Growth trajectories and asthma/rhinitis in children: a longitudinal study in Taiwan

Yang-Ching Chen[1,2,7], Tsan-Hon Liou[3], Pau-Chung Chen[4,5], Bor-Luen Chiang[6], Yao-Hsu Yang[6], Hsien-Yu Fan[1] and Yungling Leo Lee[7,8]

Affiliations: [1]Taipei City Hospital, ZhongXing Branch, Taipei, Taiwan. [2]School of Nutrition and Health Sciences, College of Nutrition, Taipei Medical University, Taipei, Taiwan. [3]Graduate Institute of Injury Prevention and Control, Taipei Medical University, Taipei, Taiwan. [4]Institute of Occupational Medicine and Industrial Hygiene and Dept of Public Health, National Taiwan University College of Public Health, Taipei, Taiwan. [5]Dept of Environmental and Occupational Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan. [6]Dept of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan. [7]Institute of Epidemiology and Preventive Medicine, National Taiwan University College of Public Health, Taipei, Taiwan. [8]Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.

Correspondence: Yungling Leo Lee, 17 Xuzhou Road, Zhongzheng District, Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei 100, Taiwan.
E-mail: leolee@ntu.edu.tw

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ABSTRACT Studies have reported the effect of body weight in early childhood on asthma. However, the effect of growth patterns during school age on asthma and rhinitis has yet to be explored. We sought to investigate whether various growth patterns predict incident asthma and rhinitis.

We conducted a nationwide longitudinal study (Taiwan Children Health Study) in 14 Taiwanese communities. Body mass index (BMI) z-scores of 4422 children aged 6–11 years were collected annually and distinct growth trajectory classes were identified using a latent generalised mixture model. Pulmonary function and exhaled nitric oxide fraction (F_{ENO}) levels were also measured. Whether different growth trajectory classes predict incident asthma and rhinitis at age 12, 15 and 18 years was determined using a discrete time hazard model.

Four growth trajectory classes were identified. Persistently overweight children exhibited significantly increased risks of asthma and rhinitis at age 12 years. Furthermore, being persistently overweight had a long-term effect on incident asthma (hazard ratio 2.47, 95% CI 1.18–5.12) and rhinitis (hazard ratio 1.44, 95% CI 1.12–1.84) in adolescence and early adulthood. Children in high BMI classes exhibited significantly lower pulmonary functions compared with normal growth children. F_{ENO} levels were lower in children in the high BMI classes and higher in children showing declining obesity compared with normal growth children.

Persistently overweight children exhibited incident asthma and rhinitis in adolescence and early adulthood.

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Introduction

Growing evidence supports the association between obesity and asthma in children [1]. In addition, most prospective studies have suggested that obesity antedates the development of asthma [2]. However, growth is dynamic in children. Using body mass index (BMI) trajectories can better describe the longitudinal development of a population, as well as the variation of individual development, compared with a single measurement of BMI. In addition, previous studies using concurrent BMI as a predictor for asthma might have problems in reverse causality [3]. BMI developmental course might better reflect the time period of gaining excess weight and the cumulative risk of asthma development. Considering the current obesity pandemic [4], determining whether elevated BMI in childhood, adolescence or young adulthood contributes independently to the risk of asthma is crucial.

Researchers have explored the associations between growth trajectory and asthma, but such studies were conducted on populations with different age ranges by using different analytical methodologies. A birth cohort study following children from 1 to 18 years of age reported that children with early persistent obesity since age 1–4 years exhibited a 2.2-fold increased risk of asthma compared with those with normal weight [5]. Furthermore, the critical period for a different growth pattern was age 1–4 years. A European study conducted on a large joint birth cohort [6] reported that children with a rapid BMI gain trajectory class in the first 2 years of life exhibited a higher risk of incident asthma within the first 6 years of life than did children with a less pronounced weight gain slope in childhood. Previous studies have focused on adiposity measurements during infancy and early childhood. However, no study has explored the relationships between growth trajectories during school age and incident asthma. The history of asthma during adolescence is different from that during early childhood [7].

Allergic rhinitis is one of the most common atopic diseases among children and its prevalence is increasing worldwide [8]. 80% patients with allergic rhinitis exhibit symptoms of rhinitis since childhood and rhinitis mainly affects children aged 9–17 years [9]. Allergic rhinitis can severely affect the quality of life of children and their performance in school [10]. However, in contrast to reports on the strong association between obesity and asthma [11], studies on obesity and allergic rhinitis have reported inconsistent results [12, 13]. No study has investigated the effect of growth trajectories on allergic rhinitis. Adiposity-related increased level of inflammation and oxidative stress in airways of children might induce the occurrence of allergic rhinitis [14].

We performed a nationwide longitudinal study (Taiwan Children Health Study (TCHS)) in 14 representative communities in Taiwan. To investigate which growth pattern during school age may be associated with the risk of asthma and allergic rhinitis, we examined the growth trajectories at age 6–11 years and their relation to active asthma and allergic rhinitis at age 12 years. We then used these growth classes in the second step as a long-term predictor for incident asthma and allergic rhinitis at age 12, 15 and 18 years in a survival model. Furthermore, the TCHS data can be used to analyse the differences in pulmonary function performance levels and airway inflammation status among various growth trajectory classes.

Methods

Study design and data collection

We conducted the nationwide TCHS on children from elementary and middle schools in 14 Taiwanese communities during 2007–2010. The TCHS involved a multipurpose nationwide design comprising two cohorts, and it focused on atopic diseases, adiposity growth, pubertal development, and certain social and behavioural issues in children [15]. Cohort 1 enrolled 12-year-old children and Cohort 2 enrolled 10-year-old children. The baseline response rates for Cohorts 1 and 2 were 86.5% and 75.5%, respectively. In Cohort 1, follow-up surveys were conducted on children aged 15 and 18 years. In Cohort 2, follow-up surveys were conducted on children aged 11 and 12 years. The parents or guardians of each participating student provided written informed consent and completed a written questionnaire. The TCHS protocol was approved by the Institutional Review Board at National Taiwan University Hospital and it complied with the principles outlined in the Declaration of Helsinki [16].

BMI measurements

In both cohorts, the growth trajectory was assessed annually at age 6–11 years by using BMI ($kg \cdot m^{-2}$; n=4422). From 2010 to 2012, the BMI levels of Cohort 2 were measured annually during school visits [17]. For earlier data on BMI growth in both cohorts, body height and weight data were retrospectively retrieved from the participants' elementary school health records. The BMI data were transformed into standardised BMI z-scores according to the World Health Organization (WHO) growth standards for school-aged children and adolescents [18, 19]. The prevalences of overweight and obesity were defined according to three criteria: Taiwanese growth charts [20], WHO [19] and International Obesity Task Force

(IOTF) criteria [21]. A child being overweight was defined by BMI between the 85th and 95th percentile of age- and sex-specific BMI, and childhood obesity was defined by BMI ⩾95th percentile of age- and sex-specific BMI according to the growth charts for children.

Outcome definition

A parent-reported questionnaire was used for defining phenotypes of asthma and rhinitis in children aged 12 and 15 years [22]. Active asthma cases were distinguished from normal children by asking two questions: "Has a doctor ever diagnosed your child as having asthma?" and "Did your child ever experience difficulty breathing, or did you observe any wheezing or whistling from his or her chest in the past 12 months?". If the answers were "Yes" to both questions, we classified the child as an active asthma case. Moreover, exercise-induced asthma was defined as a positive answer to the question "Did your child ever experience whistling from his or her chest during or after exercise in the past 12 months?". Allergic rhinitis was also determined by a positive answer to the question "Has a doctor ever diagnosed your child as having allergic rhinitis?". If the answer was "Yes", we then asked when was the first time that the child had been diagnosed with allergic rhinitis. We clarified active allergic rhinitis cases as diagnosed in the past 1 year. We obtained the answers to the same questions from children aged 18 years in the survey, rather than using a parent-reported questionnaire. We initially combined Cohorts 1 and 2 to determine which growth trajectory class across the ages 6–11 years would affect active asthma/rhinitis at age 12 years. We followed up Cohort 2 children until age 12 years; therefore, to determine whether various growth trajectory classes across the ages 6–11 years would predict incident asthma/rhinitis phenotypes in later life (at age 12, 15 and 18 years), we can only use Cohort 1.

In the questionnaire, we also identified the age of initial physician-diagnosed asthma/rhinitis. For the participants in Cohort 1, incident asthma phenotypes were calculated by excluding the history of asthma before age 11 years (n=113). Incident allergic rhinitis was calculated by excluding the history of rhinitis before age 11 years (n=204). Incident asthma/rhinitis phenotypes were determined when the answer was "Yes" to ever physician-diagnosed asthma/rhinitis and exercise-induced asthma questions during the follow-up period.

We used exhaled nitric oxide fraction (F_{ENO}) levels as a surrogate marker of airway inflammation [23]. One NIOX MINO Airway Inflammation Monitor (Aerocrine, Solna, Sweden) was used in the 2012 survey of Cohort 2. The standard procedures for measuring the F_{ENO} levels were based on the recommendations made by the American Thoracic Society and European Respiratory Society [24].

Pulmonary function tests were conducted according to our previously standardised protocol [25]. The forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio demonstrated the most significant associations with BMI [17]. Therefore, the FEV_1/FVC ratio was used as a surrogate marker for pulmonary function performance.

Statistical analysis

In the TCHS, we identified distinct growth trajectory patterns across the ages 6–11 years according to individual BMI z-score trajectories by using the latent growth mixture model (LGMM) [26]. The LGMM, an extension of random effects of the latent class growth model, refers to modelling with latent variables that are used to identify heterogeneous subgroups with similar developmental trajectories (online supplementary figure E1) [27]. The random effects are allowed to have different distributions among individuals belonging to different trajectory classes. Missing data were appropriately handled in the LGMM with the assumptions of missing at random. Furthermore, to assess model adequacy, the Bayesian Information Criterion (BIC) and Lo–Mendell–Rubin (LMR) tests were used [28]. Lower BIC test values, with significant results in the LMR test for a k-class model compared with a $k-1$-class model, suggested that the model fitted the data adequately when an additional latent class was included. LGMM analysis was conducted using Mplus software version 7 (www.statmodel.com).

For the present study, we attempted initially to determine which growth trajectory class across the ages 6–11 years would affect active asthma/rhinitis at age 12 years in the TCHS by using multivariate logistic regression. Our statistical models were adjusted for several potential confounders, such as sex, age, parental education, family income, household environmental tobacco smoke, birthweight, gestational age, breastfeeding and asthma oral steroid use. Moreover, to determine whether various growth trajectory classes across the ages 6–11 years would predict incident asthma/rhinitis phenotypes in later life (at age 12, 15 and 18 years), we used the discrete time hazard model (DTHM) [29] in Cohort 1. The DTHM is a survival analysis model that enables estimating hazard ratios (HRs) and 95% confidence intervals when an event occurrence may be considered in a discrete period. The model was weighted by individual class probabilities for each of the four trajectory classes to account for the uncertainty in classifying a child into a particular trajectory class. The comparisons of FEV_1/FVC ratios and F_{ENO} levels among different growth

trajectory classes were analysed using multivariate ANOVA. Descriptive analysis, logistic regression and DTHM analysis were conducted using SAS software version 9.3 (www.sas.com). On the basis of a two-sided estimation, statistical significance was set at 5%.

Results

In this study, the TCHS population comprised 4422 children with available data for both growth trajectory classes (age 6–11 years) and asthma/rhinitis phenotypes (age 12 years). Table 1 presents the characteristics of participants aged 12 years. Although Cohorts 1 and 2 were enrolled from the same 14 communities, the participants aged 12 years were recruited in 2007 and 2012, respectively. During this 5-year time gap, we observed a higher level of parental education and family income in Cohort 2 as compared with Cohort 1. In the TCHS, 4.0% of children aged 12 years had active asthma, 5.9% had exercise-induced asthma and 9.7% had active allergic rhinitis. In Cohort 1, the follow-up rate was 93.5% for children aged 15 years and 71.3% for children aged 18 years. When children with a history of asthma were excluded, the incidences of asthma were 10.6, 4.7 and 6.6 per 1000 person-years at age 12, 15 and 18 years, respectively. When children with a history of allergic rhinitis were excluded, the incidences of physician-diagnosed allergic rhinitis were 62.1, 20.4 and 21.4 per 1000 person-years at age 12, 15 and 18 years, respectively.

Growth trajectory classes

After conducting model adequacy assessment through the BIC and LMR tests [28], we determined four growth trajectory classes (figure 1). Both cohorts demonstrated similar trajectory patterns (online supplementary figures E2 and E3); therefore, these cohorts were combined to further analyse the growth trajectories at age 6–11 years and their relations to active asthma and allergic rhinitis at age 12 years. Online supplementary tables E1 and E2 list the detailed estimates of growth parameters in the four trajectory classes derived through the LGMM, and online supplementary table E3 lists the model fit indices. The first trajectory class (Class 1, n=2098, 47.4%) was characterised by children with normal growth, aged 6–11 years and demonstrating BMI z-scores of nearly zero. However, when three criteria were used to define overweight or obese children (table 2), 5.6% of the children in Class 1 were identified

TABLE 1 Characteristics of participants aged 12 years in the Taiwan Children Health Study

	Cohort 1	Cohort 2	Cohorts 1 and 2
Subjects	1008	3414	4422
Age years	12.7±0.3	12.1±0.3	12.3±0.4
Male	503 (49.9)	1736 (50.9)	2239 (50.6)
BMI kg·m^{-2}	20.6±4.3	19.0±3.9	19.4±4.0
Parental education years			
Senior high school or below	668 (66.3)	1785 (52.3)	2453 (55.5)
College or university	305 (30.3)	1344 (39.4)	1649 (37.3)
Post-graduate school	35 (3.5)	285 (8.4)	320 (7.2)
Family income NTD			
<600 000	614 (60.9)	1657 (48.5)	2271 (51.4)
600 001–1 000 000	277 (27.5)	1175 (34.4)	1452 (32.8)
⩾1 000 001	117 (11.6)	582 (17.1)	699 (15.8)
Birthweight g	3193.2±445.5	3132.2±455.8	3150.4±453.5
Gestational age weeks	39.1±1.4	38.5±1.8	38.7±1.7
Breastfeeding	468 (46.4)	1213 (51.8)	1681 (50.2)
Oral steroid use in past 1 year	11 (1.1)	19 (0.56)	30 (0.68)
Household cigarette smoke	468 (46.4)	1252 (36.7)	1720 (38.9)
Active asthma	34 (3.4)	122 (4.2)	156 (4.0)
Exercise-induced asthma	44 (4.4)	193 (6.5)	237 (5.9)
Active allergic rhinitis	32 (3.2)	349 (11.9)	381 (9.7)
FEV_1/FVC %	91.0 (5.4)	91.9 (6.6)	91.7 (6.3)
F_{ENO} ppb		11.7 (18.0)	
Trajectory class			
Class 1	446 (44.3)	1652 (48.4)	2098 (47.4)
Class 2	209 (20.7)	671 (19.7)	880 (19.9)
Class 3	322 (31.9)	1008 (29.5)	1330 (30.1)
Class 4	31 (3.1)	83 (2.4)	114 (2.6)

All data are presented as n, mean±SD or n (%). The numbers of participants do not add up to the total number because of missing data. BMI: body mass index; NTD: new Taiwan dollar; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; F_{ENO}: exhaled nitric oxide fraction.

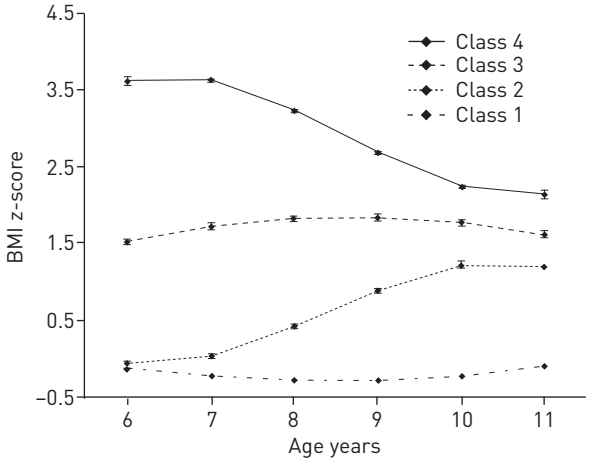

FIGURE 1 Age- and sex-specific body mass index (BMI) z-score trajectory classes across the ages 6–11 years, which were estimated using the latent growth mixture model. Class 1: normal growth (47.4%); Class 2: rapid growth (19.9%); Class 3: persistently overweight (30.1%); Class 4: declining obesity (2.6%). Bars indicate 95% confidence intervals around the estimated values in each trajectory class.

as overweight at age 11 years according to the Taiwanese criteria. An increased prevalence of overweight (20.2%) was observed in normal growth children according to the IOTF criteria, suggesting that the IOTF criteria might overestimate the prevalence of overweight in normal growth children in Taiwan.

In our analysis, 880 rapidly growing children (19.9%) were categorised into Class 2. At age 6 years, children in Class 2 exhibited similar BMI z-scores to those of children in Class 1. However, because of the steepest BMI z-scores elevation, the BMI z-scores of children in Class 2 at age 11 years were >1.

Class 3 (n=1330, 30.1%), involving persistently overweight children, registered BMI z-scores indicative of long-term overweight and obesity at age 6–11 years. Children in Class 3 experienced a marginal increase in their BMI z-scores at age 6–8 years and stabilised high BMI z-scores after age 8 years.

TABLE 2 Prevalence of overweight or obese status across the ages 6–11 years by four trajectory classes[#]

Age years	Class 1			Class 2			Class 3			Class 4		
	Taiwan	WHO	IOTF	Taiwan	WHO	IOTF	Taiwan	WHO	IOTF	Taiwan	WHO	IOTF
Normal weight												
6	96.2	92.4	84.4	94.7	88.5	81.6	36.7	22.4	13.1	4.3	2.3	1.6
7	98.8	94.4	88.1	96.2	86.5	80.3	34.0	13.2	6.2	5.3	2.5	0.0
8	99.8	96.7	91.0	86.6	71.7	63.5	26.9	5.9	2.0	9.6	2.2	2.3
9	99.4	96.4	90.6	67.1	52.8	41.7	23.0	5.4	2.2	17.3	13.5	11.9
10	91.6	87.7	80.3	58.6	43.3	32.4	37.4	24.6	17.7	27.4	17.8	16.9
11	88.1	80.8	71.2	54.2	41.6	28.0	40.2	32.1	23.7	29.4	22.0	17.8
Overweight												
6	3.3	5.9	14.3	4.6	8.1	16.3	38.8	26.1	42.9	18.9	8.6	10.9
7	1.2	5.1	11.7	3.3	10.2	18.1	40.4	24.3	40.0	20.2	5.3	9.8
8	0.2	3.3	9.0	11.0	15.6	29.3	39.0	26.7	40.8	15.8	6.8	9.8
9	0.6	3.4	9.3	22.3	19.1	39.1	35.1	24.6	38.6	13.6	4.7	10.3
10	4.5	5.3	14.5	25.3	21.7	42.2	26.3	21.1	37.9	16.9	11.9	18.7
11	5.6	8.8	20.2	25.1	23.6	46.0	23.4	21.0	36.1	11.9	12.7	18.6
Obese												
6	0.5	1.7	1.3	0.7	3.4	2.1	24.5	51.5	44.0	76.8	89.1	87.5
7	0.0	0.5	0.2	0.5	3.3	1.6	25.6	62.5	53.8	74.5	92.2	90.2
8	0.0	0.0	0.0	2.4	12.7	7.2	34.1	67.4	57.2	74.6	91.0	87.9
9	0.0	0.2	0.1	10.6	28.1	19.2	41.9	70.0	59.2	69.1	81.8	77.8
10	3.9	7.0	5.2	16.1	35.0	25.4	36.3	54.3	44.4	55.7	70.3	64.4
11	6.3	10.4	8.6	20.7	34.8	26.0	36.4	46.9	40.2	58.7	65.3	63.6

Data are presented as %. Definitions of overweight or obesity were demonstrated by three different criteria: Taiwan: new growth charts for Taiwanese children; WHO: World Health Organization Growth Standards; IOTF: International Obesity Task Force Asian cut-off point. [#]: Class 1: normal growth (n=2098); Class 2: rapid growth (n=880); Class 3: persistently overweight (n=1330); Class 4: declining obesity (n=114).

TABLE 3 Odds ratios of asthma/rhinitis phenotypes according to the various growth trajectory classes in children aged 12 years (Cohorts 1 and 2)

Trajectory class	Active asthma[#]	Exercise-induced asthma[#]	Active allergic rhinitis[¶]
Class 1 (reference)	1	1	1
Class 2	1.29 (0.82–2.02)	1.12 (0.77–1.61)	1.12 (0.90–1.38)
Class 3	1.54 (1.05–2.26)	1.42 (1.04–1.93)	1.25 (1.03–1.53)
Class 4	0.85 (0.25–2.87)	0.96 (0.37–2.44)	1.11 (0.69–1.77)

Data are presented as odds ratios with 95% confidence intervals. See figure 1 and table 2 for details of trajectory classes. [#]: logistic regression models were adjusted for sex, age, parental education, family income, household environmental tobacco smoke, birthweight, gestational age, breastfeeding and asthma oral steroid use; [¶]: logistic regression models were adjusted for sex, age, parental ducation, family income, household environmental tobacco smoke, birthweight, gestational age and breastfeeding.

In contrast to the children in Classes 2 and 3, those in Class 4 (n=114, 2.6%) demonstrated a significant decline in the BMI z-scores from >3.5 to <3. These few children who were originally considered extremely obese might experience a natural growth in height or a lifestyle modification, thus reducing their BMI z-scores.

Growth trajectory and asthma

The children in Class 3 exhibited significantly increased risks of active asthma (odds ratio (OR) 1.54, 95% CI 1.05–2.26) and exercise-induced asthma (OR 1.42, 95% CI 1.04–1.93) (table 3). Table 4 details the survival analysis of the effect of the BMI trajectory across the ages 6–11 years on incident asthma during adolescence or early adulthood. After excluding children with a history of asthma, being in Class 3 (*i.e.* the persistently overweight trajectory class) would significantly increase the risk of incident asthma (HR 2.47, 95% CI 1.18–5.12) and incident exercise-induced asthma (HR 1.40, 95% CI 1.01–1.95).

Growth trajectory and allergic rhinitis

The children in Class 3 exhibited a significantly increased risk of active allergic rhinitis (OR 1.25, 95% CI 1.03–1.53) (table 3). When these children were followed longitudinally up to age 18 years, we determined that they exhibited an increased risk of incident allergic rhinitis (HR 1.44, 95% CI 1.12–1.84) (table 4).

Pulmonary function test and airway inflammation in four growth trajectory classes

Our data suggested an inverse relationship between the growth trajectory classes and FEV_1/FVC ratios (online supplementary table E6 and figure 2a). Children in Classes 2, 3 and 4 exhibited significantly lower FEV_1/FVC ratios than did those in Class 1 ($p<0.001$). Compared with children in Class 1, those in Class 3 exhibited lower F_{ENO} levels (online supplementary table E6 and figure 2b). Children who experienced a reduction in their BMI z-scores (Class 4) exhibited increased F_{ENO} levels.

TABLE 4 Hazard ratios of asthma/rhinitis phenotypes for the different growth trajectory classes in Cohort 1 aged 12, 15 and 18 years

Trajectory class	Incident asthma[#]	Incident exercise-induced asthma[#]	Incident allergic rhinitis[¶]
Class 1 (reference)	1	1	1
Class 2	1.77 (0.75–4.15)	0.90 (0.60–1.35)	1.14 (0.85–1.52)
Class 3	2.47 (1.18–5.12)	1.40 (1.01–1.95)	1.44 (1.12–1.84)
Class 4	1.82 (0.38–8.63)	1.68 (0.83–3.40)	1.50 (0.85–2.64)

Data are presented as hazard ratios with 95% confidence intervals. See figure 1 and table 2 for details of trajectory classes. [#]: discrete time hazard models were adjusted for sex, age, parental education, family income, household environmental tobacco smoke, birthweight, gestational age, breastfeeding, asthma oral steroid use and weighted by individual class probability; [¶]: discrete time hazard models were adjusted for sex, age, parental education, family income, household environmental tobacco smoke, birthweight, gestational age, breastfeeding and weighted by individual class probability.

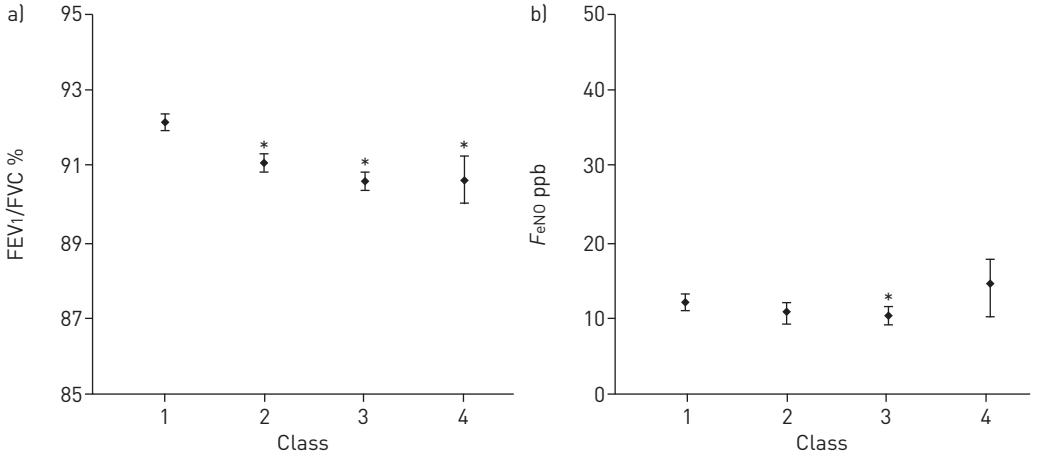

FIGURE 2 a) Forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratios and b) exhaled nitric oxide fraction (F_{eNO}) levels at age 12 years for the four growth trajectory classes (figure 1). *: significant differences ($p<0.05$) as compared with Class 1 using multivariate ANOVA (MANOVA). MANOVA tests were adjusted for sex, age, parental education, family income, household environmental tobacco smoke, birthweight, gestational age, breastfeeding and asthma oral steroid use.

Discussion

By using a novel statistical method (*i.e.* LGMM) we identified four growth pattern classes in Taiwanese children aged 6–11 years: normal growth class, rapid growth class, persistently overweight class and declining obesity class. Persistently overweight children exhibited a significantly increased risk of physician-diagnosed asthma, exercise-induced asthma and allergic rhinitis at age 12 years. Furthermore, our results suggest that the effects of being persistently overweight at age 6–11 years on asthma and rhinitis continued to adolescence and early adulthood. The period of childhood obesity at school age is critical for asthma and rhinitis later in life [30, 31].

Several studies have discovered that rapid growth during infancy significantly predicts asthma in early childhood. One study reported the critical period of infant growth to be between 0 and 2 years [6]. Other studies have indicated that this period is the first 3 months [32, 33]. Our findings that rapid growth in childhood at age 6–11 years did not significantly increase the risk of asthma are consistent with those of previous studies. Moreover, persistent overweight at age 6–11 years may originate from rapid growth in early childhood. Adiposity accumulation at age 6–11 years predicted a long-term effect on incident asthma at age 12, 15 and 18 years (table 4). This implies that the period of being overweight or obese may play different roles in the development of asthma [34]. The children in Class 2 did not exhibit a significantly increased risk of asthma, suggesting that rapid BMI growth in the age range 6–11 years might not be a critical period for asthma development. Weight reduction intervention studies have also reported that weight loss programmes facilitated enhancing symptom control of children with asthma and consequently reducing the use of rescue medications [35].

In the present study, persistently overweight children exhibited a significantly increased risk of allergic rhinitis. This risk can have long-term effects extending into young adulthood. The results of previous studies on the relationships between overweight and allergic rhinitis are not consistent. Certain studies have reported overweight as the risk factor for allergic rhinitis [14], whereas others have reported no associations between overweight and allergic rhinitis [36]. As a comorbidity of asthma, allergic rhinitis is a sequela of atopic diseases incident at the age of approximately 9–17 years. Two studies have reported significant relationships between overweight and allergic rhinitis only in children with wheeze symptoms [30, 37]. The heterogeneous findings of relevant studies may be due to the different prevalence and incidence rates of allergic rhinitis, and varied participant ages among different countries. Our result is supported by a Taiwanese study which reported that girls with high BMI exhibited an increased risk of rhinitis symptoms [38]. As a result of the high prevalence and incidence rates of allergic rhinitis in Taiwan, and the appropriate age group of participants, our longitudinal study provides an adequate design for examining the relationships between persistent overweight and allergic rhinitis.

Children in Classes 2, 3 and 4 exhibited significantly lower pulmonary function performance levels compared with those in Class 1. A study reported inverse relationships between BMI and FEV_1/FVC ratios [39]. Obesity, particularly central obesity [17], might mechanically restrict the diaphragm and limit lung expansion, reflecting impaired lung function. Children in Class 4, despite experiencing a reduction in their

BMI z-scores, exhibited an extremely higher BMI, which might cause long-term obstruction to the airway, compared with children in Class 1. Previous longitudinal studies discovered that higher weight growth in childhood was associated with higher lung volumes but increased measures of obstruction (FEV_1/FVC) [32]. Our findings are consistent with one previous study which reported that in obese individuals, lung function was significantly lower in subjects with greater years of obesity [40]. The underlying mechanism of these associations might include abnormal growth and development of lungs or immunologic or adiposity-related systemic inflammatory effects. Therefore, weight loss programmes should be encouraged to prevent future pulmonary function impairment.

According to our literature review, this is the first study exploring the difference in the airway inflammation status among various growth trajectory classes. Airway inflammation was lower in children with increased BMI z-scores, but it was higher in children with lower BMI z-scores, compared with children in Class I. This finding demonstrating an inverse relationship between obesity and airway inflammation is consistent with the results of previous studies on adults [41] and children [42]. This is because obesity obstructs the airway, affecting the measurement of exhaled nitric oxide. In children demonstrating declined BMI z-scores, the effect of obstruction in the airway by adiposity could be recovered, leading to increased F_{eNO} levels.

The strengths of our study were its nationwide, representative and longitudinal design and follow-up until age 18 years with repeated measurements of BMI and outcomes of asthma and rhinitis. We tested our hypothesis by using two statistical models (logistic regression and DTHM), and the results from these models were consistent, confirming the robustness of our findings. In addition, we conducted pulmonary function tests and collected biomarkers of airway inflammation. A limitation of our study was the use of school health records for collecting body height and weight data of children aged 6–8 years. A validation analysis was conducted by comparing the differences between our measurements and those of the school nurse. We discovered a high correlation ($r=0.92$, $p<0.001$; data not shown) between these measurements, with only a slight difference occurring between the mean value of these measurements. Moreover, we could not consider the growth factor in early childhood, which might be a crucial period for the development of asthma. However, because the prominent age of onset of allergic rhinitis is approximately 9 years, our study design provides a suitable age group for examining the relationships between different growth patterns and rhinitis. We have also adjusted several perinatal factors, such as birthweight, gestational age and breastfeeding, in the model. Another limitation in this study is that the lack of significance of the risk of asthma in Class 4 is probably due to the relatively small population size (2.6%) in this class. In addition, although concurrent BMI might influence the relationships between BMI trajectory class and asthma outcomes, we did not adjust concurrent BMI in the model because it had high collinearity with BMI trajectory class.

In conclusion, persistently overweight children aged 6–11 years exhibited significantly increased risks of asthma and rhinitis, and this effect persisted into adolescence and early adulthood. Measures for preventing obesity should be initiated during school age to reduce the incidence of asthma and rhinitis in later life.

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