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Migrant status and childhood hospitalizations for asthma and other wheezing disorders

RUNNING HEAD

Migrant status and childhood wheezing disorders

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ABSTRACT

Background

In developed Western settings, asthma is more prevalent among second-generation compared to first-generation migrants. However, these studies are difficult to interpret as they include migrants of various ethnicities and countries of origin.

Objective

We assessed the association of parental migrant status with wheezing disorders among children born in Hong Kong, a developed non-Western setting, where many children have migrant parents from mainland China of the same ethnicity.

Methods

We used Cox regression to examine the adjusted associations of parental migrant status with time to first public hospital admission for asthma, bronchitis and bronchiolitis (International

Classification of Diseases, Ninth Version Clinical Modification 466, 490 and 493) from 9 days to 12 years in a population-representative birth cohort of 8327 Chinese children in Hong Kong.

Results

Having both parents as migrants was associated with higher risk of hospitalization for asthma and other wheezing disorders, compared to both parents being Hong Kong born (hazard ratio 1.30, 95% confidence interval 1.05 to 1.60 from 9 days to 6 years), adjusted for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth, and highest parental education.

Conclusions and Clinical Relevance

In the unique, non-Western context of Hong Kong, second-generation migrants had higher risk of hospitalization for childhood wheezing disorders compared to the native population, particularly before 6 years of age. Further study is required to clarify the underlying mechanisms involved.

KEY WORDS

Asthma, epidemiology, migration, paediatrics, wheeze

INTRODUCTION

Asthma is a heterogeneous disorder characterized by recurrent, reversible airway obstruction, typically presenting with wheeze.(1, 2) It is the most common chronic disease in children.(2)

The aetiology of childhood wheezing disorders remains poorly understood; yet increasing prevalence rates in low-and-middle-income countries and striking differences in prevalence between countries suggest that yet to be discovered environmental or social factors could play an important role.(2, 3)

Migrant populations provide a natural experiment that may help to elucidate the geographic differences and secular trends in asthma.(4) Migrants to more affluent countries tend to have better health than the native or host population, known as the “healthy migrant effect”.(5-7)

However, this advantage generally dissipates with time as migrants acquire behaviours and attitudes of the native culture, a process termed “assimilation” or “acculturation”,(5, 8) or lose beneficial early life environments from their place of origin. A recent systematic review showed that asthma prevalence is lower in migrants than the native population, and higher in second-generation migrants (native-born children with at least one migrant parent) than first-generation migrants (non-native born children), such that second-generation migrants have similar rates of asthma compared to the native population.(9) Nonetheless, most studies thus far are based on developed Western countries and include migrants of various ethnicities and countries of origin, making it difficult to distinguish between the effects of attributes of migrants, assimilation,(9) and place of origin. Few studies have directly compared second-generation migrants with the native population (native-born children with native-born parents) within ethnically homogeneous populations.

Hong Kong is a developed non-Western setting with a predominantly Chinese (>95%) population, largely formed by migration from southern China in the mid-20th century, who experienced rapid economic transition from pre-industrial to post-industrial conditions over a lifetime.⁽¹⁰⁾ The prevalence of asthma is significantly higher in Hong Kong than other cities in China.⁽¹¹⁾ Grandparents and parents of children in Hong Kong may have experienced significant social re-assortment upon migration, which could affect health down the generations.⁽¹⁰⁾ Hong Kong thus enables the assessment of migration not only within an ethnically homogeneous population, but also in the unique context of its history, which has generated different patterns of confounding from those found in more commonly studied, similarly developed populations. Here we took advantage of a population-representative Chinese cohort, “Children of 1997”, to examine the associations of parental migrant status with hospitalizations for asthma and other wheezing disorders to 12 years of age. To clarify the role of language or other cultural factors, we also assessed whether parental place of birth was associated with hospitalizations for asthma and other wheezing disorders. In particular, language barriers could influence health care seeking behaviours. Cantonese, the regional dialect, is widely used in Hong Kong and neighbouring Guangdong province. The Hong Kong population largely shares culture and ethnicity with Guangdong province, although Hong Kong also has a distinct identity from the rest of China due to its unique history as a British colony.

MATERIALS AND METHODS

Sources of data

The “Children of 1997” is a population-representative Chinese birth cohort (n=8327), covering 88% of all births in Hong Kong from 1 April 1997 to 31 May 1997.⁽¹⁰⁾ The study was initially designed to examine the effects of second-hand smoke exposure and breastfeeding on infant health services utilization. Mother-infant pairs were recruited at the first postnatal visit to any of the 49 government’s Maternal and Child Health Centres in Hong Kong, which parents of all

newborns are encouraged to attend for free preventive care and vaccinations. Baseline characteristics obtained at recruitment included birth and parental characteristics, parental migration and parental education, using a standardized, self-administered questionnaire in Chinese completed by the primary caregiver (most commonly mothers). Follow-up questionnaires were administered at 3, 9 and 18 months. In 2007, a program was instituted to re-establish direct contact with the birth cohort families, and three postal surveys (surveys I to III) were conducted between 2008 and 2012. Surveys I and III both included questions about the mother's and father's place of birth. Any missing data were updated with each wave of data collection and any discrepancies between waves reconciled.

Hospital discharge data were obtained by record linkage from the Hospital Authority, which oversees all public hospitals and provides in-patient services accounting for about 90% of total bed days and 77% of all admissions in Hong Kong.⁽¹²⁾ All Hong Kong citizens are entitled to public healthcare with minimal out-of-pocket payments. Discharge records contain the date of each hospital admission and discharge, name of hospital, principal and secondary diagnoses or reasons for admission, and principal medical procedures.

Exposures

We obtained information on parental migrant status from surveys I and III in answer to the question "Where was each of your child's parents born?", supplemented by information from the baseline questionnaire (parental age, year of parental migration to Hong Kong and residency eligibility). Parental migrant status was categorized as both parents Hong Kong born (corresponding to the native population), one parent migrant, or both parents migrant (corresponding to second-generation migrant). Additionally, we assessed the associations of

mother's and father's place of birth, categorized as Hong Kong, Guangdong province in China, outside Guangdong province in China, and others.

Outcomes

Our primary outcome was public hospital admission for asthma or other wheezing disorders during 9 days to 12 years of age. Admissions were coded by physicians at discharge according to the International Classification of Diseases, Ninth Version Clinical Modification (ICD-9CM). We defined asthma and other wheezing disorders as a diagnosis of acute bronchitis and bronchiolitis (ICD-9CM 466), bronchitis, not specified as acute or chronic (ICD-9CM 490) and asthma (ICD-9CM 493). As a secondary outcome, we also considered asthma as ICD-9CM 493 only. We further considered hospitalizations to 2 years and 6 years so as to assess if associations varied by age,(13) and because the diagnosis of asthma is less reliable in children younger than 6 years.(14)

We included both day-patient and in-patient admissions. Children with no record of hospitalization were assumed to have none, although non-public hospital admission is possible but not obtainable by record linkage. We excluded hospitalizations occurring within the first 8 days of life for consistency with our previous studies. Also, as the average hospital stay of infants following Caesarean section was 7.9 days, the inclusion of hospitalizations in the immediate neonatal period could have introduced bias.

We used hospitalizations for accidents or injuries (ICD-9CM 800 to 999 or E800 to E999) as a negative control outcome,(15) because we would not expect parental migration status to be

associated with accidents or injuries. With adequate control for confounding, there should be no association of parental migrant status with hospitalizations for accidents or injuries.

Statistical analysis

We used Cox regression to examine the adjusted associations of parental migrant status and parental place of birth with time to first hospitalization, from which we report the hazard ratios (HRs) for hospitalization with associated 95% confidence intervals (CIs). Children who had withdrawn from the study were excluded, and children who died were censored at the date of death. The proportional hazards assumption was checked by Schoenfeld's global test and visual inspection of plots of $\log(-\log S)$ against time, where S is the estimated survival function. Our sample size was sufficient to detect an HR of 1.35 or 0.74 for the smallest group (one parent migrant), assuming power of 80% and an alpha of 0.05.

Model 1 was unadjusted. Model 2 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth. Model 3 further adjusted for socioeconomic position or SEP. Highest parental education was used as a proxy for early life parental SEP, which usually precedes parental migration. We also assessed whether associations varied by type of hospital at birth from the heterogeneity across strata and the significance of interaction terms. We used multiple imputation for migrant status (6.4% missing), mother's place of birth (5.8% missing), father's place of birth (4.8% missing), and potential confounders (2.7% to 4.6% missing) based on a flexible additive regression model with predictive mean matching, incorporating data on the exposures, outcomes, and potential confounders.⁽¹⁶⁾ We summarized the results from 20 imputed data sets into single estimated HRs with CIs adjusted for missing data uncertainty.⁽¹⁷⁾ As a sensitivity analysis, we performed an available case analysis for comparison, i.e. pairwise deletion of observations with missing

data. As participants with migrant parents were more likely to have left Hong Kong than those with non-migrant parents, and would therefore not attend hospital in Hong Kong, we also restricted our analysis to participants who had most likely remained in Hong Kong from birth to 12 years, i.e. those who had attended the government's Student Health Service at 12 years. Statistical analyses were conducted using Stata, version 13.0 and R, version 3.1.0.

Ethics approval was obtained from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

RESULTS

Of the original 8327 in the cohort, 29 had permanently withdrawn, 117 were known to have migrated without further contact, and 23 were known to have died as of January 2016. Of the 8298 children who remained in the study, 671 (8.1%) had a first hospitalization from 9 days to 12 years, including 429 admissions for acute bronchitis and bronchiolitis (ICD-9CM 466), 16 for bronchitis, not specified as acute or chronic (ICD-9CM 490), 219 for asthma (ICD-9CM 493), and 7 for both ICD-9CM 466 and 493. The mean age at first hospitalization was 2.1 years.

Table 1 shows the baseline characteristics of participants by parental migrant status. Most children (54.4%) had parents who were both Hong Kong born, while 20.9% had one migrant parent, and 24.6% had both parents who were migrants. Children whose parents were Hong Kong born were more likely to have been born in non-public hospitals, to have had a parental history of allergies, older mothers, younger fathers and higher parental education than children whose parents were migrants.

Table 2 shows the adjusted associations of parental migrant status with time to first hospitalization for asthma and other wheezing disorders. From 9 days to 6 years, both migrant parents were associated with higher risk of hospitalization compared to both native parents (HR 1.36, 95% CI 1.11 to 1.67), adjusted for, type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth. Further adjustment for parental SEP slightly attenuated this association (HR 1.30, 95% CI 1.05 to 1.60). Estimates from 9 days to 2 years and 12 years were similar, although estimates for >6 years to 12 years were somewhat different. One parent migrant had no clear associations with hospitalizations.

Table 3 shows the adjusted associations of parental migrant status with time to first hospitalization for asthma only. Both parents migrant was associated with higher risk of hospitalization for asthma only from 9 days to 6 years (HR 1.49, 95% CI 1.12 to 1.99). Adjustment for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth, and highest parental education attenuated the association. Estimates from 9 days to 2 years and 12 years were similar, although estimates from >6 years to 12 years were somewhat different. The available case analysis also yielded similar results overall (Tables S1 and S2).

There were no associations of parental migrant status with hospitalizations for accidents or injuries at any age (Table S3). Estimates were consistently close to null.

Children whose mothers were born outside the neighbouring Guangdong province in China had higher risk of hospitalization for wheezing disorders from 9 days to 12 years (Table 4), but adjustment for potential confounders attenuated the association. We did not find associations of father's place of birth with wheezing disorders (Table 5), although estimates for birth outside

Guangdong province in China were in the direction of higher risk. Estimates were similar for asthma only (Tables S4 and S5). None of the above associations varied by type of hospital at birth (data not shown).

DISCUSSION

In this population-representative Chinese birth cohort in the unique non-Western economically developed setting of Hong Kong, second-generation migrants had higher risk of hospitalization for childhood wheezing disorders than children with native born parents, particularly before 6 years of age. Estimates for children whose parents were born outside the neighbouring Guangdong province in China were also in the direction of higher risk, compared to children with Hong Kong-born mothers.

Our findings are largely consistent with two observational studies in Europe and North America,(18, 19) showing higher risk of asthma among second-generation migrants compared to native-born children with native-born parents. A cross-sectional study in Sweden showed higher risk of asthma medication among native-born children with migrant parents from South Asia (odds ratio 1.26, 95% CI 1.16 to 1.37), but not parents who migrated from elsewhere, potentially suggesting a genetic propensity for asthma among the South Asian population.(18) On the other hand, other cross-sectional studies have not found associations of second-generation migrant status with asthma or wheeze among children in Italy(20, 21) and the United States,(22) although these studies did not distinguish between ethnicity or parental nativity.(9) Another cross-sectional study in the United States showed that while children born to migrant mothers had lower risk of reported asthma than did children of American mothers, children of non-Mexican Hispanic mothers were more likely to have asthma than children of non-Hispanic white mothers.(23) Similarly, a survey of children born in Australia showed that children born to Asian-born mothers had higher risk of food allergy than children whose

mothers were born in Australia, New Zealand or England.(24) Parental nativity, or country of origin, predicted risk of asthma or allergy, potentially because the health of migrants reflects the general environmental and socioeconomic conditions of their countries of origin.(23) In addition, language barriers and/or less access to health care among migrant parents could have led to under-reporting of asthma or wheeze.(20, 21, 23) Finally, reverse causation is a limitation of all cross-sectional studies; it is possible that wheeze preceded migration, especially among children whose families had only recently migrated.

In addition to being prospective and population-representative, our cohort has the advantages of being ethnically homogeneous with a low attrition rate (0.3%). Participants in the cohort were all entitled to free MCHC services and highly subsidized public hospital services in Hong Kong; thus, differential access to care by parental migrant status was unlikely. Cases of childhood wheezing disorders were ascertained from physician-coded diagnoses, avoiding bias from self-report. Nonetheless, several limitations deserve discussion. First, hospitalizations generally represent relatively severe or poorly controlled cases. We can therefore only provide a comparison of rates, and not an estimate of the absolute effect of parental migrant status on wheezing disorders. Second, we do not have information on admissions to non-public hospitals, which may be more likely for families with non-migrant parents or higher SEP. As in previous studies,(13, 25) we adjusted for indicators of non-public hospital use (type of hospital at birth and SEP), which means we have compared children within type of hospital use and SEP. Furthermore, public hospitals account for the majority of hospitalizations in Hong Kong, and the associations of parental migrant status or place of birth with hospitalizations did not vary by type of hospital at birth. Third, residual confounding is possible, and we did not have information on all factors that could affect both parental migration and current risk of wheezing disorders. However, we attempted to minimize confounding by adjusting for a range of confounders, including parental SEP. We did not find associations of parental migrant status

with hospitalizations for accidents or injuries, suggesting adequate control for SEP. Fourth, the diagnosis of asthma and wheezing disorders is difficult, especially in younger children, because of non-specific symptoms and the lack of definitive diagnostic tests. We have thus included and excluded hospitalizations for bronchitis and bronchiolitis in our analysis, obtaining similar results using both outcomes. We have also considered time to first hospitalization to 2 years, 6 years and 12 years, again arriving at similar results for both definitions. Misclassification of wheezing disorders is possible, but bias would not be a concern unless the physician based the diagnoses on the parents' migrant status, which is unlikely. Fifth, our estimates for one-parent and both-parents migrants were in the direction of lower risk from >6 years to 12 years, contrary to our results from 9 days to 2 years, 6 years and 12 years. However, the available case analysis yielded estimates in the direction of higher risk for both parents migrant. To account for the possibility that participants with migrant parents were more likely to have left Hong Kong than non-migrant families, we restricted our analysis to participants who were in Hong Kong at 12 years and found similar results (data not shown). It is possible that migrant parents were more likely to have difficulty completing the questionnaires, generating more missing data on migrant status than non-migrant parents. Nonetheless, given the small number of events from >6 years to 12 years, these results should be interpreted with caution. Sixth, we do not have information on whether attendance at the MCHCs differed by parental migrant status, although differential access to care is unlikely as the service is free of charge. Finally, we did not distinguish between third and higher-generation migrants among the children with Hong Kong-born parents. However, only 7.2% of these children had Hong Kong-born grandparents, and we only had information on grandparental migrant status for 57% of participants.

Evidence from developed Western settings shows that first-generation migrants to countries with higher asthma prevalence initially have lower prevalence of asthma, but this prevalence gradually approximates that of the host population over time.(5, 9) The underlying mechanisms remain unclear, although environmental factors of the host country, such as exposure to different air pollutants, are thought to play a role in reprogramming the immune system.(5, 9)

Our prospective study within an ethnically homogeneous population further shows that the risk of wheeze among second-generation migrants could even exceed that of the native population.

We suggest several possible explanations for our findings. First, migrants may have experienced different exposures in early life, which could result in adaptive responses of the offspring's immune system that lead to permanent changes in lung development.(26) Second, the process of migration itself may have induced higher levels of maternal stress, which could modulate immune system and lung development in the offspring.(27) Third, the effects of acculturation, or the changes that migrants experience as they adopt the culture of the host society,(28) may extend beyond first-generation migrants and apply even to ethnically homogeneous populations. China is a culturally heterogeneous country with distinct provincial and regional identities,(29) whereas Hong Kong's unique history as a former British colony has produced a community of Chinese residents who see themselves as different from their counterparts in mainland China.(30) Further research distinguishing between these possibilities could help to guide interventions for the prevention of childhood wheezing disorders.

CONCLUSIONS

In a large, population-representative birth cohort in the ethnically homogeneous, developed setting of Hong Kong, second-generation migrants had higher risk of hospitalization for childhood wheezing disorders than children with native born parents. Future studies should focus on elucidating the mechanisms involved so as to guide preventive interventions for childhood wheezing disorders.

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AUTHOR CONTRIBUTIONS

JYYL and CMS had substantial contributions to the conception and design of this study. JYYL analysed and interpreted the data. GML had substantial contributions to the conception and design of the original study and the interpretation of data. CMS had substantial contributions to the interpretation of data. JYYL drafted the article, and the other authors reviewed it critically for important intellectual content. All authors gave final approval of the version to be published and agree to be responsible for the reported research.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Table 1. Baseline characteristics for 8298 children in Hong Kong's "Children of 1997" birth cohort

Characteristics			Migrant status						
			Both parents Hong Kong born		One parent migrant		Both parents migrant		P value ^a
			(n = 4228)		(n = 1626)		(n = 1914)		
n	%		n	%	n	%	n	%	
Infant characteristics									
Type of hospital at birth									
Public	5285	70.9	2347	58.4	1240	78.9	1698	91.2	<0.001
Non-public	2171	29.1	1675	41.7	332	21.1	164	8.8	
Parental characteristics									
Parental history of allergies									
Neither parent	4434	59.1	2127	51.2	993	63.1	1314	73.7	<0.001
Mother only	1069	14.2	694	16.7	207	13.2	168	9.4	
Father only	1332	17.7	851	20.5	258	16.4	223	12.5	
Both parents	673	9.0	480	11.6	115	7.3	78	4.4	
Mother's age at birth, years									
24 or below	907	11.9	408	9.7	256	16.0	243	13.1	<0.001
25-29	2350	30.7	1072	25.6	579	36.1	699	37.6	
30-34	2980	38.9	1901	45.4	502	31.3	577	31.1	
35 or above	1415	18.5	808	19.3	268	16.7	339	18.3	
Father's age at birth, years									
24 or below	286	3.7	184	4.4	51	3.2	51	2.8	<0.001
25-29	1025	13.4	539	12.9	193	12.0	293	15.8	
30-34	2599	34.0	1695	40.5	447	27.9	457	24.6	

35 or above	3739	48.9	1771	42.3	914	57.0	1054	56.8	
Highest parental education									
Grade 9 or below	2283	29.8	712	17.0	624	38.9	947	51.0	<0.001
Grade 10-11	3287	42.9	1962	46.8	658	41.0	667	35.9	
Grade 12 or above	2089	27.3	1522	36.3	324	20.2	243	13.1	

^a *P* values obtained from chi-squared tests for categorical variables.

Table 2. Adjusted associations of migrant status with public hospital admissions for asthma and other wheezing disorders (ICD-9CM 466, 490 and 493) in 8298 children (after multiple imputation)

Migrant status	Age	Events	Model 1		Model 2		Model 3	
			HR	95% CI	HR	95% CI	HR	95% CI
Both parents Hong Kong born	9 days to 2 years	415	1	Referent	1	Referent	1	Referent
One parent migrant			1.37	1.07, 1.76	1.15	0.89, 1.50	1.10	0.84, 1.43
Both parents migrant			1.64	1.30, 2.06	1.32	1.03, 1.69	1.22	0.95, 1.58
Both parents Hong Kong born	9 days to 6 years	625	1	Referent	1	Referent	1	Referent
One parent migrant			1.31	1.07, 1.61	1.16	0.94, 1.45	1.13	0.91, 1.40
Both parents migrant			1.59	1.32, 1.91	1.36	1.11, 1.67	1.30	1.05, 1.60
Both parents Hong Kong born	9 days to 12 years	671	1	Referent	1	Referent	1	Referent
One parent migrant			1.23	1.01, 1.51	1.1	0.89, 1.36	1.06	0.86, 1.31
Both parents migrant			1.49	1.25, 1.79	1.29	1.06, 1.56	1.22	1.002, 1.50
Both parents Hong Kong born	>2 years to 6 years	273	1	Referent	1	Referent	1	Referent
One parent migrant			1.14	0.84, 1.56	1.12	0.80, 1.56	1.10	0.78, 1.53
Both parents migrant			1.45	1.09, 1.91	1.38	1.02, 1.87	1.34	0.98, 1.84
Both parents Hong Kong born	>6 years to 12 years	74	1	Referent	1	Referent	1	Referent
One parent migrant			0.94	0.51, 1.73	0.66	0.32, 1.34	0.64	0.31, 1.32
Both parents migrant			0.83	0.47, 1.44	0.80	0.40, 1.59	0.81	0.40, 1.65

Abbreviations: CI, confidence interval; HR, hazard ratio.

Model 1 is unadjusted.

Model 2 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth.

Model 3 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth and highest parental education.

Table 3. Adjusted associations of migrant status with public hospital admissions for asthma (ICD-9CM 493) in 8298 children (after multiple imputation)

Migrant status	Age	Events	Model 1		Model 2		Model 3	
			HR	95% CI	HR	95% CI	HR	95% CI
Both parents Hong Kong born	9 days to 2 years	52	1	Referent	1	Referent	1	Referent
One parent migrant			1.44	0.71, 2.93	1.24	0.59, 2.63	1.10	0.52, 2.36
Both parents migrant			1.83	0.97, 3.43	1.61	0.81, 3.23	1.34	0.66, 2.74
Both parents Hong Kong born	9 days to 6 years	260	1	Referent	1	Referent	1	Referent
One parent migrant			1.15	0.83, 1.59	1.05	0.75, 1.47	1.03	0.73, 1.45
Both parents migrant			1.49	1.12, 1.99	1.35	0.98, 1.86	1.33	0.96, 1.84
Both parents Hong Kong born	9 days to 12 years	307	1	Referent	1	Referent	1	Referent
One parent migrant			1.08	0.80, 1.45	0.98	0.72, 1.34	0.97	0.71, 1.33
Both parents migrant			1.32	1.01, 1.72	1.19	0.89, 1.59	1.16	0.86, 1.57
Both parents Hong Kong born	>2 years to 6 years	225	1	Referent	1	Referent	1	Referent
One parent migrant			1.06	0.75, 1.49	1.02	0.70, 1.48	0.99	0.68, 1.44
Both parents migrant			1.33	0.97, 1.81	1.28	0.91, 1.80	1.24	0.88, 1.75
Both parents Hong Kong born	>6 years to 12 years	69	1	Referent	1	Referent	1	Referent
One parent migrant			0.89	0.48, 1.65	0.71	0.35, 1.43	0.69	0.34, 1.41
Both parents migrant			0.83	0.46, 1.50	1.14	0.56, 2.31	1.13	0.55, 2.35

Abbreviations: CI, confidence interval; HR, hazard ratio.

Model 1 is unadjusted.

Model 2 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth.

Model 3 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth and highest parental education.

Table 4. Adjusted associations of mother's place of birth with public hospital admissions for asthma and other wheezing disorders (ICD-9CM 466, 490 and 493) in 8298 children (after multiple imputation)

Mother's place of birth	Age	Events	Model 1		Model 2		Model 3	
			HR	95% CI	HR	95% CI	HR	95% CI
Hong Kong	9 days to 2 years	415	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.06	0.82, 1.37	1.05	0.81, 1.35	1.04	0.81, 1.35
Outside Guangdong province in China			1.26	0.92, 1.74	1.21	0.88, 1.66	1.20	0.87, 1.65
Other			0.74	0.36, 1.51	0.74	0.36, 1.53	0.74	0.36, 1.54
Hong Kong	9 days to 6 years	625	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.03	0.84, 1.27	1.03	0.83, 1.27	1.02	0.83, 1.26
Outside Guangdong province in China			1.28	0.98, 1.67	1.24	0.95, 1.62	1.23	0.94, 1.60
Other			0.75	0.42, 1.33	0.75	0.42, 1.34	0.75	0.42, 1.34
Hong Kong	9 days to 12 years	671	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.03	0.84, 1.27	1.03	0.83, 1.27	1.02	0.83, 1.26
Outside Guangdong province in China			1.32	1.02, 1.72	1.29	0.99, 1.67	1.28	0.99, 1.66
Other			0.70	0.39, 1.25	0.71	0.40, 1.26	0.71	0.40, 1.26
Hong Kong	>2 years to 6 years	273	1	Referent	1	Referent	1	Referent
Guangdong province in China			0.82	0.59, 1.15	0.79	0.56, 1.12	0.79	0.56, 1.12
Outside Guangdong province in China			1.20	0.81, 1.76	1.19	0.80, 1.78	1.18	0.79, 1.76
Other			0.90	0.41, 1.97	0.90	0.41, 1.96	0.90	0.41, 1.96
Hong Kong	>6 years to 12 years	74	1	Referent	1	Referent	1	Referent
Guangdong province in China			0.63	0.30, 1.34	0.49	0.19, 1.26	0.47	0.18, 1.21
Outside Guangdong province in China			1.50	0.78, 2.87	1.30	0.53, 3.19	1.38	0.54, 3.50

Other	NA	NA	NA	NA	NA	NA
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Abbreviations: CI, confidence interval; HR, hazard ratio; NA, not available.

Model 1 is unadjusted.

Model 2 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth.

Model 3 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth and highest parental education.

Table 5. Adjusted associations of father's place of birth with public hospital admissions for asthma and other wheezing disorders (ICD-9CM 466, 490 and 493) in 8298 children (after multiple imputation)

Father's place of birth	Age	Events	Model 1		Model 2		Model 3	
			HR	95% CI	HR	95% CI	HR	95% CI
Hong Kong	9 days to 2 years	415	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.12	0.86, 1.45	1.10	0.85, 1.43	1.10	0.86, 1.43
Outside Guangdong province in China			1.10	0.71, 1.70	1.05	0.68, 1.63	1.05	0.68, 1.63
Other			0.85	0.33, 2.23	0.90	0.34, 2.35	0.90	0.34, 2.35
Hong Kong	9 days to 6 years	625	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.05	0.84, 1.32	1.04	0.83, 1.30	1.04	0.83, 1.30
Outside Guangdong province in China			1.12	0.78, 1.60	1.08	0.75, 1.56	1.08	0.75, 1.56
Other			0.93	0.43, 1.98	0.96	0.45, 2.07	0.97	0.45, 2.09
Hong Kong	9 days to 12 years	671	1	Referent	1	Referent	1	Referent
Guangdong province in China			1.00	0.80, 1.25	0.99	0.80, 1.23	0.99	0.80, 1.23
Outside Guangdong province in China			1.08	0.76, 1.53	1.04	0.73, 1.48	1.05	0.74, 1.49
Other			0.87	0.41, 1.84	0.90	0.42, 1.91	0.91	0.43, 1.93
Hong Kong	>2 years to 6 years	273	1	Referent	1	Referent	1	Referent
Guangdong province in China			0.83	0.59, 1.17	0.85	0.60, 1.21	0.84	0.59, 1.20
Outside Guangdong province in China			1.23	0.74, 2.04	1.28	0.77, 2.14	1.26	0.75, 2.12
Other			1.06	0.35, 3.24	1.09	0.36, 3.33	1.09	0.36, 3.33

Hong Kong			1	Referent	1	Referent	1	Referent
Guangdong province in China	>6 years to 12	74	0.79	0.42, 1.48	0.89	0.41, 1.95	0.91	0.41, 2.02
Outside Guangdong province in China	years		1.35	0.51, 3.62	1.06	0.36, 3.14	1.04	0.34, 3.21
Other			1.29	0.16, 10.57	1.19	0.11, 12.59	1.05	0.10, 11.66

Abbreviations: CI, confidence interval; HR, hazard ratio.

Model 1 is unadjusted.

Model 2 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth and father's age at birth.

Model 3 adjusted for type of hospital at birth, parental history of allergies, mother's age at birth, father's age at birth and highest parental education.