

## Association between overweight and asthma or allergy: Results from a prospective 27-year post-bronchiolitis follow-up.

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### Abstract

The aim of the study was to evaluate the association between weight status and asthma, allergy and respiratory symptoms in young adults with bronchiolitis in infancy. At age 26-29 years, a questionnaire was sent to 78 study subjects hospitalized for bronchiolitis at age <24 months, and 59(76%) of them answered. Asthma, allergy and respiratory symptoms were compared between overweight or obese and normal weight groups constructed by body mass index (BMI). Corresponding data were available from the follow-up visit at age 18-20 years. Population controls matched for sex and birth month and place were recruited for this 26-29 years study. Thirty-two study subjects (54.4%) were overweight (BMI >25 kg/m<sup>2</sup>) and 8(13.6%) obese (BMI >30 kg/m<sup>2</sup>) at age 26-29 years. Overweight was present in 21/52 study subjects (40.4%) at age 18-20 years. Overweight or obesity had no association with doctor-diagnosed or self-reported asthma or allergy, or the use of inhaled corticosteroids, at either age. The negative results were confirmed by adjusted analyses at age 26-29 years. Overweight or obesity at age 18-20 years did not predict asthma 8 years later. Overweight or obesity had no association with asthma or allergy in young adults hospitalized for bronchiolitis in infancy.

**Keywords:** Adulthood, asthma, bronchiolitis, obesity, overweight

Accepted May 07 2012

### Introduction

The prevalence of overweight and obesity among children and young adults has increased like an epidemic in western countries concomitantly with the asthma and allergy epidemics [1, 2]. Epidemiological studies have shown a modest association between overweight or obesity and prevalent or incident asthma in adults [1, 3] but the studies in children have given conflicting results [2, 4-8]. In a recent meta-analysis pooling adult studies, overweight (body mass index, BMI >25 kg/m<sup>2</sup>) carried in mean a 1.5-fold risk and obesity (BMI >30 kg/m<sup>2</sup>) a 1.9-fold risk for incident asthma within a year [9].

There may even be a dose-response relationship of increasing asthma prevalence with increasing BMI [10], and obese asthma has been suggested as a new phenotype of adult asthma [11].

We have prospectively followed a group of children hospitalized for bronchiolitis at <24 months of age. The prevalence of doctor-diagnosed asthma was 30% (self-reported asthma 41%) when the study subjects were 18-

20 years old [12]. When the study subjects were 26-29 years old, we carried out a questionnaire study to find out their asthma and allergy status, compared with population controls. Doctor-diagnosed asthma was present in 20% (self-reported in 41%) of the former bronchiolitis patients and in 5% (10%) of the population controls [13].

The weights and heights were measured at the control visit at 18-20 years of age and were asked in the posted questionnaire at 26-29 years of age, allowing the calculation of BMI at both ages. Weight and height data were available from the population controls at 26-29 years of age.

The aim of the present study was to evaluate the association between weight status and asthma and allergy in the former bronchiolitis patients at 18-20 and 26-29 years of ages.

### Materials and methods

#### Design

Eighty-three children were hospitalized for bronchiolitis at <24 months of age during a 12-month study period in

1981-1982 at Kuopio University Hospital (Finland) [14, 15]. The diagnostic criteria were the presence of respiratory infection and expiratory wheezing and/or prolonged expiration. Subsequent follow-up visits have been organized regularly, including a clinical study in 2000 when the former bronchiolitis patients were 18-20 years old [12].

The present study was carried out in 2008 when the study subjects were 26-29 years old. A questionnaire was sent to 78 former bronchiolitis patients with the current address available, and 59(76%) of them answered [13].

For this study, population controls, matched for sex, birth month and birth place, were obtained by a 4:1 ratio from the Population Register Centre (Finland). A questionnaire was sent to 328 subjects and 121(37%) answered. None had been hospitalized for wheezing or other respiratory symptoms at <24 months of age. From them, a control group of 105 subjects (60 females; 2 controls for each case, and all 61 males who answered; 1.65 controls for the cases) was constructed, as described recently [13].

#### **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 symptoms suggestive for atopic dermatitis, and the presence of seasonal nose and/or eye symptoms suggestive for allergic rhinitis and/or conjunctivitis, respectively [13]. Doctor-diagnosed asthma and the time when asthma diagnosis was done (during preceding 12 months, during preceding 24 months or ever in life) were specifically asked. The presence of symptoms and the use of asthma medication were recorded only for the preceding 12 months. The reported daily consumption of at least one cigarette during the preceding 12 months was defined as current smoking [13]. In addition, the attendants were asked to measure and record their actual weights and heights.

#### **Definition of asthma and allergy**

Bronchial asthma was defined by two different ways reflecting the degree of certainty of the diagnosis, as published previously [13].

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-demand bronchodilators during the preceding 12 months, or asthma diagnosed by a doctor previously and the presence of wheezing symptoms, pro-

longed cough or repeated night cough during the preceding 12 months (current doctor-diagnosed asthma included by both criteria).

Nose and eye symptoms which occurred apart from infection during spring or summer seasons were accepted as allergic [13]. Atopic dermatitis was regarded if the subjects reported itching dermatitis in typical areas [13].

#### **Definition of weight status**

BMI was calculated by the equation (weight in kg / the square of height in meters). Overweight was defined as BMI >25 kg/m<sup>2</sup> and obesity as BMI > 30 kg/m<sup>2</sup> [16].

#### **Statistics**

The data were analyzed using the SPSS 14.0 statistical package (SPSS Inc., Chicago, IL, USA). Analysis of variance was used for continuous variables, and Pearson's Chi square test or Fisher's exact test for discrete variables. Logistic regression, adjusted for age, sex, smoking, group (case, control) and allergic rhinoconjunctivitis (or self-reported asthma), was used to analyze the association between weight status and asthma (or allergic rhinoconjunctivitis, respectively) at 26-29 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 and Kuopio University Hospital. The participants accepted the use of the collected data by undersigning a specific permission form posted with the study questionnaire.

#### **Results**

The mean BMI of the former bronchiolitis patients was 25.95 kg/m<sup>2</sup> at 26-29 years of age; 54.4% were overweight (BMI >25 kg/m<sup>2</sup>) and 13.6% were obese (BMI >30 kg/m<sup>2</sup>). The figures were 24.17 kg/m<sup>2</sup>, 37.2% and 11.1% at 18-20 years of age, respectively. There were no significant differences in BMIs between the study subjects and controls at 26-29 years of age, or between the measurements at 26-29 and 18-20 years of ages in the study subjects (Table 1).

There were no significant differences between overweight and normal weight former bronchiolitis patients in respiratory symptoms or allergic manifestations at 26-29 years of age (Table 2) or eight years earlier at 18-20 years of age (Data not shown). The results remained negative at both ages, when obese children were compared with normal weight children (Data not shown). Surprisingly, current smoking was more common in former bronchiolitis patients than in controls, again with no significant difference between overweight and normal weight subjects (Table 2). As expected, previous asthma and current whe-

**Table 1.** Weight data expressed as body mass index in the study subjects at 18-20 and 26-29 years of age, and in population controls at 26-29 years of age

Body mass index (kg/m <sup>2</sup> )	Former bronchiolitis group at 26-29 years of age N=5	Control group <sup>A</sup> at 26-29 years of age N=105	P value <sup>B</sup>	Former bronchiolitis group at 18-20 years of age N=54	P value <sup>C</sup>
Body mass index (mean, SD)	25.95 (4.41)	25.51(5.12)	0.22	24.17 (5.12)	0.25
Body mass index >25	32 (54.4%)	42 (40.4%)	0.07	20 (37.0%)	0.35
Body mass index >30	8 (13.6%)	17(16.2%)	0.50	6 (11.1%)	0.58

<sup>A</sup> population controls collected for the study at 26-29 years of age

<sup>B</sup> between bronchiolitis and control groups

<sup>C</sup> between measurements at 26-29 and 18-20 years of ages in the bronchiolitis group

**Table 2.** Respiratory and allergic manifestations in relation to overweight in the 58 former bronchiolitis patients at 26-29 years of age and in 105 population controls

Manifestations	Former bronchiolitis group: Normal weight N=26	Former bronchiolitis group: Overweight <sup>A</sup> N=32	P value <sup>B</sup>	Control group N= 105
Wheezing symptoms	14 (53.8%) <sup>1</sup>	11 (34.4%)	0.14	22 (20.9%) <sup>1</sup>
Prolonged cough	1 (3.8%)	5 (15.6%)	0.14	6 (5.7%)
Night cough	2 (7.7%)	3 (9.4%)	0.82	6 (5.7%)
Previous asthma	16/25 (61.5%) <sup>2</sup>	16 (50%) <sup>3</sup>	0.29	6 (5.7%) <sup>2,3</sup>
Allergic rhinitis	14 (53.8%)	14 (43.8%)	0.44	45/104 (42.9%)
Allergic conjunctivitis	10 (38.5%)	18 (56.3%)	0.18	38 (36.2%)
Atopic dermatitis	4 (15.4%)	8 (25%)	0.37	18 (17.1%)
Current smoking	11 (42.3%) <sup>4</sup>	12 (37.5%) <sup>5</sup>	0.71	18 (17.1%) <sup>4,5</sup>

Overweight = BMI >25 kg/m<sup>2</sup>; obesity = BMI >30 kg/m<sup>2</sup>

<sup>A</sup> obesity included

<sup>B</sup> between normal weight and overweight subjects in bronchiolitis group

Normal weight bronchiolitis group vs. control group: <sup>1</sup>p=0.001, <sup>2</sup>p<0.001, <sup>4</sup>p=0.006; and overweight bronchiolitis group vs. control group: <sup>3</sup>p<0.001, <sup>5</sup>p=0.015

**Table 3.** Outcome of the former bronchiolitis patients at 26-29 years of age in relation to weight status

Outcomes	Normal weight N=26	Overweight N=32	P value	Control group N=105
Current doctor-diagnosed asthma	8 (30.8%) <sup>1</sup>	4/31(12.5%)	0.10	5/104 (4.8%) <sup>1</sup>
Current self-reported asthma	13 (50%) <sup>2</sup>	11 (34.4%) <sup>3</sup>	0.23	7/104 (6.7%) <sup>2,3</sup>
Use of inhaled corticosteroids	6 (23.1%) <sup>4</sup>	3 (9.4%)	0.15	4/104 (3.8%) <sup>4</sup>
Current rhinoconjunctivitis	15 (57.7%)	20 (62.5%)	0.71	47/104 (44.8%)

Overweight = BMI >25 kg/m<sup>2</sup>; obesity = BMI >30 kg/m<sup>2</sup>

Normal weight bronchiolitis group vs. control group: <sup>1</sup>p<0.001, <sup>2</sup>p<0.001, <sup>4</sup>p=0.001; and overweight bronchiolitis group vs. control group: <sup>3</sup>p<0.001

**Table 4.** Logistic regression: Self-reported asthma at 26-29 years of age in relation to overweight and obesity in the combined group of cases and controls

Body mass index (kg/m <sup>2</sup> )	Self-reported asthma at the age of 26-29 years		
	Yes N=31	OR (95%CI)	No N=132
BMI > 25	14	0.91 (0.41-2.03) <sup>1</sup> 0.54 (0.21-1.40) <sup>2</sup>	60
BMI > 30	7	1.85 (0.69-4.96) <sup>1</sup> 2.03 (0.61-6.78) <sup>2</sup>	18

OR=odds ratio, CI=95% confidence interval

<sup>1</sup> adjusted for sex and age (continuous).

<sup>3</sup> adjusted for sex, age group (case, control), smoking (yes, no) and rhinoconjunctivitis (yes, no).

ezing symptoms were more common in former bronchiolitis patients than in controls (Table 2).

Overweight had no significant association with doctor-diagnosed asthma, self-reported asthma or the use of inhaled corticosteroids in the former bronchiolitis patients at 26-29 years of age (Table 3). The result remained negative when obese subjects were compared with normal weight subjects (Data not shown). As expected, asthma by all definitions was more common in the former bronchiolitis patients than in controls; however, in overweight study subjects the difference was significant only for self-reported asthma (Table 3).

Overweight had no significant association with doctor-diagnosed asthma, self-reported-asthma or the use of inhaled corticosteroids at 18-20 years of age (Data not shown). Overweight or obesity at 18-20 years of age did not predict asthma at 26-29 years of age (Data not shown).

Since identical data on current disease modifying and/or confounding factors were available from former bronchiolitis patients and controls at 26-29 years of age, we combined cases and controls and evaluated the association of overweight and/or obesity with self-reported asthma and allergic rhinoconjunctivitis by logistic regression (Table 4). No significant associations were found in analyses adjusted for age, sex, smoking, group (case, control) and allergic rhinoconjunctivitis (Table 4), or correspondingly, adjusted for age, sex, smoking, group (case, control) and asthma (Data not shown). Similar analyses were done also for doctor-diagnosed asthma, and no significant associations were found (Data not shown).

## Discussion

There are two main, clearly negative results in the present study. First, the presence of doctor-diagnosed asthma or self-reported asthma, and the use of inhaled corticosteroids had no association with overweight or obesity in young adults who had been hospitalized for bronchiolitis in infancy. In addition, overweight or obesity at age 18-20

years had no association with asthma or allergy at age 26-29 years. Second, no significant association was found between weight status and atopic dermatitis, allergic rhinitis or allergic conjunctivitis. The results were similar at both 18-20 and 26-29 years of ages.

Epidemiological studies have confirmed that there is a significant association between overweight and prevalent or incident asthma in adults, but the effect is only modest [17]. In a recent meta-analysis, overweight (BMI >25 kg/m<sup>2</sup>) increased the risk of asthma on average to 1.5-fold and obesity (BMI >30 kg/m<sup>2</sup>) on average to 1.9-fold [9]. In some studies, asthma has markedly improved after weight loss, and this reversibility offers strong evidence that overweight is a risk factor for asthma [17, 18]. The role of overweight in allergy is less clear. Atopic sensitization has been connected with marked obesity [19], but allergic rhinitis and allergic asthma merely with underweight [20].

In a Finnish prospective cohort study including children and adults, asthma was associated with increasing BMI and prior excessive weight gain, but not earlier than at 24-39 years of age [21]. In the present study, overweight at 18-20 years of age was not associated with an increased asthma risk at 26-29 years of age. Our study subjects were just at the lower level of the observed age window [21], and the association between overweight and asthma may appear later. In the Finnish cohort study, no association was found between obesity-related biomarkers and asthma or allergy [21].

Over half of the former bronchiolitis patients were overweight (BMI >25 kg/m<sup>2</sup>), and 13.6% were obese (BMI >30 kg/m<sup>2</sup>). The figures were nearly identical with those in population controls and in line with available population data from Finland. In 2007, BMI was >25 kg/m<sup>2</sup> in 50.3% of males and in 34.2% of females aged 25-34 years [22]. In our later post-bronchiolitis cohort, previous or current overweight or obesity did not increase the risk of asthma or bronchial hyper-responsiveness at 12.3 years of age [23] but was associated with reduced lung function [24]. In addition, preliminary evidence was found that

obesity may decrease the risk of allergy [23]. The increases in BMI may have been too small to induce significant overweight-related effects in both our cohorts.

As expected, asthma and respiratory symptoms were, irrespective of the current weight status, more common in the former bronchiolitis patients than in controls. Surprisingly, as many as 40% of the former bronchiolitis patients smoked, and smoking was significantly more common than in controls. The figure was 30% eight years earlier at age 18-20 years [12]. According to a recent Finnish study, 26% of men and 17% of women smoke daily [25], which is in line with the controls of the present study.

The main shortcoming of the present study is the small number of study subjects. There were only 5-7 asthma patients among the controls, which on the other hand, is in agreement with the 6% asthma frequency in young Finnish adults [26]. Though asthma was common due to the selected material consisting of former bronchiolitis patients, the study obviously was underpowered to find all existing differences. Unexpectedly, asthma by all definitions and at both ages was even more common in normal weight than in overweight subjects. Thus, the low statistical power of the study is not the main reason for the negative results. The data at 26-29 years of age, including the weight and height data, were collected only by the posted questionnaire. However, self-reported weight and height correlated well with measured height and weight in a validation study [27], in line with many other studies [17].

The main strength of the present study is the long prospective follow-up from infancy to the median age of 27 years. In fact, this study is the longest prospective post-bronchiolitis follow-up thus far published. The definitions of asthma were rather strict, and the diagnosis was never based on respiratory symptoms alone, which are known to be non-specific especially in obese patients [28] and in smokers [29]. Recent observations have suggested that asthma is not over-diagnosed more often in obese than in non-obese patients. Among 540 adults with doctor-diagnosed asthma, the diagnosis could be confirmed by serial lung function measurements and bronchial challenges in 68% obese and in 71% non-obese subjects [30].

In conclusion, overweight or obesity had no association with doctor-diagnosed or self-reported asthma or allergy at 18-20 or 26-29 years of age in study subjects hospitalized for bronchiolitis in infancy and prospectively followed thereafter.

### **Acknowledgements**

The authors are grateful to Anneli Paloranta, RN, for her skillful work during the study.

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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.

**Funding:** Kuopio University Hospital (EVO grant, code 440071), The National Foundation for Pediatric Research in Finland, The National Graduate School of Clinical Investigation in Finland and The Kerttu and Kalle Viik's Foundation.