight status and allergy is less studied. Many authors have failed to confirm the association between overweight and allergic diseases or atopic sensitization (7,8) or opposite to the expectations, and underweight has been associated with atopic sensitization (9) and allergic rhinitis (10) at school age. However, overweight has been associated with atopic dermatitis (10,11) and food allergy in teenagers (12). In some studies, the association between excessive weight gain and allergy has been gender dependent, presenting only in girls and young women (4,11).

We have prospectively followed up a group of children treated in hospital for bronchiolitis at <24 months of age. Asthma was present in 32/81 (39.5%) study subjects at median age of 12.3 years (13). When the former bronchiolitis patients were 15–18 years of age, we carried out a questionnaire study to evaluate their asthma and allergy status, compared to population controls. Doctor-diagnosed asthma was present in 20/67 (29.9%) (self-reported asthma in 43, 64.2%) of the former bronchiolitis patients and in 8/155 (5.2%) (self-reported asthma in 17, 11.0%) of the population controls (14).

The weight and height were asked in the posted questionnaire at the age of 15–18 years allowing the calculation of the body mass index (BMI) and age- and sex-specific

## Key notes

In a postbronchiolitis cohort, overweight or obesity had no association with

- Doctor-diagnosed or self-reported asthma.
- The use of inhaled steroids as maintenance medication for asthma.
- Allergy symptoms in adolescence.

standard deviation scores (BMI-SDS) for both cases and controls.

The hypothesis of the study was that overweight or obesity may be associated with an increased asthma risk in adolescent after early-life wheezing. The aim of the present study was to evaluate the association between weight status and asthma and/or allergy in the former bronchiolitis patients at 15–18 years of age, compared with population controls.

## SUBJECTS AND METHODS

### Study design

One hundred children were hospitalized for wheezing and recruited into this follow-up study at one to 23 months of age in 1992–1993 in Kuopio University Hospital (Finland). They have been followed up at two immediate and three later clinical follow-up visits at the median ages of 4.0 (15), 7.2 (16) and 12.3 years (13).

The present study was carried out in 2008 when the study subjects were 16.5 (median) years of age (range 15.1–18.1). On average, the follow-up time from the hospitalization for wheezing in infancy was 15.6 years. The questionnaire was sent to 96 study subjects with current address available and 67 (70%) (45 males and 22 females) answered (14). The weight and height data were available from 60 of them.

For the present study, nonselected population-based controls, born like the study subject in the primary area of Kuopio University Hospital and matched for gender and birth month, were obtained by the ratio 4:1 for the cases from the Population Register Centre (Finland). The questionnaire was sent to 396 controls and 155 (39%) answered (14). The weight and height data were available from 152 of them.

### Questionnaire data

The questionnaire comprised questions on the presence of wheezing symptoms, prolonged (>4 weeks) cough apart from infection, repeated night cough apart from infection, the use of maintenance medication for asthma, the use of on-demand medication for asthma, the presence of skin, nose and eye symptoms suggestive for atopic dermatitis or allergic rhinitis and/or conjunctivitis, respectively (17). Nose and eye symptoms had to be seasonal, occurring in spring or summer time, to be accepted as allergic. Atopic dermatitis was regarded if the subjects reported itching eczema in typical areas. The reported daily consumption of at least one cigarette during the preceding 12 months was defined as current smoking (17). The presence of symptoms and the use of asthma medication were recorded only for the preceding 12 months. In addition, the attendants were asked to measure and record their actual weights and heights.

Allergic rhinitis was defined by the presence of seasonal nose symptoms and allergic conjunctivitis by the presence of seasonal eye symptoms, respectively. Allergic rhinoconjunctivitis was defined as the presence of either allergic rhinitis or conjunctivitis.

Bronchial asthma was defined by two different ways reflecting the degree of certainty of the diagnosis (1). Current doctor-diagnosed asthma: either asthma diagnosed by a doctor during the preceding 24 months or the use of maintenance medication for asthma during the preceding 12 months (2). Current self-reported asthma: either a weekly use of on-demanded bronchodilating drugs or asthma diagnosed by a doctor previously and the presence of wheezing symptoms, prolonged cough or repeated night cough during the preceding 12 months (current doctor-diagnosed asthma included by both criteria) (17).

Body mass index (BMI) was calculated by using the equation: weight (kg)/height (m)<sup>2</sup>. Age- and sex-specific BMI standard deviation score (BMI-SDS), also called Z score, was assessed for all study subjects and controls using the recently published population-based Finnish growth references (18). BMI-SDS >1.16 in females and >0.78 in males corresponds BMI >25 kg/m<sup>2</sup> in young adults and means overweight, and BMI-SDS >2.10 in females and >1.70 in males corresponds BMI >30 kg/m<sup>2</sup> in young adults and means obesity (18).

### Statistics

The data were analysed using the SPSS 14.0 statistical package (SPSS Inc., Chicago, IL, USA). Analysis of variance was used for continuous data, and Pearson's chi-square test and Fisher's exact test for discrete data.

Logistic regression, adjusted for age, sex, hospitalization for wheezing at <24 months of age, current smoking and current allergic rhinoconjunctivitis (or with current asthma, correspondingly), was used to analyse the association between weight status and asthma or allergy at 15–18 years of age in the combined group consisting of cases and controls.

### Ethics

This follow-up study was approved by the Ethics Committee of Kuopio University Kuopio University Hospital. The attendants accepted the use of the collected data by undersigning a specific permission form, posted with the study questionnaire.

## RESULTS

Weight and height data were available from 60 former bronchiolitis patients and from 152 population controls. Only three of the former bronchiolitis group were obese (BMI-SDS >2.11 in females and >1.70 in males), and 11 (18.3%) were overweight (BMI-SDS >1.16 in females and >0.78 in males). There were no significant differences between the groups in BMI-SDS or in the presence of overweight or obesity (Table 1). There were only four subjects (two in both groups, all males) who were underweight (BMI-SDS less than -1.83).

In the former bronchiolitis group, only 2 (14.3%) of the overweight subjects reported current wheezing symptoms vs. 20 (43.5%) in normal weight subjects ( $p = 0.047$ ). There were no other significant differences in respiratory or

**Table 1** Weight data expressed as body mass index in the 60 former bronchiolitis patients and 152 population-based controls at 15–18 years of age

| Weight status      | Bronchiolitis group N = 60 | Control group N = 152 | p-value <sup>#</sup> |
|--------------------|----------------------------|-----------------------|----------------------|
| BMI-SDS (mean, SD) | 0.15 (0.95)                | 0.22 (0.90)           | 0.47                 |
| Overweight         | 11 (18.3%)                 | 23 (14.8%)            | 0.42                 |
| Obesity            | 3 (5.0%)                   | 5 (3.2%)              | 0.33                 |

BMI, means body mass index; SDS, means standard deviation score.

Overweight: BMI-SDS >1.61 in females and >0.78 in males corresponding BMI >25 kg/m<sup>2</sup> in young adulthood (obesity included).

Obesity: BMI-SDS >2.10 in females and >1.70 in males corresponding BMI >30 kg/m<sup>2</sup> in young adulthood.

<sup>#</sup>Pearson chi-square test.

allergic symptoms or manifestations between the overweight and normal weight former bronchiolitis patients (Table 2). One of the three obese former bronchiolitis patients reported previous asthma, but no one had current wheezing symptoms or allergic rhinitis or conjunctivitis. The two underweight former bronchiolitis patients reported previous asthma, current wheezing symptoms and allergic rhinitis.

Current doctor-diagnosed asthma, current self-reported asthma and use of inhaled steroids were more common in normal weight former bronchiolitis patients than in population controls (Table 3). The figures were rather similar in normal weight and in overweight former bronchiolitis patients. Current rhinoconjunctivitis was more common in controls than in cases (Table 3).

Like in the postbronchiolitis study subjects, there were no significant associations between overweight or obesity and doctor-diagnosed asthma, self-reported asthma, use of asthma medication or presence of allergic rhinoconjunctivitis in the controls (data not shown).

**Table 2** Respiratory and allergic manifestations in relation to overweight in the 60 former bronchiolitis and in 152 population-based controls

| Manifestations          | Bronchiolitis group: normal weight N = 46 (%) | Bronchiolitis group: overweight <sup>†</sup> N = 14 (%) | p-value* | Control group N = 152 (%) |
|-------------------------|-----------------------------------------------|---------------------------------------------------------|----------|---------------------------|
| Wheezing symptoms       | 20 (43.5) <sup>1</sup>                        | 2 (14.3)                                                | 0.047    | 20 (13.2) <sup>1</sup>    |
| Prolonged cough         | 5 (10.9)                                      | –                                                       | 0.33     | 13 (8.6)                  |
| Night cough             | 4 (8.7)                                       | 1 (7.1)                                                 | 1.00     | 7 (4.6)                   |
| Previous asthma         | 30 (65.2) <sup>2</sup>                        | 9 (64.3) <sup>4</sup>                                   | 0.95     | 16 (10.5) <sup>2,4</sup>  |
| Allergic rhinitis       | 17 (37.0)                                     | 3 (21.4)                                                | 0.35     | 47 (30.9)                 |
| Allergic conjunctivitis | 9 (19.6)                                      | 4 (28.6)                                                | 0.47     | 38 (25.0)                 |
| Atopic dermatitis       | 10 (21.7)                                     | 5 (35.7)                                                | 0.29     | 32 (21.1)                 |
| Current smoking         | 14 (30.4) <sup>3</sup>                        | 1 (7.1)                                                 | 0.16     | 26 (17.1) <sup>3</sup>    |

<sup>†</sup>Overweight = BMI-SDS >1.16 in females and >0.78 in males corresponding BMI >25 kg/m<sup>2</sup> in young adulthood (obesity included).

\*p-values between normal weight and overweight in bronchiolitis group; Pearson chi-square test or Fisher's exact test.

Statistical significance between normal weight bronchiolitis group and control group: <sup>1</sup>p < 0.001, <sup>2</sup>p < 0.001, <sup>3</sup>p = 0.049, and overweight bronchiolitis group vs. control group: <sup>4</sup>p < 0.001.

Weight and height data were available from the control visit at 12–13 years of age for 57 of the 60 former bronchiolitis patients. Overweight or obesity at that age did not predict current asthma by either definition or allergic rhinoconjunctivitis (data not shown).

Since identical current questionnaire data were available from former bronchiolitis patients and population controls, we combined the cases and controls when evaluating the association between overweight and self-reported asthma or allergic rhinoconjunctivitis by logistic regression (Table 4). The result was negative; no significant associations were found in analyses adjusted for age, sex, group (case or control), smoking (yes, no) and allergic rhinoconjunctivitis (or self-reported asthma, respectively), first separately for each confounder (data not shown) and then including all confounders in the same model.

## DISCUSSION

There are two main, unquestionably negative results in the present study on the association between overweight or obesity and asthma or allergy in former bronchiolitis patients prospectively followed up from infancy to the median age of 16.5 years. First, the presence of doctor-diagnosed and self-reported asthma and the use of inhaled corticosteroids had no association with overweight or obesity in adolescence, though the prevalence of asthma differed between cases and controls. Second, no significant association was found between overweight or obesity and allergy by any definition. Against expectations, allergic rhinoconjunctivitis was even more common in controls. All main results were confirmed as negative by adjusted multivariate analyses.

Epidemiological studies have revealed an association between excessive weight gain and presenting or emerging asthma, at least when asthma has been assessed by symptom history or drug consumption (2,3,19). Even a dose–response relationship between increasing asthma occurrence with increasing BMI has been suggested in adults (4,20). In a meta-analysis, overweight (BMI >25 kg/m<sup>2</sup>) increased the risk of emerging asthma in mean to 1.5-fold and obesity (BMI >30 kg/m<sup>2</sup>) in mean to 1.9-fold (21). In addition, asthma has improved after weight loss, and this reversibility offers strong evidence that overweight may be a significant risk factor for asthma (22). The conflicting results obtained from epidemiological studies made in large population samples and from clinical asthma studies, like the present study, may be due to different statistical powers in the analyses. Our results were negative also in the combined analyses including both cases and controls, which were done to check the constancy of the results after increasing statistical power. In addition, asthma was by all definitions even more common in normal weight than in overweight study subjects, though statistical significance was not reached.

Most studies, independently from the design, have failed to reveal an association between overweight or obesity and allergic diseases or atopic sensitization (7,8), or opposite to

**Table 3** Asthma by different definitions in the former bronchiolitis patients and controls at 15–18 years of age

| Outcomes                        | Normal weight<br>N = 46 (%) | Over weight <sup>#</sup><br>N = 14 (%) | p-value* | Control group<br>N = 152 (%) |
|---------------------------------|-----------------------------|----------------------------------------|----------|------------------------------|
| Current doctor-diagnosed asthma | 16 (34.8) <sup>1</sup>      | 4 (28.6) <sup>5</sup>                  | 0.67     | 8 (5.3) <sup>1,5</sup>       |
| Current self-reported asthma    | 30 (65.2) <sup>2</sup>      | 9 (64.3) <sup>6</sup>                  | 0.95     | 17 (11.2) <sup>2,6</sup>     |
| Use of inhaled corticosteroids  | 16 (34.8) <sup>3</sup>      | 4 (28.6) <sup>7</sup>                  | 0.67     | 7 (4.6) <sup>3,7</sup>       |
| Current rhinoconjunctivitis     | 7 (15.2) <sup>4</sup>       | 3 (21.4)                               | 0.59     | 34 (22.4) <sup>4</sup>       |

For asthma definitions, see the text.

<sup>#</sup>Overweight = BMI-SDS >1.16/0.78; obesity = BMI-SDS >2.10/1.70.

\*p-values between normal weight and overweight in bronchiolitis group; Pearson chi-square test or Fisher's exact test.

Statistical significance between normal weight bronchiolitis group and control group: <sup>1</sup>p < 0.001, <sup>2</sup>p < 0.001, <sup>3</sup>p < 0.001, <sup>4</sup>p = 0.31, and between overweight bronchiolitis group and control group: <sup>5</sup>p = 0.001, <sup>6</sup>p < 0.001, <sup>7</sup>p = 0.008.

**Table 4** Logistic regression: self-reported asthma and allergic rhinoconjunctivitis at 15–18 years of age in relation to overweight in the combined group of cases and controls

| Weight status      | Current self-reported asthma at the age of 15–18 years |                                                    |               |
|--------------------|--------------------------------------------------------|----------------------------------------------------|---------------|
|                    | Yes<br>N = 56                                          | OR (95% CI)                                        | No<br>N = 156 |
| Overweight present | 10                                                     | 0.99 (0.46–2.12)*<br>0.76 (0.30–1.93) <sup>†</sup> | 24            |
| Weight status      | Current rhinoconjunctivitis at the age of 15–18 years  |                                                    |               |
|                    | Yes<br>N = 44                                          | OR (95% CI)                                        | No<br>N = 168 |
| Overweight present | 7                                                      | 0.72 (0.30–1.75)*<br>0.70 (0.28–1.73) <sup>‡</sup> | 35            |

OR, odds ratio; CI = 95%, confidence interval.

\*With no adjustments.

<sup>†</sup>Adjusted for sex, age, smoking (yes, no), allergic rhinoconjunctivitis (yes, no) and hospitalization for bronchiolitis in infancy (case, control).

<sup>‡</sup>Adjusted for sex, age, smoking (yes, no), self-reported asthma (yes, no) and hospitalization for bronchiolitis in infancy (case, control).

the expectations, underweight has merely been associated with atopic sensitization (9) or allergic rhinitis (11) at school age. In some studies, the association between excessive weight gain and allergy has been gender dependent, presenting only in girls at teenage and in young women (23,24). The present results were similarly negative for both females and males. In a Finnish study in 18- to 25-year-old young adults, the risk of asthma increased linearly by BMI in men but not in women, and the risk of allergic

rhinoconjunctivitis and atopic dermatitis increased linearly by BMI in women but not in men, which suggests different effects of body fat on asthma and on atopic disease (4).

Four years earlier, overweight was not associated with increased asthma risk (25) but was associated with reduced lung function (26) in this same postbronchiolitis cohort. Preliminary evidence was found that obesity may be associated with a decreased risk of atopic dermatitis and atopic sensitization to inhaled allergens (25). However, the results of the two phases of the study are not well comparable. The study 4 years earlier was a clinical study, the number of attending former bronchiolitis patients was 82, but no population controls were enrolled, and the national BMI-SDS references were not yet available. Therefore, British references were used instead. In addition, some children were prepubertal and some were at puberty (25). The present study is a questionnaire study, the study subjects had passed puberty, and population controls and population-based national BMI-SDS references were available. The number former bronchiolitis patients with weight and height data available at both occasions has decreased to 57, and overweight or obesity 4 years earlier did not predict current asthma by any definition. The new, less strict national BMI references allow more weight gain than the international references; accordingly, the number of children assessed as overweight has decreased from 33.3% to 18.3%, and only 5% were now assessed as obese. Previous or current overweight does not increase asthma or allergy risk of former bronchiolitis patients at the mean age of 16.5 years, as was seen also at the median ages of 7.3 and 12.3 years (25).

The negative results of the present study must be interpreted with caution. Due to the small number of former bronchiolitis patients and the rarity of asthma in controls, the study may be under-powered to find some true but small differences between overweight and normal weight children. The high dropout rates, 37.5% in cases and 61% in controls invited to the study, may bias the results. On the other hand, the rate of doctor-diagnosed asthma in the controls (5.3%) was nearly identical to the rate of self-reported doctor-diagnosed asthma (3–5%) in the population (27). There may be a risk of understating the weight in questionnaire studies, but in a validation study, self-reported weight and height correlated well with measured weight and height (28). One reason for the negative results of the study may be the highly selected study group, that is, subjects hospitalized for severe wheezing in early life. In them, overweight and obesity may be a less important risk factor than, for example, heredity, viral disease or smoke exposure in early childhood.

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Saari MD provided the population-based weight and height data and participated in data analysis and interpretation of the results. Eija Piippo-Savolainen MD PhD participated in study planning, data collection and writing. Prof Matti Korppi supervised the study, contributing to the analytical framework and to writing the manuscript.

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## CONFLICT OF INTEREST

The authors do not have any conflict of interests or any financial relationship with a commercial entity that has an interest in the subjects of this manuscript.

## References

1. Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005; 115: 897–909.
2. Flaherman V, Rutherford GW. A meta-analysis of the effect of high weight on asthma. *Arch Dis Child* 2006; 91: 334–9.
3. Noal RB, Menezes AMB, Macedo SEC, Dumith SC. Childhood body mass index and risk of asthma in adolescence: a systematic review. *Obesity Rev* 2011; 12: 93–104.
4. Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M. Body mass index and physical activity in relation to asthma and atopic diseases in young adults. *Respir Med* 2006; 100: 1518–25.
5. Lugogo NL, Kraft M, Dixon AE. Does obesity produce a distinct asthma phenotype? *J Appl Physiol* 2010; 108: 729–34.
6. Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Siega-Riz A, 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.
7. Jarvis D, Chinn S, Potts J, Burney P. Association of body mass index with respiratory symptoms and atopy: results from the European Community Respiratory Health Survey. *Clin Exp Allergy* 2002; 32: 831–7.
8. Ma J, Xiao L, Knowles SB. Obesity, insulin resistance and the prevalence of atopy and asthma in US adults. *Allergy* 2010; 65: 1455–63.
9. Van Gysel D, Govaere E, Verhamme K, Doli E, De Baets F. Body mass index in Belgian schoolchildren and its relationship with sensitization and allergic symptoms. *Pediatr Allergy Immunol* 2009; 20: 246–53.
10. Silverberg JL, Kleiman E, Lev-Tov H, Silverberg NB, Durkin HG, Joks R, et al. Association between obesity and atopic dermatitis in childhood: a case-control study. *J Allergy Clin Immunol* 2011; 127: 1180–6.
11. Kusunoki T, Morimoto T, Nishikomori R, Heike T, Ito M, Hosoi S, et al. Obesity and the prevalence of allergic diseases in schoolchildren. *Pediatr Allergy Immunol* 2008; 19: 527–34.
12. Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Siega-Riz A, et al. Association of obesity with IgE levels and allergy symptoms in children and adolescents: results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol* 2009; 123: 1163–9.
13. Hyvärinen MK, Kotaniemi-Syrjänen A, Reijonen TM, Korhonen K, Korppi MO. Teenage asthma after severe early childhood wheezing: an 11-year prospective follow-up. *Pediatr Pulmonol* 2005; 40: 316–23.
14. Ruotsalainen M, Sidoroff V, Piippo-Savolainen E, Hyvärinen M, Korppi M. Adolescent asthma is more common after rhinovirus than respiratory syncytial virus bronchiolitis. *Pediatr Pulmonol* doi: 10.1002/ppul.22692. [Epub ahead of print].
15. Reijonen TM, Kotaniemi-Syrjänen A, Korhonen K, Korppi M. Predictors of asthma three years after hospital admission for wheezing in infancy. *Pediatrics* 2000; 106: 1406–12.
16. Kotaniemi-Syrjänen A, Reijonen TM, Korhonen K, Korppi M. Wheezing requiring hospitalization in early childhood: predictive factors for asthma in a six-year follow-up. *Pediatr Allergy Immunol* 2002; 13: 418–25.
17. Ruotsalainen M, Piippo-Savolainen E, Hyvärinen MK, Korppi M. Adulthood asthma after wheezing in infancy: a questionnaire study at 27 years of age. *Allergy* 2010; 65: 503–9.
18. Saari A, Sankilampi U, Hannila M, Kiviniemi V, Kesseli K, Dunkel L. New Finnish growth references for children and adolescents aged 0 to 20 years: length/height-for-age, weight-for-length/height, and body mass index-for-age. *Ann Med* 2011; 43: 235–48.
19. Beuther DA. Recent insight into obesity and asthma. *Curr Opin Pulmon Med* 2010; 16: 64–70.
20. Coogan PF, Palmer JR, O'Connor GT, Rosenberg L. Body mass index and asthma incidence in the Black Women's Health Study. *J Allergy Clin Immunol* 2009; 123: 89–95.
21. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007; 175: 661–6.
22. Eneli IU, Skybo T, Camargo CA. Weight loss and asthma: a systematic review. *Thorax* 2008; 63: 671–6.
23. Schachter LM, Peat JK, Salome CM. Asthma and atopy in overweight children. *Thorax* 2003; 58: 1031–5.
24. Hancox RJ, Milne BJ, Poulton R, Taylor DR, Greene JM, McLachlan CR, et al. Sex differences in the relation between body mass index and asthma and atopy in a birth cohort. *Am J Respir Crit Care Med* 2005; 171: 440–5.
25. Sidoroff V, Hyvärinen MK, Piippo-Savolainen E, Korppi M. Overweight does not increase asthma risk but may decrease allergy risk at school age after infantile bronchiolitis. *Acta Paediatr* 2012; 46: 435–41.
26. Sidoroff V, Hyvärinen MK, Piippo-Savolainen E, Korppi M. Lung function and overweight in school aged children after early childhood wheezing. *Pediatr Pulmonol* 2011; 46: 435–41.
27. Huurre TM, Aro HM, Jaakkola JJ. Incidence and prevalence of asthma and allergic rhinitis. a cohort study in Finnish adolescents. *J Asthma* 2004; 41: 311–7.
28. Hu FB, Willet WC, Li T, Stampfer MJ, Colditz G, Manson JE. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med* 2004; 351: 2694–703.