Increased prevalence of pre-school wheeze is not explained by time trends in body mass index

To the Editor:

Overweight and obesity have been associated with asthma, particularly in adults [1–4]. In children, findings are less consistent [2, 5–7]. Different mechanisms have been proposed to explain this association, including lung mechanics, systemic inflammation and associated comorbidities [1, 2, 8]. In a previous study, we showed that the prevalence of pre-school wheeze doubled in two cohorts in Leicestershire, UK, born 8 years apart [9]. This increase could not be attributed to differences in environmental exposures, socioeconomic status or vaccination status [9, 10]. Because body mass index (BMI) is increasing across the globe [2], we hypothesised that BMI played a role. We therefore sought to determine whether higher BMI in the second cohort could explain the increase in prevalence of pre-school wheezing and asthma.

Our data come from the Leicester Respiratory Cohorts, two population-based random samples of children living in Leicestershire [11]. Cohort 1 included children born in 1985–1989; cohort 2 included children born in 1993–1997. At the time the first respiratory questionnaire was administered (1990 and 1998), children were 1–4 years old. An identical study protocol was followed for both cohorts [11]. Parents completed a postal questionnaire that asked for detailed information on respiratory symptoms and environmental exposures. Routine data, including demographic and ethnic information, and data on growth and immunisations, were available from the Leicestershire Health Authority Database. Height and weight had been measured and recorded independently by health visitors. We used the measurements made closest to the date of the questionnaire for analyses. The Leicestershire Health Authority Research Ethics Committee (Leicester, UK) approved the study.

We included white pre-school children aged 1–4.99 years, with completed questionnaires and at least one valid measurement of height and weight (table 1) [9, 11]. BMI was calculated from growth measurements, as weight in kilograms divided by height in meters squared. We used z-scores from the World Health Organization (WHO) growth standards as reference values for BMI [12]. We also computed BMI categories (underweight, normal weight, overweight and obese) from WHO [12] to investigate whether outcomes were associated with extreme values (overweight, obese and underweight) rather than a linear trend.

Main outcomes were prevalence of current wheeze (previous 12 months) and doctor-diagnosed asthma. Secondary outcomes were frequent wheeze (three or more episodes in previous 12 months), multiple-trigger wheeze and hospital admission for wheeze (ever in life).

We calculated odds ratios for time trends (1998 versus 1990) in current wheeze and doctor-diagnosed asthma with multivariable logistic regression, with and without adjusting for BMI z-scores and BMI categories. We repeated the unadjusted analysis, comparing children with and without valid BMI measurements to check for systematic differences between the groups. Sensitivity analyses were performed for the secondary outcomes. We controlled for various potential confounding factors (sex, age, pets, pre-and post-natal exposure to smoke, gas cooking, attending nursery care, parental education, and crowding).

In total, we posted 1650 questionnaires to cohort 1, of which 1422 (86%) were returned. We posted 2522 questionnaires to cohort 2, of which 2127 (84%) were returned. For the analysis, we excluded data from children aged less than 1 and more than 5 years, leaving 1136 children in cohort 1 and 2084 children in cohort 2. In cohort 1, 978 children, and in cohort 2, 1819 children had valid measurements for height and weight.

Between 1990 and 1998, mean BMI z-scores increased from -0.693 (95% CI -0.143–0.004) to 0.104 (95% CI 0.052–0.156) (p<0.001) (table 1). In the same period, prevalence of current wheeze rose from 11.9% to 26.3% and doctor-diagnosed asthma rose from 11.0% to 18.6% (both p<0.001) (table 1). Prevalence of secondary outcomes also increased (table 1).

In cohort 1 (1990), there was no association between current wheeze or doctor-diagnosed asthma and BMI z-score (p=0.297 and p=0.443, respectively) or BMI categories. In cohort 2 (1998), current wheeze and doctor-diagnosed asthma were associated with BMI z-scores; the odds ratio was 1.16 for wheeze (95% CI 1.05–1.27, p=0.002) and 1.13 for asthma (95% CI 1.02–1.25, p=0.025) per 1 z-score of BMI. When looking
at BMI categories, we found that compared to children of normal weight, obese children had odds ratios of 1.57 (95% CI 1.16–2.12, p = 0.003) for wheeze and 1.68 (95% CI 1.21–2.35, p = 0.002) for asthma. Overweight and underweight were not associated with these outcomes (p = 0.337 and p = 0.282 for current wheeze, and p = 0.994 and p = 0.815 for doctor-diagnosed asthma, respectively).

Last, we compared the prevalence of respiratory outcomes between 1990 and 1998. When we compared 1998 to 1990, the unadjusted odds ratios were 2.73 (95% CI 2.19–3.41) for current wheeze and 1.79 (95% CI 1.42–2.26) for doctor-diagnosed asthma (fig. 1). We repeated this analysis, comparing children with and without valid BMI measurements, with similar findings (data not shown). The results were unchanged when we adjusted for BMI z-scores (adjusted odds ratios were 2.68 (95% CI 2.15–3.35) for current wheeze and 1.77 (95% CI 1.40–2.24) for doctor-diagnosed asthma) and for BMI categories (fig. 1). Adjusting for other potential confounders also did not change the odds ratios. The results of sensitivity analyses for secondary outcomes were similar to primary outcomes (data available from the authors).

In summary, we found: 1) prevalence of reported wheeze and doctor-diagnosed asthma in preschool children increased significantly between 1990 and 1998, and BMI rose over the same period; 2) BMI and respiratory outcomes were associated in the more recent cohort but not in the earlier one; and 3) no evidence that increased BMI explains the marked increase in wheeze and asthma prevalence over this 8-year period.

### TABLE 1 Demographic data, body mass index (BMI) and respiratory morbidity in the two cohorts

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects n</td>
<td>978</td>
</tr>
<tr>
<td>Year of questionnaire survey</td>
<td>1990</td>
</tr>
<tr>
<td>Age years</td>
<td>2.99 [2.92–3.06]</td>
</tr>
<tr>
<td>Males</td>
<td>50.6 [49.5] [47.5–53.8]</td>
</tr>
<tr>
<td>BMI z-scores</td>
<td>-0.69 [0.143–0.004]</td>
</tr>
<tr>
<td>Current wheeze</td>
<td>11.9 [116] [9.9–13.9]</td>
</tr>
<tr>
<td>Doctor-diagnosed asthma</td>
<td>11.0 [108] [9.1–13.0]</td>
</tr>
<tr>
<td>Frequent wheeze</td>
<td>6.1 [60] [4.6–7.6]</td>
</tr>
<tr>
<td>Multiple-trigger wheeze</td>
<td>5.1 [50] [3.7–6.5]</td>
</tr>
<tr>
<td>Hospital admission for wheeze</td>
<td>3.4 [33] [2.2–4.5]</td>
</tr>
</tbody>
</table>

Data are presented as mean [95% CI] or % [n] [95% CI], unless otherwise stated. #: three or more episodes in the previous 12 months; †: wheezing occurring also between episodes of respiratory infections.

![ FIGURE 1 Odds ratios and 95% confidence intervals describing the trend of respiratory outcomes (1998 versus 1990) unadjusted, adjusted for body mass index (BMI) z-scores and adjusted for BMI categories.](image-url)
We believe this is the first study to examine the possibility that BMI explains time trends in wheezing illness in toddlers. Chinn and Rona [5] conducted a comparable study for schoolchildren with similar findings. They also found that BMI and asthma were associated in obese children only in the more recent cohort (1994) and not in the earlier cohort (1982). Also in their population, rising BMI did not explain trends in respiratory outcomes.

Most other studies examined the relationship between BMI and asthma in a single cohort only, and focused on older children or adults. Associations were not consistent in children and were found mainly for pre-adolescents [2, 6, 7]. In a birth cohort, Noal et al. [7] found that obesity and wheezing were associated in 11-year-olds but not in 15-year-olds. Guerra et al. [6] reported that obesity at age 11 years predicted persistence of wheeze and asthma during puberty.

Our study was strengthened by the use of identical methodology in both cohorts; cohort 2 had been designed to assess time trends [9]. We used objective measurements of weight and height, which were assessed independently from the outcomes. We were, however, limited by parent-reporting of respiratory outcomes. We lacked data on maternal adiposity, which has been associated with transient wheeze in the offspring and could be a confounder [13]. As with all questionnaire-based surveys, a non-response bias could have affected our results. However, our response rate was high (84–86%) so our sample remains highly representative. BMI could not be calculated in 13%, because measurements of height and weight had not been taken on the same date, but missingness was not associated with the outcome and can hardly have affected the results.

If BMI is associated with wheeze or asthma, the connection is recent, because it was only seen in our second cohort. This could possibly be explained by lifestyle factors that differ between obese children and children of normal weight, and have emerged only recently, such as differences in diet, exercise habits or time spent indoors. The lack of consistency in the relationship between BMI and wheeze over time, also observed by Chinn and Rona [5], makes a causal association less likely. Our data do not exclude, however, that the association between BMI and wheeze may be relevant for very obese children, or for adults and adolescents [7, 14]. Neither do they contradict an association of birth weight and weight gain during early childhood with childhood asthma, as found in a recent meta-analysis including data from the Leicester cohorts [15]. Finally, BMI might be associated with specific phenotypes of wheezing illness only. In summary, our study suggests that the generational increase in BMI does not explain the increasing prevalence of wheezing in Leicestershire pre-school children throughout the 1990s.

Generational increase in BMI cannot explain increasing prevalence of wheezing in preschool children in the 1990s http://ow.ly/xc0Yw

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References
1 Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. Am J Respir Crit Care Med 2006; 174: 112–119.
3 Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. Am J Respir Crit Care Med 2007; 175: 661–666.
5 Chinn S, Rona RJ. Can the increase in body mass index explain the rising trend in asthma in children? Thorax 2001; 56: 845–850.


Beuther DA. Recent insight into obesity and asthma. Curr Opin Pulm Med 2010; 16: 64–70.


