

Prevalence of respiratory and atopic disorders in Chinese schoolchildren

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Summary

Background Epidemiological surveys have shown that the prevalence of asthma in the Asian population is relatively low. Within the Chinese population, schoolchildren from Hong Kong were found to have the highest rate of asthma.

Objective To compare the prevalence of respiratory and atopic disorders, and to assess the role of atopy in the development of asthma, in Chinese schoolchildren from Hong Kong, Beijing and Guangzhou.

Methods Community-based random samples of schoolchildren aged 9–11 years from three Chinese cities (Hong Kong, Beijing and Guangzhou) were recruited for study using the International Study of Asthma and Allergies in Childhood (ISAAC) Phase II protocol. Subjects were studied by parental questionnaires ($n = 10902$), skin-prick tests ($n = 3479$) and skin examination ($n = 3479$).

Results The prevalence rates of current wheeze, speech limiting wheeze, rhinoconjunctivitis and flexural dermatitis were significantly more common in Hong Kong than in Beijing or Guangzhou. The atopy rate was also higher in Hong Kong (41.2%) than in Beijing (23.9%) or Guangzhou (30.8%). Atopy was strongly correlated with current wheeze (OR 7.74; 95% CI = 5.70–10.51). Subgroup analyses of children from Hong Kong revealed that children born in mainland China who had subsequently migrated to Hong Kong had a significantly lower rate of allergic symptoms and atopy than those children born in Hong Kong.

Conclusion Using a standardized written questionnaire along with a skin prick test and skin examination, we confirmed that the prevalence of asthma, allergic diseases and atopy was highest in schoolchildren from Hong Kong. Atopic sensitization is an important factor associated with asthma in Chinese children.

Keywords: asthma, atopy, ISAAC, children, Chinese

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Introduction

Asthma is one of the most common chronic disorders in childhood. Phase I of the International Study of Asthma and Allergies in Childhood (ISAAC) developed simple stan-

dardized methods for measuring prevalence of childhood asthma, allergic rhinitis and atopic eczema for international comparison [1]. The prevalence rates of asthma in 13–14-year-old schoolchildren were found to vary widely from the highest of 36.7% in Scotland to the lowest of 1.6% in India [2]. In general, the high rates of asthma symptoms were usually found in Western countries where the predominant language is English. In contrast, the prevalence of asthma

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and allergic disease in Asian populations has been reported to be lower than that in the West. Within the Chinese population, the prevalence rate of asthma was found to be highest in Hong Kong Chinese children [3]. The 12-month prevalence of wheeze in 13–14-year-old schoolchildren as identified by the ISAAC video questionnaire was 10.1% in Hong Kong, while the average rate in mainland China was only 2.0%, with the highest rate of 3.3% in Beijing and the lowest of 1.3% in Chongqing. A similar magnitude of difference was identified by the ISAAC written questionnaire [2]. Given the similar genetic background, environmental factors are likely to be important, resulting in the observed difference within the same ethnic group. The differences in the prevalence rates within and across different ethnic groups provide opportunities to study the potential environmental factors important in the pathogenesis of asthma and allergies.

ISAAC Phase II study has been designed to assess the prevalence of objective markers of atopic diseases and to investigate the possible determinants of atopic conditions in different population groups. A detailed protocol has been developed for use in 9–11-year-old children [4]. In the present paper, we report findings of a cross-sectional study in Chinese schoolchildren from three cities (Hong Kong, Beijing and Guangzhou) using the ISAAC Phase II written questionnaire supplemented with skin prick test and skin examination.

Subjects and methods

Study area and populations

The studies were conducted in three cities: Hong Kong (6.7 million inhabitants), Guangzhou (10 million) and Beijing (12 million). Guangzhou is situated approximately 200 km north of Hong Kong and has a similar climate to Hong Kong. In each of the cities, random samples of schoolchildren were recruited for the studies using primary schools as sampling units as described previously [3]. Schoolchildren aged 10 years (10 years 0 months to 10 years 11 months) were targeted for the study following the ISAAC protocol. In participating schools, students of grade 5 were selected for the study, as the majority of students would be in the target age range. A total of 11 608 children were invited to participate and 10 902 agreed to enrol in the study, representing an overall participation rate of 94% (Hong Kong, 97%; Beijing, 92%; Guangzhou, 93%).

Questionnaires

Each subject was given an ISAAC Phase II questionnaire [4] to be completed by the parents or guardians. The written questionnaire was translated into Chinese following the

ISAAC protocol. This involved an independent person who was bilingual to translate the original English questionnaire into Chinese. Another bilingual person then back translated this into English. The translated questionnaire was pilot tested in a group of parents, and necessary modifications were made before the survey was carried out. The ISAAC Phase II questionnaire asked for information on demography, symptoms of wheeze, asthma, rhinitis and eczema, along with various possible risk factors, including perinatal history, immunization history, family history of allergic diseases and environmental exposure. 'Current' symptoms referred to symptoms in the past 12 months. For those subjects recruited in Hong Kong, an additional question on the place of birth was also included, as a proportion of children are recent immigrants from China. Subgroup analyses will allow us to detect any possible effect of migration from mainland China to Hong Kong.

Skin prick test and physical examination

In Hong Kong and Guangzhou, 2023 (65%) and 2823 (79%) subjects also gave consent for skin prick test, respectively. Random subgroups of at least 1000 subjects were recruited from Hong Kong and Guangzhou for skin prick test. In Beijing, 1063 subjects from 13 schools were invited for skin prick test and 1044 (98%) gave consent to be tested. The sensitivity to eight common aeroallergens was assessed: *Dermatophagoides pteronyssinus*, *D. farinae*, cat, *Alternaria tenuis*, mixed tree pollen, mixed grass pollen, cockroach, and mixed moulds. Standardized allergen extracts and control solutions were obtained from ALK (Hørsholm, Denmark). Histamine (10 mg/mL) and diluent were used as positive and negative control. A drop of each allergen extract was brought into the skin of the volar side of the left forearm using ALK lancets. After 15 min, the weal reaction was measured as the mean of the longest diameter and the length of the perpendicular line through its middle. A weal size ≥ 3 mm after subtraction of the negative control is considered positive. Subjects with one or more positive reactions were considered atopic. All children who underwent skin prick tests were also examined for visible flexural dermatitis according to a photographic protocol as described in the ISAAC Phase II protocol [4]. The following five sites were examined for the presence or absence of signs of flexural dermatitis: (a) around the eyes; (b) around the sides and front of the neck; (c) in front of elbows; (d) behind the knees; and (e) in front of the ankles.

The written questionnaire surveys were conducted between October 1997 and February 1998. Skin prick tests and skin examinations were performed between March and May 1998. The study protocol was approved by the ethics committees of the participating institutions. Informed parental consent was obtained from parents or guardians before the studies were carried out.

Data analyses

All data were entered into a computer twice by two independent investigators. Data were categorized and analysed using the Statistical Package for the Social Sciences (SPSS) for windows [5]. The chi-squared test was used to compare prevalence rates between study areas. Logistic regression with adjustment for age and gender was used to estimate risk factors for various atopic symptoms. Estimates of odds ratio (ORs) and 95% confidence intervals (95% CIs) were based on asymptomatic likelihood theory. A *P*-value less than 0.05 was considered to be significant.

Results

The age and sex distributions of participating children in the three cities are shown in Table 1. Prevalence estimates of symptoms and diagnoses of asthma were lower in Beijing and Guangzhou than in Hong Kong, reaching statistical significance for the following symptoms in the past year: wheeze, speech-limiting wheeze, exercise-induced wheeze, runny nose with itchy eyes (rhinoconjunctivitis) and flexural dermatitis (Table 2). In line with the questionnaire results, visible signs of flexural dermatitis were significantly more prevalent in Hong Kong (3.4%) than in Beijing (1.1%) or Guangzhou (0.8%).

A total of 3479 children from three cities underwent skin prick tests. The prevalence of allergic symptoms and

asthma in the subgroup of children from Hong Kong and Beijing who also underwent skin testing was not significantly different from that in the whole group. For children recruited from Guangzhou, the prevalence of current wheeze and asthma ever was higher than that in the whole group from Guangzhou who participated in the written questionnaire survey. Atopy defined as having at least one positive skin test was significantly more common in Hong Kong when compared with Beijing and Guangzhou (Table 3). In particular, sensitivity against *D. pteronyssinus* and *D. farinae* were significantly more common in Hong Kong than in Beijing or Guangzhou. The prevalence of sensitivity against mixed moulds was highest in Beijing and it was significantly higher than in Hong Kong or Guangzhou. Multiple logistic regression analyses revealed that atopy was strongly correlated with current wheeze (OR 7.74; 95% CI = 5.70–10.51; *P* < 0.001), current rhinoconjunctivitis (OR 2.76; 95% CI = 2.23–3.41; *P* < 0.001), current flexural dermatitis (OR 2.54; 95% CI = 1.59–4.07; *P* < 0.001) and asthma ever (OR 5.06; 95% CI = 3.88–6.60; *P* < 0.001).

For those subjects recruited in Hong Kong, 511 children (16%) were born outside and subsequently emigrated to Hong Kong. Most (440, 86%) of them were born in the southern coastal provinces of mainland China. For these 440 subjects, the median age of migration to Hong Kong was 3.4 years. Being born in Hong Kong was significantly associated with current wheeze (OR 4.07; 95% CI = 1.93–8.97; *P* < 0.001), current rhinoconjunctivitis (OR 1.70; 95% CI = 1.24–2.34; *P* < 0.001) and current flexural dermatitis (OR 2.42; 95% CI = 1.23–4.93; *P* = 0.006). Table 4 shows the differences of responses to the questionnaire between children born in Hong Kong and mainland China. Most parameters of allergic symptoms were significantly more common in children born in Hong Kong. Table 5 shows the differences in atopy rate and allergic sensitization between the two subgroups. Children born in Hong Kong had a significantly higher rate of atopy and allergic sensitization to *D. pteronyssinus* and *D. farinae*. The prevalence rates of sensitization to various antigens in children born in mainland China were similar to those in Guangzhou or Beijing (Table 3). For those subjects who also underwent skin testing (*n* = 1341), being born in Hong Kong remained significantly associated with current wheeze even after adjustment for their atopic status (OR 2.86; 95% CI = 1.05–7.79; *P* = 0.04).

Discussion

The prevalence of asthma and allergic diseases in childhood has been extensively investigated in different parts of the world. Many surveys consistently reported an increase in the prevalence of asthma in the UK, Australia,

Table 1. Demographic characteristics of the study population

	Hong Kong		Beijing		Guangzhou	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
<i>Written questionnaire</i>						
<i>Age (yr)</i>						
< 9	63	2.0	8	0.2	164	4.6
10	2454	78.9	2756	65.2	3205	89.9
> 11	593	19.1	1463	34.6	196	5.5
<i>Sex</i>						
Male	1659	53.3	2139	50.6	1780	49.9
Female	1451	46.7	2088	49.4	1785	50.1
Total	3110	–	4227	–	3565	–
<i>Skin test & examination</i>						
<i>Age (yr)</i>						
≤ 9	29	2.1	3	0.3	48	4.3
10	1228	91.6	708	67.8	1041	95.2
≥ 11	84	6.3	333	31.9	5	0.5
<i>Sex</i>						
Male	711	53.0	528	50.6	591	54.0
Female	630	47.0	516	49.4	503	46.0
Total	1341	–	1044	–	1094	–

Table 2. Prevalence of symptoms and diagnoses of respiratory and allergic disorders and of visible flexural dermatitis in schoolchildren by study area

	Hong Kong		Beijing		Guangzhou	
	%	95% CI	%	95% CI	%	95% CI
Symptoms in last 12 months						
Wheeze*	5.8	5.0–6.7	3.8	3.3–4.4	3.4	2.8–4.1
≥ 4 attacks of wheezing	1.4	1.0–1.9	0.9	0.6–1.2	0.5	0.3–0.8
Speech limiting wheezing*	1.8	1.3–2.3	0.5	0.3–0.7	0.4	0.3–0.7
Exercise-induced wheezing*	7.7	6.8–8.7	4.5	3.9–5.2	3.1	2.5–3.7
Runny nose with itchy eyes*	15.0	13.9–16.4	6.7	5.9–7.5	7.4	6.6–8.3
Flexural dermatitis*	3.8	3.1–4.5	2.2	1.8–2.7	1.8	1.4–2.3
Asthma ever	7.7	6.8–8.6	6.4	5.7–7.2	4.4	3.8–5.1
Visible flexural dermatitis (n)*		1341		1044		1094
Yes	3.4	2.5–4.5	1.1	0.5–1.9	0.8	0.4–1.6

* The prevalence rates of these symptoms and signs were significantly higher ($P < 0.01$) in Hong Kong than in Beijing or Guangzhou.

Scandinavia, Israel and Taiwan [6–12]. Phase I of the ISAAC developed a standardized questionnaire to measure prevalence of various childhood allergic conditions, such that meaningful international comparisons were possible. ISAAC Phase I results revealed that the prevalence rates of asthma vary widely across the world. For children aged 13–14 years, the highest prevalence was about 20 times

higher than in the centre with the lowest prevalence, with an eight-fold variation seen between the 10th and 90th percentiles (3.9–30.6%) [13]. Similar variations in the prevalence rates of allergic rhinitis and eczema were noted. These wide variations of asthma prevalence between populations and the recent increasing trend within populations are unlikely to be explained by genetic factors.

Table 3. Prevalence of symptoms and atopic sensitization in schoolchildren who had skin prick tests in the three cities

	Hong Kong		Beijing		Guangzhou	
	%	95% CI	%	95% CI	%	95% CI
Symptoms in last 12 months						
Wheeze	8.2	6.2–9.8	3.4	2.4–4.6	8.5	6.9–10.3
Runny nose with itchy eyes	16.8	14.8–18.9	7.9	6.3–9.7	9.1	7.4–10.9
Flexural dermatitis	5.3	4.2–6.6	1.8	1.1–2.8	2.7	1.8–3.8
Asthma ever	9.6	8.1–11.3	6.3	4.9–8.0	8.5	6.9–10.3
Atopic sensitization						
Atopy						
≥ 1 positive skin test*	41.2	38.6–43.8	23.9	21.4–26.6	30.8	28.1–33.7
<i>D. pteronyssinus</i> *	34.1	31.5–36.7	7.5	5.9–9.3	20.0	17.7–22.5
<i>D. farinae</i> *	25.9	23.6–28.3	5.7	4.3–7.2	17.9	15.7–20.3
Cat	3.7	2.8–4.9	5.6	4.3–7.1	4.3	3.2–5.7
Cockroach	11.5	9.8–13.3	13.3	11.3–15.6	17.3	15.1–19.7
Mixed grass pollen	0.7	0.4–1.4	1.2	0.7–2.1	1.1	0.6–1.9
<i>A. tenuis</i>	0.4	0.1–0.9	1.5	0.9–2.5	0.9	0.4–1.7
Mixed moulds	0.4	0.2–1.0	3.2	2.2–4.4	1.2	0.6–2.0
Mixed tree pollen	0.1	0.0–0.4	1.0	0.5–1.8	0.5	0.2–1.2

*Atopy and sensitization to *D. pteronyssinus* and *D. farinae* were significantly more common ($P < 0.01$) in Hong Kong than in Beijing and Guangzhou.

Table 4. Comparison of children born in Hong Kong and mainland China: response to written questionnaire within the group of subjects recruited from Hong Kong

	Mainland China <i>n</i> = 440		Hong Kong <i>n</i> = 2599		OR*
	%	95% CI	%	95% CI	
Asthma ever	2.1	0.9–3.8	8.6	7.6–9.8	0.22
Wheeze ever	3.9	2.3–6.1	13.0	11.8–14.4	0.27
Wheeze in past year	1.4	0.5–2.9	6.5	5.6–7.5	0.20
Exercise-induced wheeze in past year	6.6	4.6–9.3	8.0	7.0–9.1	NS
Nocturnal cough in past year	7.1	4.8–9.8	15.0	13.7–16.5	0.43
Rhinitis ever	12.3	9.3–15.7	35.2	33.4–37.1	0.26
Rhinitis in past year	16.4	13.0–20.1	30.0	28.2–31.9	0.46
Rhinoconjunctivitis in past year	9.1	6.6–12.2	16.2	14.8–17.6	0.52
Itchy rash ever	3.6	2.1–5.8	6.1	5.2–7.1	NS
Itchy rash in past year	1.8	0.8–3.6	5.0	4.2–5.9	0.35
Itchy flexural rash in past year	1.1	0.4–2.6	4.3	3.6–5.2	0.26
Eczema ever	11.6	8.8–15.0	19.3	17.8–20.8	0.55

95% CI = 95% confidence interval; OR = odds ratio; NS = not significant. *All parameters except as specified as NS are significantly lower ($P < 0.01$) in children born in mainland China.

Environmental factors are likely to be more important, such that modification of these environmental factors offers possible opportunities for prevention. The Phase II ISAAC protocol has been developed to assess the possible environmental risk factors, which could be important in the pathogenesis of asthma. Measures of bronchial hyper-responsiveness and skin testing are also being used to determine whether they support the questionnaire results. As documented in the Phase I study, the Chinese population in different regions had a four-fold difference in asthma prevalence in children aged 13–14 years. Hong Kong has

the highest prevalence rates of asthma, allergic rhinitis and eczema among the Chinese centres that participated in the survey [2]. Such differences in the prevalence rates within a specific ethnic group offer great opportunity to study the possible environmental risk factors.

The results of this study confirmed that the prevalence rates of wheeze, rhinoconjunctivitis and flexural dermatitis were more common in Hong Kong than in Beijing or Guangzhou. For the first time in the Chinese population, the questionnaire results were confirmed by physical examination demonstrating that schoolchildren in Hong

Table 5. Comparison of children born in Hong Kong and mainland China: rate of atopy and allergic sensitization within the group of subjects recruited from Hong Kong for skin prick tests

Allergen*	Mainland China <i>n</i> = 109		Hong Kong <i>n</i> = 1232		OR
	%	95% CI	%	95% CI	
Atopy					
≥ 1 positive skin test result	22.0	14.6–31.0	42.9	40.5–45.7	0.38
<i>D. pteronyssinus</i>	15.6	9.4–23.8	35.7	33.1–38.4	0.33
<i>D. farinae</i>	12.8	7.2–20.6	27.0	24.6–29.6	0.40
Cockroach	13.8	7.9–21.7	11.3	9.6–13.2	NS

95% CI = 95% confidence interval; OR = odds ratio; NS = not significant.

*The prevalence rates of atopy, sensitization to *D. pteronyssinus* and *D. farinae* were significantly lower ($P < 0.01$) in children born in mainland China. Sensitization to other allergens tested was uncommon (data not shown) and not significantly different between the two groups of children.

Kong have the highest prevalence of visible flexural dermatitis. Within the group of children recruited from Hong Kong, children born in Hong Kong have higher prevalence of current wheeze, rhinoconjunctivitis and flexural dermatitis than those children born in mainland China and subsequently emigrated to Hong Kong (Table 4). The prevalence rates of various atopic symptoms of children born in mainland China were comparable with those of children from Beijing or Guangzhou. Since these children were exposed to living conditions in China before emigrating to Hong Kong, the differences in the prevalence rates of various symptoms confirm that early life experience and environmental factors are important determinants of subsequent development of asthma and allergic diseases. Either risk factors in Hong Kong or protective factors in mainland China could be responsible for the differences.

The results of the skin prick test revealed that atopy and allergic sensitization to *D. pteronyssinus* and *D. farinae* were more common in Hong Kong than in Beijing or Guangzhou. The differences in the prevalence of atopy and allergic sensitization could not be explained by the differences in the age and sex distribution of the study populations. There was selection bias in the group recruited from Guangzhou because subjects who underwent skin testing had higher prevalence of current wheeze and asthma ever when compared with the whole group from Guangzhou who participated in the questionnaire survey. Despite such bias, the atopy rate and prevalence of allergic sensitization to house dust mite are still significantly higher in Hong Kong than in Guangzhou (Table 3). Furthermore, seasonal variation could not be the reason for the differences because skin prick tests were carried out in the same season (spring, 1998) of the year in all three cities.

In line with the questionnaire results of asthma and allergic symptoms, the prevalence of atopy and sensitization to house dust mite of children born in mainland China who subsequently emigrated to Hong Kong were similar to those of schoolchildren from Beijing and Guangzhou. In contrast, sensitivity to moulds and tree pollen were more commonly found in Beijing than in Hong Kong. Hong Kong is a highly urbanized city and most people live in multi-storey apartments; therefore, it is not surprising that sensitivity to tree pollen is relatively uncommon.

A recent study of 9–11-year-old children from Leipzig, a city of former East Germany, demonstrated significant increase in atopic sensitization but no significant change in the prevalence of asthma or bronchial hyper-responsiveness 5 years after German unification [14]. Their results suggested that factors operating early in life may be particularly important for the development of childhood asthma, whereas the prevalence of atopic sensitization may be affected by environmental exposure occurring beyond

infancy in addition to early life factors. In our study sample of children born in mainland China who subsequently migrated to Hong Kong, the majority (85%) of them moved to Hong Kong after their first birthday and the median age of migration was 3.4 years. The lower prevalence of allergic sensitization in these children compared with those born in Hong Kong suggested that early life experience is also an important determinant of development of atopy and allergic sensitization in our population.

There has only been one small comparative study of Chinese children investigating the role of atopy in the manifestations of allergic diseases [15]. In that study, a total of 2208 Chinese schoolchildren aged 12–18 years were recruited from Hong Kong, Malaysia and San Bu, China. Written questionnaires on respiratory and allergic symptoms were completed by parents and a subsample ($n = 1442$) underwent skin prick testing to common inhaled allergens. The prevalence of asthma was highest in Hong Kong (7% for asthma ever), intermediate in Malaysia (3%) and low in San Bu (2%). The atopy rate in Hong Kong (58%) was significantly higher than in San Bu, China (49%). Furthermore, a higher proportion of students in Hong Kong had severe degree of reactivity on skin test than the other two populations. However, the prevalence of atopy in Malaysia was very high (64%) and yet the prevalence of asthma was low. Nevertheless, within each study population, allergen sensitization remained a significant risk factor associated with asthma. The difference in the atopy rate of the current study and the previous study could be due to difference in the age ranges of the studied subjects, different sources of the allergen extracts used for skin testing, as well as the total number of antigens being tested.

Although the importance of atopy as a determinant of asthma has been questioned, cross-sectional studies in Caucasian children suggested that 25% to 63% of asthma cases could be attributable to atopy [16]. Our results clearly demonstrated that the prevalence of asthma symptoms and atopy were highest in Hong Kong. The prevalence rates of asthma symptoms and atopy in the subgroup of children born in mainland China who subsequently emigrated to Hong Kong were also significantly lower than those born in Hong Kong. We have also demonstrated a significant correlation between atopy and allergic symptoms, including wheezing, rhinoconjunctivitis and flexural dermatitis. Therefore, the difference in the prevalence of allergen sensitization and atopy among different Chinese populations may be one of the factors contributing to the differences in the prevalence of asthma and allergies. However, the difference in atopy rate cannot be explained by the difference in allergen exposure because we previously have shown that domestic indoor levels of aero-allergens in Hong Kong and Guangzhou were similar [17]. In addition to allergen exposure, other factors such as

early viral infections, breast feeding and dietary factors are likely to modify the susceptibility in the development of allergen sensitization.

Since the diagnosis of asthma is primarily made on the basis of combined information from history, physical examination and respiratory function tests [18], the method of choice for population prevalence comparisons is still the use of standardized written or video symptom questionnaires. Testing for bronchial hyper-responsiveness (BHR) is only used as a supplement to such questionnaires in epidemiological surveys. We have previously validated that the ISAAC video questionnaire and ISAAC written questionnaire correlated with BHR in secondary schoolchildren in Hong Kong [19]. The age group of the current study is different from those children in the previous study. Therefore, further validation study for the prediction of BHR by the ISAAC written questionnaire in the age group of the current study is necessary.

In conclusion, we have evaluated three populations of Chinese schoolchildren using a standardized written questionnaire supplemented with skin prick test and skin examination. We confirmed that the prevalence of asthma, allergic diseases and atopy was highest in schoolchildren from Hong Kong. Our findings support the importance of early life experience in the development of allergic sensitization and asthma. Although the role of atopy as a determinant of asthma has been questioned, the results of skin prick tests suggest that atopic sensitization is an important factor associated with the development of asthma in our population. Data on present and previous living and exposure conditions of the subjects have been collected by written questionnaires. Subgroups of children have also been recruited for bronchial challenge tests. Further aetiological analyses will be performed to reveal the possible determinants for asthma, atopy and bronchial hyper-reactivity in Chinese children.

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