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# Joint effects of birth outcomes and childhood body mass index on respiratory symptoms

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**ABSTRACT: Thinness in infancy and higher childhood body mass index (BMI) are risk factors for poor respiratory health. However, few studies have examined the joint effects of birth outcomes and childhood BMI on the occurrence of respiratory symptoms.**

**A total of 78,011 Taiwanese middle-school children were investigated between 1995 and 1996 in a nationwide International Study of Asthma and Allergies in Childhood (ISAAC) survey, with standardised height/weight measurement. Their survey data was compared successfully with the birth registration dataset.**

**Childhood BMI was positively associated with all respiratory symptoms, with greater effects and significant risks associated with serious phenotypes in the video questionnaire. Children with a history of low birth weight (LBW), those who were born prematurely (pre-term), or those who were small for gestational age (SGA) were also more likely to have allergic respiratory symptoms. As birthweight and gestational age were not positively associated with childhood BMI, we proposed that LBW, pre-term birth and childhood BMI were independent factors for respiratory symptoms.**

**LBW, pre-term birth and childhood BMI are all independent risk factors for respiratory symptoms in children. Children with a history of LBW, pre-term birth or SGA and a higher current BMI might have larger respiratory burden.**

**KEYWORDS: Birthweight, body mass index, children, ISAAC questionnaire, small for gestational age**

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Childhood obesity is the most common metabolic disease in the world, and has increased in prevalence over several decades [1–3]. The prevalence and incidence of allergic respiratory symptoms in children are also steadily increasing worldwide [4–6], which has led to the hypothesis that the two epidemics are somehow related [2, 3, 7, 8]. Systematic immunological changes of pro-inflammatory cytokines, which could influence respiratory health, have been suggested as a possible mechanistic link between the two [9–14].

Birthweight is a recognised indicator of pre-natal growth, nutritional status *in utero* and maternal health, and is a sensitive marker of fetal respiratory and immune system development [13, 14]. Lower birthweight has been suggested as a risk factor for respiratory diseases in children through the mechanism of impaired fetal respiratory function [14, 15]. Pre-term birth, quantified as gestational age, might predispose children to respiratory tract infections and increase their risk of allergic respiratory symptoms [16–18]. To date, only one epidemiological study has investigated the joint effects of birthweight/gestational age and obesity on respiratory health in children [13].

This study had three objectives: 1) to determine the effects of childhood body mass index (BMI) on allergic respiratory symptoms; 2) to examine the association between birthweight, gestational age and allergic respiratory symptoms; and 3) to explore the joint effects of birthweight, gestational age and childhood BMI. Data was obtained from the standardised International Study of Asthma and Allergies in Childhood (ISAAC) written and video questionnaires, used in the 1995–1996 national survey in Taiwan.

## METHODS

### *Study design*

Between November 1995 and March 1996, a nationwide ISAAC mass screening survey of

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middle-school children (aged 13–16 yrs) in Taiwan was conducted to learn more about allergic respiratory diseases and symptoms. A total of 800 middle schools and >1 million children were recruited. The standardised ISAAC-Chinese version written questionnaire was taken home by children and answered by parents. Approximately 10% of the children were randomly selected to perform height/weight measurement and pulmonary function tests during school visits, using standardised techniques. The study protocol has been described in detail previously [4, 19]. Classroom incentives but not individual incentives were used to encourage participation.

### Definitions of health outcomes

The written questionnaire consisted of the ISAAC core questions on allergic respiratory symptoms. Children were considered to have asthma if there was an affirmative answer to the question ''Has your index child (*i.e.* a child who took the questionnaire home) ever being diagnosed as having asthma by a physician in the lifetime?'' Ever wheeze was defined by the question ''Has your index child ever had wheeze or whistling in the chest at any time in the past?'' and current wheeze referred to wheeze or whistle occurring in the previous year. Night wheeze was defined by the question ''Has your index child ever had sleep disturbance owing to wheeze at night in the previous 12 months?''; and severe wheeze by ''Has your index child ever had a severe wheeze or shortness of breath in the past 12 months?'' Wheeze with exercise was defined by the question ''Has your index child ever had a wheeze or whistling with or after exercise?'' Night cough was defined by the question ''Has your index child ever had cough seriously at night in the previous 12 months when he/she did not have a cold or the flu?''. In our study, asthma, night wheeze, severe wheeze and night cough are considered to be ''serious phenotypes'' [20, 21].

As recommended by the ISAAC protocol, video questionnaires were also administered to all school children. The video questionnaire showed five scenes related to allergic respiratory symptoms: 1) wheeze at rest; 2) wheeze and shortness of breath with exercise; 3) night wheeze; 4) night cough; and 5) severe wheeze and shortness of breath. Children answered specific questions after viewing each scene. The ISAAC written and video questionnaires have been validated and are widely used around the world. We could find corresponding questions to the definitions for all allergic respiratory symptoms in both written and video questionnaires [4]. The study protocol was approved by the Institutional Review Board at the National Taiwan University College of Public Health.

### Birthweight, gestational age and BMI measurement

The survey data was compared with the birth registration dataset, which comprises child's date of birth, birth order, mother's childbearing status, birthweight and gestational age. Birthweight was divided into three groups (<3,000 g, 3,000–3499 g, and ⩾3,500 g), which provided an adequate distribution for analysis. Gestational age was categorised into pre-term (<37 completed gestational weeks), term (37–41 gestational weeks) and post-term (⩾42 gestational weeks). Low birthweight (LBW) denotes a birthweight of <2,500 g. Small for gestational age (SGA) was defined as a birthweight of less than the $10^{th}$ percentiles of birthweight standards for each specific completed week of gestation, stratified by sex [22].

To determine the relationship between childhood BMI and diagnosed asthma, we plotted a histogram for the asthma probability by using childhood BMI as the independent variable. To achieve a good fit of the relationship, we adjusted estimates of these distributions by spline smoothing interpolation method using R software version 2.13.1 (R Development Core Team 2011; R Foundation for Statistical Computing, Vienna, Austria) (fig. 1). The relationship between the probability of doctor-diagnosed asthma and childhood BMI showed a ''linear'' trend. We then decided to analyse childhood BMI as a continuous variable using a sex- and age-specified z-score in our study.

### Statistical analysis

Unconditional logistic regression models were used to assess the individual and joint effects of childhood BMI on the occurrence of allergic respiratory symptoms. All of the models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema. Subjects with missing covariate information were included in the model using missing indicators [23]. All analyses were performed by SAS software version 9.1 (SAS Institute Inc., Cary, NC, USA). A two-sided p-value of <0.05 was considered statistically significant.

## RESULTS

In total, 990,512 children completed the ISAAC questionnaires, and 85,604 children had their height and weight measured. After excluding duplicates and missing linkages in the birth registration dataset (n=4,963) and those with invalid birthweight or gestational age (n=2,630), data from 78,011 children remained for analyses. Table 1 shows the characteristics of our study participants. Mean±SD birthweight for these children was 3,272.9±459.6 g, and gestational age was 39.7±1.2 weeks. LBW occurred in 3.7% of children and pre-term birth in 2.3% of children. There were 8,200 children (~10.5%) with SGA at birth. Their average height was 159.9±7.7 cm, average weight was 52.8±11.3 kg and average BMI was 20.6±3.5 kg·m$^{-2}$.

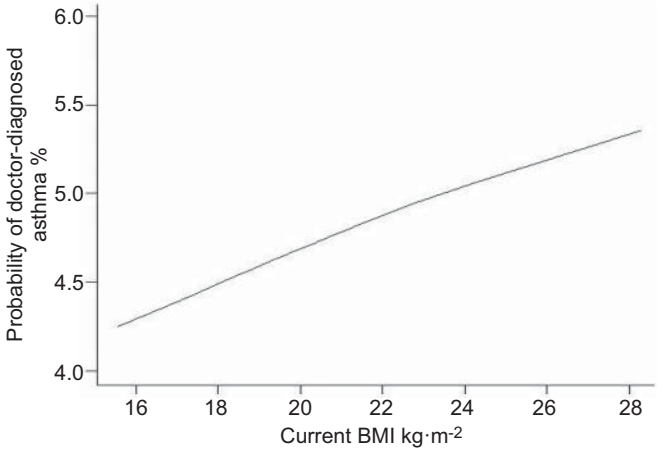


**FIGURE 1.** A spline interpolation curve demonstrating the relationship between probability of doctor-diagnosed asthma and childhood body mass index (BMI). The probability was adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema.

**TABLE 1** Characteristics of 78,011 middle-school students in Taiwan from 1995 to 1996

| | |
|---|---|
| **At birth** | |
| Weight g | 3272.9±459.6 |
| <3000 | 16009 (20.5) |
| 3000–3499 | 35759 (45.9) |
| ⩾3500 | 26243 (33.6) |
| Gestational age weeks | 39.7±1.2 |
| <37 | 1822 (2.3) |
| 37–42 | 74007 (94.9) |
| ⩾42 | 2182 (2.8) |
| LBW | 2897 (3.7) |
| Pre-term# | 1822 (2.3) |
| SGA | 8200 (10.5) |
| **Current assessment** | |
| Age yrs | |
| 13 | 20849 (26.7) |
| 14 | 26545 (34.0) |
| 15 | 25500 (32.7) |
| 16 | 5117 (6.6) |
| Height cm | 159.9±7.7 |
| Weight g | 52.8±11.3 |
| BMI | 20.6±3.5 |
| **Parental education level yrs** | |
| <7 | 18544 (23.8) |
| 7–9 | 19952 (25.6) |
| 10–12 | 26017 (33.4) |
| ⩾13 | 13498 (17.3) |
| **Number of smokers at home** | |
| 0 | 34802 (44.6) |
| 1 | 25403 (32.6) |
| ⩾2 | 17806 (22.8) |
| **Incense burning** | |
| Yes | 41427 (53.1) |
| **Active smoking** | |
| Yes | 1718 (2.2) |
| **Alcohol use** | |
| Yes | 1016 (1.3) |
| **History of rhinitis** | |
| Yes | 17185 (22.3) |
| **History of eczema** | |
| Yes | 5892 (7.6) |

Data are presented as mean±SD or n (%). LBW: low birthweight (denotes birthweight <2,500 g); SGA: small for gestational age; BMI: body mass index. #: pre-term denotes gestational age <37 weeks.

The relationships between sex- and age-specified z-score of childhood BMI and allergic respiratory symptoms are presented in table 2. After adjustment for potential confounders, we found that childhood BMI is positively associated with all allergic respiratory symptoms, with greater effects on serious phenotypes, such as severe wheeze (odds ratio (OR) 1.08), night wheeze (OR 1.05) and night cough (OR 1.14) in both written and video questionnaires. Childhood BMI also showed significant higher risk in relation with serious phenotypes, such as severe wheeze and night cough in the video questionnaire. In other words, the video questionnaire answered by children themselves correlates better with childhood BMI than the written questionnaire reported by parents.

**TABLE 2** Association between sex- and age-specified z-score of childhood body mass index and respiratory outcomes

| | Written questionnaire | Video questionnaire |
|---|---|---|
| **Ever wheeze** | 1.07** (1.04–1.09) | 1.10** (1.06–1.13) |
| **Current wheeze** | 1.06* (1.01–1.11) | 1.06* (1.00–1.13) |
| **Night wheeze** | 1.00 (0.94–1.07) | 1.05* (1.01–1.10) |
| **Severe wheeze** | 1.03 (0.95–1.12) | 1.08** (1.04–1.11) |
| **Wheeze with exercise** | 1.16** (1.13–1.19) | 1.16** (1.14–1.19) |
| **Asthma** | 1.02 (0.98–1.06) | |
| **Night cough** | 1.08** (1.05–1.10) | 1.14** (1.10–1.17) |

Data are presented as OR (95% CI). All models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema. *: $p<0.05$; **: $p<0.01$.

Table 3 shows the association between birthweight, gestational age and allergic respiratory symptoms in childhood. Children with a birthweight <3,000 g had a significantly increased risk of asthma (OR 1.17, 95% CI 1.07–1.28) and night cough (OR 1.08, 95% CI 1.02–1.15). A gestational age of >37 weeks was significantly associated with night wheeze (OR 1.43, 95% CI 0.95–2.15) and night cough (OR 1.19, 95% CI 1.03–1.37). Children with a history of LBW, pre-term birth or SGA were more likely to have allergic respiratory symptoms, such as night cough (LBW: OR 1.11, 95% CI 0.99–1.25; pre-term birth: OR 1.18, 95% CI 1.02–1.36; and SGA: OR 1.10, 95% CI 1.03–1.19). SGA more profoundly affects most of the allergic respiratory symptoms than LBW and pre-term birth, and is a better predictor than birthweight and gestational age.

Tables 4 and 5 show the effects of LBW, pre-term birth and sex- and age-specified z-score of childhood BMI on the risks of allergic respiratory symptoms in childhood. Children without a LBW history had a greater effect on asthma (OR 1.02, 95% CI 0.99–1.06) and night cough (written questionnaire: OR 1.08, 95% CI 1.05–1.10; video questionnaire: OR 1.14, 95% CI 1.10–1.18). The findings were consistent among children with joint exposure of pre-term history and childhood BMI (table 5). The effects of SGA and sex- and age-specified z-score of childhood BMI were also analysed (table 6). Compared with those without a history of SGA, children with a history of SGA had significant risk of serious phenotypes, such as asthma (OR 1.02, 95% CI 0.99–1.06) in the written questionnaire, and severe wheeze (OR 1.09, 95% CI 1.05-1.12) and night cough (OR 1.14, 95% CI 1.11–1.18) in the video questionnaire. The relationship between risk and serious phenotypes, such as asthma, night wheeze, severe wheeze and night cough, among children without LBW, pre-term birth or SGA history was significant.

## DISCUSSION

Children of LBW, pre-term birth or higher BMI were found to be at increased risk of allergic respiratory symptoms. Furthermore, children with history of LBW, pre-term birth or SGA and a higher current BMI had greater risks of respiratory outcomes compared with those without LBW, pre-term birth or SGA and a lower BMI.

**TABLE 3** Association between birth conditions and respiratory outcomes

| | Ever wheeze | Current wheeze | Night wheeze | Severe wheeze | Wheeze with exercise | Asthma | Night cough |
|---|---|---|---|---|---|---|---|
| **Written questionnaire** | | | | | | | |
| Birthweight g | | | | | | | |
| <3000 | 1.06 (0.99–1.14) | 0.97 (0.85–1.11) | 1.08 (0.90–1.28) | 1.12 (0.89–1.41) | 1.11 (1.03–1.19) | 1.17 (1.07–1.28) | 1.08 (1.02–1.15) |
| 3000–3499 | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
| ⩾3500 | 1.02 (0.96–1.08) | 1.00 (0.89–1.12) | 1.05 (0.90–1.22) | 1.23 (1.01–1.49) | 1.07 (1.01–1.15) | 0.97 (0.90–1.05) | 1.03 (0.97–1.08) |
| Gestational age weeks | | | | | | | |
| <37 | 1.09 (0.93–1.29) | 0.97 (0.71–1.33) | 1.43 (0.95–2.15) | 1.40 (0.86–2.28) | 1.04 (0.86–1.25) | 1.15 (0.93–1.42) | 1.19 (1.03–1.37) |
| 37–42 | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
| ⩾42 | 1.07 (0.92–1.24) | 1.05 (0.80–1.39) | 0.89 (0.61–1.31) | 0.94 (0.58–1.52) | 1.13 (0.96–1.33) | 1.14 (0.94–1.37) | 1.15 (1.01–1.31) |
| LBW | | | | | | | |
| Not LBW | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
| LBW | 1.11 (0.97–1.27) | 1.01 (0.79–1.31) | 1.21 (0.87–1.69) | 0.99 (0.64–1.52) | 1.07 (0.92–1.24) | 1.10 (0.92–1.31) | 1.11 (0.99–1.25) |
| Pre-term[#] | | | | | | | |
| Not pre-term | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
| Pre-term | 1.09 (0.92–1.29) | 0.97 (0.71–1.32) | 1.43 (0.95–2.16) | 1.40 (0.86–2.28) | 1.04 (0.86–1.25) | 1.15 (0.93–1.42) | 1.18 (1.02–1.36) |
| SGA | | | | | | | |
| Not SGA | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
| SGA | 1.10 (1.01–1.19) | 1.03 (0.88–1.20) | 1.01 (0.82–1.24) | 0.92 (0.70–1.21) | 1.15 (1.06–1.26) | 1.17 (1.05–1.30) | 1.10 (1.03–1.19) |
| **Video questionnaire** | | | | | | | |
| Birthweight g | | | | | | | |
| <3000 | 1.05 (0.96–1.14) | 0.92 (0.77–1.10) | 1.12 (1.00–1.25) | 1.03 (0.94–1.12) | 1.14 (1.07–1.21) | | 1.09 (1.00–1.20) |
| 3000–3499 | ref. | ref. | ref. | ref. | ref. | | ref. |
| ⩾3500 | 1.03 (0.96–1.11) | 0.95 (0.82–1.10) | 1.00 (0.90–1.10) | 0.99 (0.92–1.07) | 1.06 (1.00–1.12) | | 0.92 (0.85–1.00) |
| Gestational age weeks | | | | | | | |
| <37 | 1.01 (0.82–1.25) | 1.00 (0.65–1.54) | 1.03 (0.77–1.36) | 0.99 (0.80–1.21) | 1.12 (0.97–1.31) | | 1.09 (0.87–1.36) |
| 37–42 | ref. | ref. | ref. | ref. | ref. | | ref. |
| ⩾42 | 1.09 (0.91–1.30) | 1.38 (0.93–2.03) | 1.09 (0.86–1.39) | 1.00 (0.84–1.20) | 1.01 (0.88–1.16) | | 1.15 (0.95–1.39) |
| LBW | | | | | | | |
| Not LBW | ref. | ref. | ref. | ref. | ref. | | ref. |
| LBW | 1.07 (0.90–1.26) | 0.98 (0.70–1.38) | 1.12 (0.90–1.40) | 1.00 (0.84–1.18) | 1.16 (1.02–1.30) | | 1.23 (1.04–1.46) |
| Pre-term[#] | | | | | | | |
| Not pre-term | ref. | ref. | ref. | ref. | ref. | | ref. |
| Pre-term | 1.01 (0.82–1.25) | 0.99 (0.64–1.52) | 1.02 (0.77–1.36) | 0.99 (0.80–1.21) | 1.12 (0.97–1.31) | | 1.08 (0.87–1.35) |
| SGA | | | | | | | |
| Not SGA | ref. | ref. | ref. | ref. | ref. | | ref. |
| SGA | 1.09 (0.98–1.21) | 1.00 (0.81–1.24) | 1.17 (1.02–1.34) | 1.08 (0.98–1.20) | 1.16 (1.08–1.25) | | 1.19 (1.07–1.32) |

Data are presented as OR (95% CI). LBW: low birthweight (denotes birth weight <2,500 g); SGA: small for gestational age; ref.: reference group. [#]: pre-term denotes gestational age <37 weeks. All models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema.

The effects of childhood BMI on allergic respiratory symptoms were modified by SGA, and showed significant risks among children without SGA history. To the best of our knowledge, this is the first study that investigates the individual and joint effects of birthweight, gestational age and BMI on respiratory health in children.

The strengths of our study include the large sample size, the use of standardised questionnaires and appropriate adjustment for potential confounders. Data was obtained from a large-scale, nationwide survey and participating children were representative of the native population of Taiwan. The ISAAC questionnaire has been validated and used for 13- to 14-yr-old children throughout the world [24, 25]. The prevalence of allergic respiratory symptoms in children by both ISAAC written and video questionnaires was simultaneously evaluated, and it was found that the self-reported video questionnaire correlated better with childhood BMI than the parental written questionnaire (table 2). Parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema were associated with childhood respiratory outcomes from a previous study [6], and we have effectively adjusted these factors in all analyses to minimise the confounding effects.

Our study confirms that higher BMI is associated with an increased risk of allergic respiratory symptoms in children (table 2). Birthweight and gestational age also showed obvious effects on respiratory outcomes (table 3). The above findings were

**TABLE 4** Effects of low birthweight (LBW)[#] and sex- and age-specified z-score of childhood body mass index on respiratory outcomes

| | Written questionnaire | Video questionnaire |
|---|---|---|
| **Ever wheeze** | | |
| LBW | 0.97 (0.84–1.11) | 1.02 (0.86–1.20) |
| Not LBW | 1.07** (1.04–1.10) | 1.10** (1.06– 1.13) |
| **Current wheeze** | | |
| LBW | 1.13 (0.85–1.51) | 1.04 (0.71–1.53) |
| Not LBW | 1.06* (1.01–1.11) | 1.07* (1.00–1.14) |
| **Night wheeze** | | |
| LBW | 1.01 (0.68–1.50) | 0.96 (0.76–1.20) |
| Not LBW | 1.01 (0.95–1.08) | 1.06* (1.01–1.10) |
| **Severe wheeze** | | |
| LBW | 0.72 (0.43–1.22) | 0.85 (0.71–1.02) |
| Not LBW | 1.04 (0.96–1.13) | 1.09** (1.05–1.12) |
| **Wheeze with exercise** | | |
| LBW | 1.05 (0.91–1.21) | 1.13* (1.01–1.27) |
| Not LBW | 1.16** (1.13–1.19) | 1.17** (1.14–1.19) |
| **Asthma** | | |
| LBW | 0.96 (0.81–1.15) | |
| Not LBW | 1.02 (0.99–1.06) | |
| **Night cough** | | |
| LBW | 1.12* (1.00–1.26) | 1.13 (0.96–1.33) |
| Not LBW | 1.08** (1.05–1.10) | 1.14** (1.10–1.18) |

Data are presented as OR (95% CI). [#]: birthweight <2,500 g. All models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema. *: $p<0.05$; **: $p<0.01$.

**TABLE 5** Effects of pre-term[#] and sex- and age-specified z-score of body mass index on respiratory outcomes

| | Written questionnaire | Video questionnaire |
|---|---|---|
| **Ever wheeze** | | |
| Pre-term | 0.95 (0.80–1.12) | 0.95 (0.76–1.18) |
| Not pre-term | 1.07** (1.04–1.10) | 1.10** (1.07–1.13) |
| **Current wheeze** | | |
| Pre-term | 1.08 (0.76–1.54) | 0.89 (0.53–1.49) |
| Not pre-term | 1.06* (1.01–1.11) | 1.07* (1.00–1.14) |
| **Night wheeze** | | |
| Pre-term | 0.82 (0.52–1.30) | 0.94 (0.70–1.27) |
| Not pre-term | 1.01 (0.95–1.08) | 1.05* (1.01–1.10) |
| **Severe wheeze** | | |
| Pre-term | 0.96 (0.54–1.70) | 0.93 (0.74–1.15) |
| Not pre-term | 1.03 (0.95–1.12) | 1.08** (1.05–1.11) |
| **Wheeze with exercise** | | |
| Pre-term | 1.05 (0.87–1.25) | 1.12 (0.97–1.29) |
| Not pre-term | 1.16** (1.13–1.19) | 1.17** (1.14–1.19) |
| **Asthma** | | |
| Pre-term | 0.90 (0.72–1.14) | |
| Not pre-term | 1.02 (0.99–1.06) | |
| **Night cough** | | |
| Pre-term | 1.02 (0.89–1.17) | 1.26* (1.04–1.54) |
| Not pre-term | 1.08** (1.05–1.10) | 1.13** (1.10–1.17) |

Data are presented as OR (95% CI). All models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema. [#]: pre-term denotes gestational age <37 weeks. *: $p<0.05$; **: $p<0.01$.

consistent with previous studies which suggested that birthweight, gestational age and childhood BMI were associated with chronic conditions of later life, such as coronary heart disease [26], type-2 diabetes [27] and respiratory health [13]. The joint effects of birthweight and gestational age on the relationship between BMI and childhood diseases have never been previously examined.

Childhood asthma is a complex disease that includes distinct respiratory symptoms with potentially different aetiologies, such as childhood obesity [2, 3, 5, 6]. In accordance with previous epidemiological studies [8, 28–30], our data show that a higher childhood BMI is associated with an increased risk for allergic respiratory symptoms and showed significant trends on serious phenotypes. Possible explanations for the increased risk in obese children might be systematic immunological changes through higher levels of proinflammatory cytokines, such as leptin, interleukin-18 and tumour necrosis factor-α [9–14]. This immunological change, an important element of asthma pathophysiology, may affect airway function in the short and long term [9, 11–13]. Conversely, obesity has also been noted to adversely affect lung function by decreasing expiratory flow rates and reducing airway calibre, leading to a worsening of respiratory symptoms [9, 31].

Children with LBW and pre-term birth history are considered to have poor pre-natal growth and development of the fetal respiratory/immune systems, which increases the risk of respiratory tract infections [13, 14, 16–18]. Our results are consistent with previous studies that suggested that children with histories of not only LBW and pre-term birth, but also SGA, a synthetic indicator of birthweight and gestational age, had increased risks of allergic respiratory symptoms [13–18, 32]. Impaired growth *in utero*, resulting in LBW and earlier gestational age, is associated with diminished surfactant activity and pulmonary cellularity, due to the fact that the lungs of immature neonates are not fully developed either anatomically or immunologically [13, 16–18].

There is a direct relationship between birthweight, childhood BMI and obesity in adult life, suggesting that appropriate intervention in infancy could prevent subsequent obesity [13, 14, 33, 34]. In our data, although LBW and higher BMI were associated with allergic respiratory symptoms, we found that birthweight was positively related to childhood BMI (online supplementary table S1). A number of environmental and nutritional factors might influence the development of childhood obesity [13, 14, 33, 34], and LBW has not been found to be a cause of obesity in children [33, 35]. Therefore, we concluded that birthweight, gestational age and childhood BMI are independent predictors for allergic respiratory symptoms.

When the effect of childhood BMI was further stratified by LBW, pre-term birth or SGA history, a modified effect of LBW, pre-term birth or SGA was shown on the association between childhood BMI and allergic respiratory symptoms (tables 4–6). Respiratory

**TABLE 6** Effects of being small for gestational age (SGA) and sex- and age-specified z-score of childhood body mass index on respiratory outcomes

| | Written questionnaire | Video questionnaire |
|---|---|---|
| **Ever wheeze** | | |
| SGA | 1.06 (0.98–1.15) | 1.06 (0.96–1.17) |
| Not SGA | 1.07** (1.04–1.10) | 1.10** (1.07–1.14) |
| **Current wheeze** | | |
| SGA | 1.08 (0.92–1.26) | 1.04 (0.84–1.29) |
| Not SGA | 1.06* (1.00–1.11) | 1.07* (1.00–1.14) |
| **Night wheeze** | | |
| SGA | 0.94 (0.77–1.15) | 0.96 (0.84–1.10) |
| Not SGA | 1.01 (0.95–1.08) | 1.07** (1.02–1.12) |
| **Severe wheeze** | | |
| SGA | 0.91 (0.69–1.19) | 1.02 (0.93–1.13) |
| Not SGA | 1.04 (0.96–1.14) | 1.09** (1.05–1.12) |
| **Wheeze with exercise** | | |
| SGA | 1.11* (1.02–1.20) | 1.15** (1.07–1.23) |
| Not SGA | 1.16** (1.13–1.20) | 1.17** (1.14–1.20 |
| **Asthma** | | |
| SGA | 1.01 (0.91–1.13) | |
| Not SGA | 1.02 (0.99–1.06) | |
| **Night cough** | | |
| SGA | 1.08* (1.01–1.16) | 1.09 (0.99–1.20) |
| Not SGA | 1.08** (1.05–1.10) | 1.14** (1.11–1.18) |

Data are presented as OR (95% CI). All models were adjusted for parental education level, number of smokers at home, incense burning, active smoking, alcohol use and history of rhinitis and eczema. *: $p<0.05$; **: $p<0.01$.

symptoms were highly correlated with childhood obesity through the effects of high levels of leptin and proinflammatory cytokines [9, 11–13]. Our findings are in line with the hypothesis that children with a history of obesity in infancy and childhood have higher risks of respiratory health outcomes synergistically.

There are some limitations to our study. The cross-sectional design would not provide a direct casual link between childhood BMI and allergic respiratory symptoms. Our findings are consistent with many longitudinal and cross-sectional studies, showing that childhood obesity is strongly linked with poor respiratory health [28, 29]. Another potential bias is the imprecise assessment of allergic respiratory symptoms reporting by the questionnaire. However, ISAAC questionnaires have been widely used to define respiratory outcomes in epidemiological studies in children [4, 19]. The ISAAC questionnaire has been validated and used for 13- to 14-yr-old children throughout the world [24, 25]. The development of a standardised video questionnaire for self-completion by children offers a further advantage of minimising the cultural and linguistic gap [25]. We also proved that the video questionnaire reported by children themselves is a better predictor of childhood BMI (table 2).

In conclusion, the large-scale nationwide ISAAC survey in Taiwan resulted in some important and novel findings. Our study suggests that LBW, pre-term birth and childhood BMI are independent risk factors for allergic respiratory symptoms in children. Children with histories of LBW, pre-term birth or SGA, and a higher current BMI would have larger respiratory burden. We recommend that LBW, pre-term birth or SGA children should be placed on proper weight-management programmes to avoid adverse respiratory outcomes in the future.

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## STATEMENT OF INTEREST

None declared.

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