

BMJ Open Trajectories of asthma symptom presenting as wheezing and their associations with family environmental factors among children in Australia: evidence from a national birth cohort study

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ABSTRACT

Objectives Asthma is one of the greatest health burdens, yet contributors to asthma symptom trajectories are understudied in Australian children. We aimed to assess the trajectories of asthma symptom and their associations with several family environmental factors during the childhood period in Australia.

Design Secondary analysis from a cross-sequential cohort study.

Setting Nationwide representative data from the 'Longitudinal Study of Australian Children (LSAC)'.

Participants Participants from the LSAC birth cohort.

Outcome measures Asthma symptom trajectory groups.

Methods Asthma symptom presenting as wheezing, family environmental factors and sociodemographic data (2004–2018) were obtained from the LSAC. Group-based trajectory modelling was applied to identify asthma symptom trajectories and multivariable logistic regression models were used to assess the associations between these and environmental factors.

Results Of 5107 children in the LSAC cohort, 3846 were included in our final analysis. We identified three distinct asthma symptom trajectories from age 0/1 year to 14/15 years: 'low/no' (69%), 'transient high' (17%) and 'persistent high' (14%). Compared with the 'low/no' group, children exposed to 'moderate and declining' (relative risk ratio (RRR): 2.22, 95% CI 1.94 to 2.54; RRR: 1.26, 95% CI 1.08 to 1.46) and 'high and persistent' prevalence of maternal smoking (RRR: 1.41, 95% CI 1.23 to 1.60; RRR: 1.26, 95% CI 1.10 to 1.44) were at increased risk of being classified into the 'transient high' and 'persistent high' trajectories of asthma symptom. Persistently bad external dwelling conditions (RRR: 1.27, 95% CI 1.07 to 1.51) were associated with 'transient high' trajectory while 'moderate and increasing' conditions of cluttered homes (RRR: 1.37, 95% CI 1.20 to 1.56) were associated with 'persistent high' trajectory of asthma symptom. Exposure to tobacco smoke inside the house also increased the risk of being in the 'persistent high' trajectory group (RRR: 1.30, 95% CI 1.12 to 1.50).

Conclusion Poor home environment increased the risk of asthma symptom during childhood. Improving home

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This is the first study in Australia to report the trajectories of asthma symptom and several family environmental exposures among children during childhood.
- ⇒ Data used in this study were based on a nationally representative sample of Australian children, with longitudinal follow-up from 0/1 year to 14/15 years of asthma symptom and presence of family environmental factors.
- ⇒ The main limitations of this study were the missing values and participant attrition at different follow-up time points.

environment and reducing exposure to tobacco smoke may facilitate a favourable asthma symptom trajectory during childhood.

INTRODUCTION

Asthma is a heterogeneous disease usually characterised by chronic airway inflammation, with wheezing as the main symptom of any phenotype of the disease.¹ It is one of the most common chronic illnesses in children,^{2,3} presents with periodic exacerbations and remissions, and accounts for substantial medical and economic burden.⁴ Global studies of asthma in children have reported that the prevalence of asthma symptoms has increased in the last few decades, which is concerning.⁵ Australia is one of the developed countries where asthma continues to be a significant public health concern. One in every ten children in Australia currently suffer from this condition.⁶ Although mortality from asthma-related illness is low, treatment of the morbidity incurs a substantial healthcare cost

and utilisation of resources in Australia and warrants further attention.⁷

The aetiology of asthma symptoms is still unknown. However, several environmental factors have been found to be triggers of asthma symptoms.^{8–10} Over the past two decades, attention has been focused on the role of indoor environment (work, home and school) in the management of asthma symptoms.¹¹ Several studies have shown that the family or household environment, including indoor allergens, biological matter and pollutants, is an important risk factor for the development of asthma symptoms.¹² Of these, passive smoking/environmental tobacco smoking (ETS), furry pets, household size/crowding, housing condition, etc are well-evident family environmental exposures that increase the risk of asthma symptoms.^{13–20} House dust mites and fungus are also prevalent sources of indoor allergens and are the most studied allergens in the development of asthma symptoms.^{21–22} Although the association between cluttered homes and asthma symptoms has not been studied, clutter harbours dust mites, pet dander and mould, which can trigger allergic reactions, reduce air quality and increase potential asthma problems. More and closer-together items at home may increase the potential for accumulation of dust, pet dander and mould in closets, on surfaces and in crevices.²³ Thus, a cluttered home is a potential family environmental factor that could exacerbate symptoms of asthma. Besides the interior condition of the household, poor exterior may also contribute to asthma symptoms.¹⁶

Most of the previous studies focused on the immediate effect of these environmental factors on exacerbating asthma symptoms.^{12–20} However, these factors are dynamic, can change over time and have the potential to influence the trajectories of asthma symptoms. Studies have reported that several family environmental exposures, such as passive smoking/ETS,²⁴ pets at home²⁴ and dampness in the house,²⁵ were significantly associated with detrimental asthma symptom trajectories compared with relatively better asthma symptom trajectories in children. Exposure to these adverse family environmental factors during childhood can contribute to unfavourable asthma symptom trajectories as the developmental and functional growth of the lungs occurs during childhood, especially during the first few years of life.²⁶ Any insult during this period may affect the normal growth and development of the lungs and eventually contribute to chronic respiratory illnesses such as asthma.^{25–26} However, it is not well evident at which time point during childhood (such as the first year, the first 5 years and the first 15 years) environmental exposure is more associated with bad trajectories of asthma symptoms.

Although there is no permanent solution to eradicate asthma, symptoms can be controlled by appropriate management. Prevention of symptoms is the best strategy to combat this condition. To implement an appropriate and pragmatic prevention strategy, knowing the trajectories of asthma symptoms and their associations with potential environmental factors is necessary. Studying

asthma symptoms trajectories in childhood is also crucial to predicting the course and outcome of this condition.²⁷ Some previous studies followed children since birth and attempted to identify the trajectories of asthma symptoms according to age^{24–28} and showed that asthma symptoms in childhood follow different temporal trajectories. Studies in North America and England found that asthma symptoms in children usually follow three to four distinct trajectories. These include transient asthma, early-onset chronic asthma, late-onset chronic asthma and no asthma from early childhood to adolescence.^{4–24–25–28} One study described the trajectories as low progressive, early transient and early persistent asthma symptoms.²⁴ All studies showed that the prevalence was high at 2–5 years of age for all unfavourable types of asthma symptoms trajectories.^{24–28} Assessing the trajectories of different family environmental factors may also provide data on the prevalence of these exposures in a defined population over time. However, data are sparse with regard to trajectories of asthma symptoms and the potential family environmental factors and their associations among children in Australia.

To advance understanding of the different trajectories of asthma symptoms and family environmental factors and their association, conducting a population-based studies would be ideal. We analysed data from the Longitudinal Study of Australian Children (LSAC)²⁹ to assess the association between trajectories of some common family environmental factors (such as passive smoking, external and internal condition of homes, presence of pets, and living conditions) and asthma symptom among children in Australia. The LSAC is a large cohort study with a nationally representative sample of children in Australia. It aims to build an understanding of child development, inform social policy debate, and identify opportunities for intervention and prevention strategies in policy areas concerning children and their families. It is a good source of several family environmental indicators and different health outcomes, such as asthma symptom, over eight different time points (0–15 years of age).

METHODS

Data source

The LSAC is conducted in partnership with the Australian Government's Department of Social Services, the Australian Institute of Family Studies and the Australian Bureau of Statistics, with advice provided by a consortium of leading researchers from research institutions and universities throughout Australia.³⁰ Data from waves 1–8 of the 'B' cohort of the LSAC study were used. This is a 'birth cohort' in which children were recruited between 0 and 1 year of age in 2004 (wave 1). Starting with 5107 children at wave 1, the LSAC collected information from children and their families biannually at age 2/3 (wave 2), 4/5 (wave 3), 6/7 (wave 4), 8/9 (wave 5), 10/11 (wave 6), 12/13 (wave 7) and 14/15 (wave 8). Although the LSAC 'B' cohort started with 5107 children, the sample

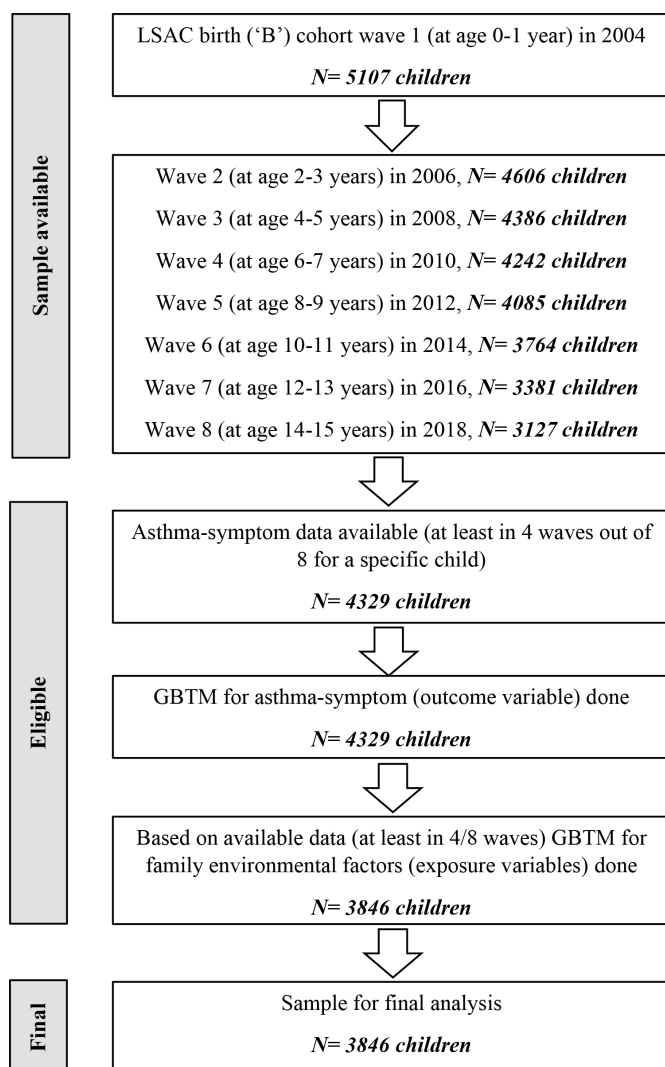


Figure 1 Study flow chart. GBTM, group-based trajectory modelling; LSAC, Longitudinal Study of Australian Children.

size decreased in every consecutive wave due to attrition. At wave 8, 3127 children remained. Before enrolling the children in this study, parents and caregivers gave informed written consent. The sampling design and field methods have been described elsewhere.²⁹

Analytical sample

Out of 5107 children, trajectory analyses for both outcome and exposure variables were conducted in 3846 children based on available data and methodological techniques (figure 1). We considered these as our analytical sample. We could not include 1261 participants from the initial cohort due to attrition or unavailability of the desired information.

Outcome measurements

We considered ‘asthma symptom’ as our initial outcome variable since asthma is a heterogeneous disease with several clinical phenotypes. A recent ‘Lancet Commission’ has discouraged using the term ‘asthma’ as a single disease and proposed a more targeted approach to think

about its mechanisms and treatment.³¹ Wheezing is the most common symptom among patients with asthma, independent of their phenotype.¹ To determine the presence of asthma symptom in participating children, we considered affirmative responses from the caregivers to the following question: ‘Has the child had an illness with wheezing in the chest which lasted for a week or more in the last 12 months?’ This is one of the standardised questions for asthma diagnosis in a community-based study. The LSAC study adopted this question from the largest study of asthma and allergy in children.³² We assessed the responses to this question from all the participants over different time points (waves) and then performed group-based trajectory modelling (GBTM)^{33 34} to assess the trajectory groups for asthma symptom and identify which child belonged to which trajectory group. Finally, different trajectory groups for asthma symptom (see the Results section) were considered as the outcome variable in this study.

Exposure measurements

The exposure variables in this study were some common family environmental factors. These family environmental exposures were considered based on literature review and availability of data in the LSAC. We evaluated the housing conditions of the participants,^{16 25} presence of a furry pet at home,^{17 24} parental cigarette smoking,^{13 24 35} household cigarette smoking²⁴ and family size^{18 36} as the family environmental factors and exposure variables in our study. A detailed list of variables with a description of the measurements is provided in online supplemental table TS1. All our exposure variables were time-variant variables that can change over time, so we considered exposure time (such as exposure in the first year of life and the first 5 years of life) and trajectory groups (see the Results section) of some environmental factors as our final exposure variables.

Adjusted variables

Existing literature has identified several demographic factors and health status or behaviour as effect modifiers. Literature suggests that the prevalence of asthma symptoms may vary by sex,³⁷ ethnicity,³⁷ poor health status or having a comorbid condition,³⁸ preterm birth³⁹ and low birth weight.⁴⁰ Maternal cigarette smoking⁴¹ and maternal asthma during pregnancy⁴² also contribute to the risk of the offspring developing asthma symptoms during childhood. These factors may alter the magnitude of the effect of the primary exposures (family environmental factors) on the outcome (asthma symptom trajectory). In our study, child factors including sex, indigenous status, health status, preterm birth and birth weight; maternal factors such as maternal smoking and maternal asthma medication during pregnancy; and family factors such as socioeconomic status according to the ‘Socio-Economic Indexes for Areas (SEIFA) economic resources’⁴³ were adjusted in the statistical models as confounder variables to determine the independent effects of family

environmental factors on the trajectories of asthma symptom. We also adjusted current medications for asthma in the regression model as these may act as an effect modifier and alter the magnitude of the effect of the primary exposures on the outcome. Among all adjusted variables, sex, indigenous status, birth weight, maternal smoking during pregnancy and maternal asthma medication during pregnancy were the time-invariant variables, while health status, current asthma medication and socioeconomic status were the time-variant variables.

Statistical analysis

The baseline demographic characteristics of the children, the prevalence of asthma symptom and the different family environmental factors over different time points are shown. Significance between the groups was measured by χ^2 for categorical variables (for group percentage) and Student's t-test for continuous variables (for group mean). $P < 0.05$ was considered significant in all univariate analyses. However, in the multivariable models, we used the Dunn-Šidák corrections⁴⁴ to control family-wise error rate at 0.05. Depending on the number of variables in the different multivariable regression models, $p < 0.003$ was considered statistically significant in the adjusted model 1, while $p < 0.004$ was considered statistically significant in models 2 and 3.

Group-based trajectory modelling

GBTM^{33 34} was conducted to identify trajectories of asthma symptom (outcome) of the participating children across eight time points (0/1, 2/3, 4/5, 6/7, 8/9, 10/11, 12/13 and 14/15 years of life) using Stata V.16.1.³³ Children were only included in the GBTM when they had a response to the 'asthma symptom question' in at least four time points out of eight (waves 1–8). GBTM was also used for time-variant environmental factors such as 'external condition of dwelling', 'home condition_cluttered', 'current smoking_mother' and 'number of people who smoke inside the house'. We could not use GBTM for other environmental factors due to significant missing values across time points (eg, current smoking_father had 30%–40% missing data across the study period), or complete absence of data at most time points (eg, furry pets at home), or where bivariate analysis showed insignificant association with the outcome in almost all time points (eg, the number of people living in the household). Detailed statistical modelling and the GBTM approach have been described elsewhere.^{28 33} However, a brief description of the statistical procedures for GBTM is provided in online supplemental text S1.

Association between different family environmental factors and asthma symptom trajectories

Multinomial logistic regression was conducted to assess the association of different family environmental factors and group trajectories of asthma symptom. The reference category for the outcome variable was the 'low prevalent/no asthma symptom' trajectory group. Risk ratio and relative

risk ratio and their 95% CI were reported for bivariable and multinomial logistic regression accordingly. Bivariate analyses were undertaken to assess the unadjusted association between different family environmental factors and asthma symptom trajectories over different time points. Three different multivariable models were constructed after adjusting for potential confounders. These models were used to measure the association between asthma symptom trajectories and exposure to different family environmental factors over the first year (0/1 year, model 1), over the first 4/5 years (model 2) and over 14/15 years (model 3). In the first and second models (models 1 and 2), we attempted to capture exposure to environmental factors during the first 1000 and first 2000 days of life. We chose these two timeframes because the first 1000 and 2000 days are critical times in a child's physical, cognitive, social and emotional health. Events that happen in the first 1000/2000 days of life would have an impact throughout life.^{45 46} In the third model, we attempted to capture variations in environmental exposure during the childhood period (up to 15 years).

Dealing with missing values

We performed multiple imputations (MI)⁴⁷ to handle missing values under the assumption of missing at random. Imputations were done for missing independent and adjusted variables using chained equations. As most of our variables were categorical, the augmented regression option was applied to handle perfect prediction. Sensitivity analyses were conducted by comparing the outputs of the final regression between complete case and imputed data for all three models (online supplemental tables TS2–TS4). Due to attrition in the LSAC cohort during the different waves and not having sufficient information on the outcome variables in our study, our analytical sample is different from the LSAC original sample. Thus, this may create selection bias and affect estimates of associations. Hence, we performed a sensitivity analysis (online supplemental tables TS5–TS7) after incorporating the inverse probability weighting (IPW) technique⁴⁸ in our regression models to control for selection bias.⁴⁹ All statistical analyses were undertaken using Stata IC V.16.1.⁵⁰

Participant and public involvement statement

Participants and the public were not involved in the development or design of this study.

RESULTS

Of 5107 children in the LSAC 'B' cohort, 3846 were included in the final analyses. Figure 1 illustrates how the analytical sample was obtained from this cohort of the LSAC study.

Baseline characteristics

Among the 3846 children in our study, 51% were male and 3% came from indigenous backgrounds. Other baseline

Table 1 Baseline characteristics of the participants (analytical sample)

Variables	Total N=3846	Group 1 n=2956	Group 2 n=409	Group 3 n=481	P value
Male sex, n (%)	1982 (51)	1486 (50)	231 (56)	265 (55)	0.016
Ethnicity: indigenous, n (%)	102 (3)	65 (2)	15 (4)	22 (5)	0.004
Birth weight, g, mean (SE)	3441 (9)	3448 (4)	3394 (11)	3451 (10)	<0.001
Preterm infants (gestational age <37 weeks)	235 (6)	161 (5)	45 (11)	29 (6)	<0.001
Presence of any medical condition, yes, n (%)	194 (5)	97 (3)	41 (10)	56 (12)	<0.001
Maternal smoking during pregnancy, yes, n (%)	470 (14)	306 (11)	82 (22)	82 (20)	<0.001
Asthma medication during pregnancy, yes, n (%)	141 (4)	83 (3)	21 (5)	37 (8)	<0.001
SEIFA economic resources					
Lowest quantile	1389 (36)	1068 (36)	140 (34)	181 (38)	0.574
Second quantile	828 (21)	628 (21)	86 (21)	114 (24)	0.462
Third quantile	749 (19)	558 (19)	105 (26)	86 (18)	0.003
Highest quantile	880 (23)	702 (24)	78 (19)	100 (21)	0.055

Comparisons done between group 1 and group 2, and between group 1 and group 3.

Group 1: low/no asthma symptom trajectory group; group 2: transient high asthma symptom trajectory group; group 3: persistent high asthma symptom trajectory group.

SEIFA, Socio-Economic Indexes for Areas.

characteristics such as birth weight, preterm infants, presence of any current medical condition, maternal smoking during pregnancy, maternal asthma during pregnancy and socioeconomic status of the parents according to the SEIFA are described in [table 1](#). These baseline characteristics were compared between different trajectory groups of asthma symptom (outcome) and all were found to be significantly different from the control group (group 1: low/no asthma symptom trajectory group) ([table 1](#)).

We also describe the baseline characteristics of the participants excluded from this study in online supplemental table TS8. The proportion of indigenous people, presence of any medical condition, maternal smoking during pregnancy, low socioeconomic condition, lower mean birth weight, preterm infants and SEIFA were significantly higher in the excluded participants compared with our analytical sample (online supplemental table TS8).

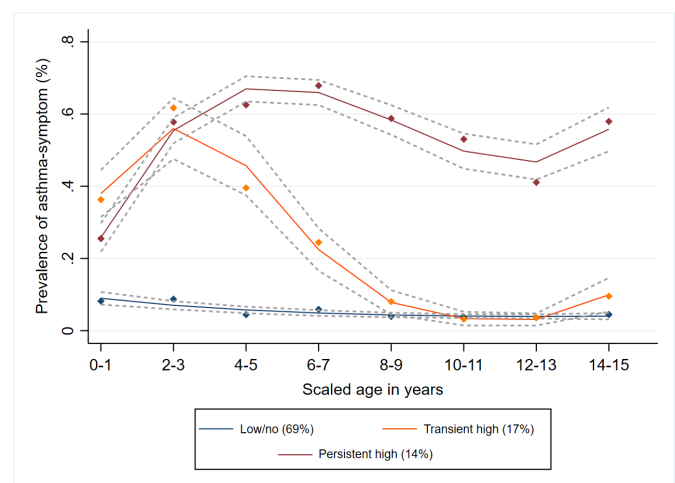
Characteristics of the asthma symptom trajectory groups

Out of 79 different trajectory models, one model had the best fit and identified three distinct trajectory groups for asthma symptom among the children in this study (online supplemental table TS9). According to the observed pattern of presence of asthma symptom, the trajectory groups were labelled as ‘low/no asthma (group 1)’, ‘transient high asthma (group 2)’ and ‘persistent high asthma (group 3)’ groups ([figure 2](#)). About 69% of the children belonged to the ‘low/no asthma’ group and these children had zero or very low prevalence of asthma symptom throughout the whole period (ages 0–15). In the ‘transient high’ group, the prevalence of symptom increased from 40% to 55% by 2/3 years and then gradually decreased. By the age of 10/11 years, the prevalence became very low or nil, but rose slightly at the age of 14/15 years. Of the

children, 14% belonged to the ‘persistent high’ asthma symptom group. In this group, the prevalence started from about 25%, gradually increased and then sustained between 65% and 45% from 4/5 years to 14/15 years.

Characteristics of the trajectory groups for family environmental exposures

We used GBTM for family environmental variables such as ‘external condition of the dwelling’, ‘home condition’, ‘current smoking_mother’ and ‘number of people who smoke inside the house’. After the same model-fitting approach as GBTM for asthma symptom trajectories, all environmental factors, except ‘external condition of the dwelling’, showed three group trajectories that fit the best model (online supplemental tables TS10–TS13). ‘External condition of the dwelling’ showed two distinct


Figure 2 Trajectory groups for asthma symptom.

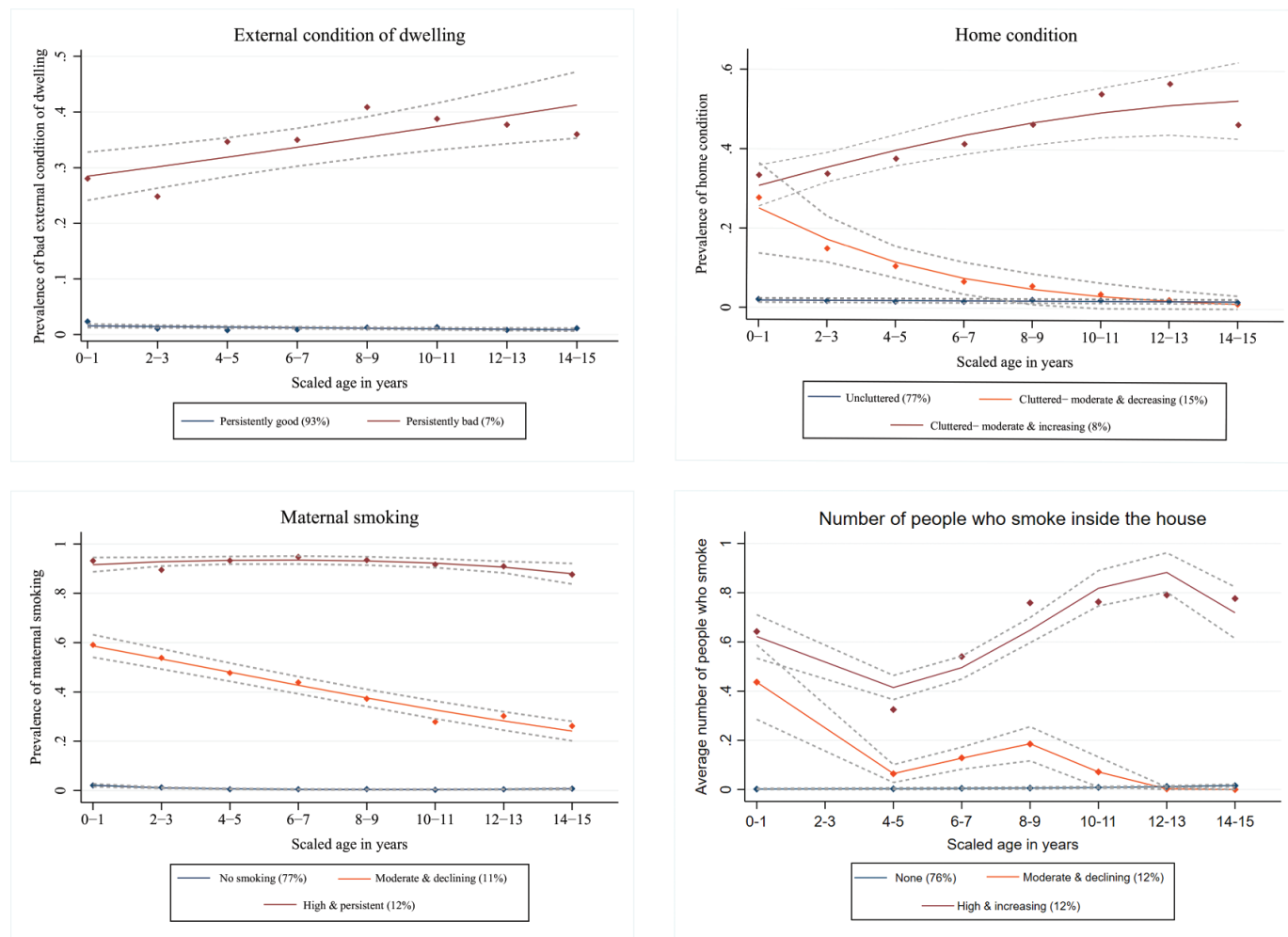


Figure 3 Trajectory groups for family environmental factors.

trajectory groups: ‘persistently good’ and ‘persistently bad’. Home condition showed three distinct trajectory groups: ‘persistently uncluttered’, ‘cluttered-moderate and decreasing’, and ‘cluttered-moderate and increasing’. ‘Maternal smoking’ also showed three distinct groups: ‘no smoking’, ‘moderate and declining’ prevalence, and ‘high and persistent’ prevalence. The trajectory groups for the ‘average number of people who smoke inside the house’ showed three distinct groups: ‘no people’, ‘moderate and declining’ and ‘high and increasing’. Projections of the trajectory groups and individual group percentages for all environmental factor trajectories are shown in [figure 3](#).

Descriptive analyses of family environmental exposures and their association with asthma symptom trajectories at different time points

In this study, we assessed the prevalence of asthma symptom and several family environmental factors at different time points (ages of the participants). The overall prevalence of asthma symptom varied from 9% to 25% at different time points. The prevalence was higher in the first 6/7 years, with a peak of 25% at age 2/3. Boys had a higher prevalence of asthma symptom than girls at almost all

time points. We found that the prevalence of maternal and paternal smoking changed remarkably over the first 14/15 years. Some other environmental exposures also showed significant changes in prevalence (>10% from the initial prevalence). Their prevalence followed a downward trend over time, with some fluctuations in between ([table 2](#)). We do not know the prevalence trend for ‘furry pet at home’ as data were available at only two time points out of eight. Among all the variables, ‘current smoking_father’ showed the highest change (reduction) over these time points. However, about 30%–40% of the responses to this question were missing at different time points.

Bivariate analyses showed that current smoking status of the mother was significantly associated with the ‘transient high’ and ‘persistent high’ asthma symptom trajectory groups compared with the ‘low/no’ asthma symptom trajectory group (control) (online supplemental table TS14). ‘Home condition_cluttered’, ‘current cigarette smoking_father’ and ‘external condition of dwelling_bad’ were also significantly associated with the ‘transient high’ trajectory group in 50% or more of the time points (online supplemental table TS14A). In the ‘persistent high’ trajectory group, other than maternal smoking, the

Table 2 Prevalence (%) of asthma symptom and family environmental exposures among the cohort over different time points

Variable	Time points							
	0/1 year	2/3 years	4/5 years	6/7 years	8/9 years	10/11 years	12/13 years	14/15 years
Asthma symptom (male, female)	16.08 (17, 13)	24.81 (26, 23)	18.73 (20, 17)	17.76 (19, 16)	12.33 (14, 10)	10.48 (11, 10)	8.76 (10, 8)	12.58 (12, 13)
External condition of dwelling, bad	4.16	2.80	3.12	3.26	3.97	3.78	3.19	3.22
Home uncluttered, no	8.53	6.37	5.74	5.38	5.93	5.97	5.78	4.72
Furry pet at home, yes	55.85	DNA	DNA	63.80	DNA	DNA	DNA	DNA
Current cigarette smoking, mother, yes	19.06	15.88	17.39	16.87	15.77	13.41	13.24	11.89
Current cigarette smoking, father, yes	25.43	20.23	19.34	15.52	14.31	13.12	11.41	9.72
Number of residents who smoke inside (mean)	0.14	DNA	0.06	0.09	0.12	0.10	0.10	0.10
Number of people in the household (mean)	4.03	4.31	4.49	4.57	4.63	4.56	4.52	4.44

DNA, data not available.

'number of residents who smoke inside' was significantly associated in most of the time points (online supplemental table TS14B).

Associations between asthma symptom trajectory groups and different family environmental factors in the multivariable models

After adjusting for potential covariates (participants' sex, indigenous status, any medical condition, current asthma medication, birth weight, preterm birth, SEIFA economic resources index for parents and asthma medication of the mother during pregnancy), three different multivariable analysis models were created based on exposure during the different time periods to assess for the independent associations between asthma symptom trajectory groups and different family environmental factors.

Model 1 shows the association of asthma symptom trajectory groups with exposure to various environmental factors in the first year of life. The unadjusted results showed that children exposed to maternal smoking in the first year of life were significantly associated with the 'transient high' trajectory group of asthma symptoms (table 3).

Model 2 shows the association of asthma symptom trajectory groups with different environmental factors exposed over the first 4/5 years. The unadjusted results showed that exposure to bad external dwelling conditions, cluttered home and maternal smoking at all time points (three out of three) had a significant association with both the 'transient high' and 'persistent high' asthma symptom trajectory groups. The association was also the same in the adjusted analysis (table 4).

Finally, model 3 shows the longitudinal association of asthma symptom trajectory groups with exposure to different environmental factors over the first 14/15 years. To assess these associations, trajectory groups of various environmental exposures were determined. Associations (relative risk ratio) were then calculated using multinomial logistic regression adjusted for potential confounders (table 5). In the unadjusted model, persistently bad external

dwelling condition, both 'moderate and decreasing' and 'moderate and increasing' conditions of cluttered home, both 'moderate and declining' and 'high and persistent' prevalence of maternal smoking, and 'high and increasing' number of people who smoke inside the house were all significantly associated with the 'persistent high' asthma symptom trajectory group compared with the 'no/low' asthma symptom trajectory group (table 5). However, after adjustment for potential confounders, 'persistently bad external condition of the dwelling' and both 'moderate and declining' and 'high and persistent' prevalence of maternal smoking trajectory groups were associated with the 'transient high' asthma symptom trajectory group (table 5). 'Moderate and increasing condition of cluttered home', both 'moderate and declining' and 'high and persistent' prevalence of maternal smoking, and 'high and increasing number of people who smoke inside the house' were also significantly associated with the 'persistent high' asthma symptom trajectory group (table 5).

DISCUSSION

In this cohort of children in Australia, three distinct trajectories for asthma symptom were identified. Around one in every seven children in this cohort belonged to a persistently high asthma symptom trajectory group. Trajectories of prevalence of some family environmental factors also showed distinct patterns. Trajectory groups that showed unfavourable family environment were significantly associated with high prevalence of asthma symptom. Among them, a higher prevalence of maternal smoking during the first 5 years or throughout childhood was the most detrimental family environmental exposure associated with all types of bad asthma symptom trajectory groups in this cohort.

Trajectories of asthma symptom and family environmental exposures

About one-third of the children in our study belonged to relatively bad asthma symptom trajectories in two distinct

Table 3 Multivariable model 1: association of different family environmental factors (exposed at age 0/1 year) with asthma symptom trajectories

Variables	Unadjusted (n=3846)		Adjusted* (n=3846)	
	Transient high	Persistent high	Transient high	Persistent high
External condition of the dwelling				
Good	1	1	1	1
Bad	1.44 (0.89 to 2.34)	1.63 (1.04 to 2.56)	1.44 (0.88 to 2.35)	1.60 (1.01 to 2.54)
Cluttered home				
No	1	1	1	1
Yes	1.33 (0.93 to 1.91)	1.67 (1.21 to 2.30)	1.31 (0.91 to 1.88)	1.59 (1.15 to 2.21)
Furry pet at home				
No	1	1	1	1
Yes	1.32 (1.06 to 1.63)	0.93 (0.76 to 1.13)	1.32 (1.06 to 1.65)	0.89 (0.73 to 1.09)
Current cigarette smoking, mother				
No	1	1	1	1
Yes	1.70 (1.29 to 2.24)	1.23 (0.94 to 1.62)	1.65 (1.25 to 2.19)	1.18 (0.89 to 1.57)
Number of residents who smoke inside the house (per unit increase)	0.99 (0.70 to 1.40)	1.04 (0.73 to 1.47)	0.99 (0.69 to 1.40)	1.01 (0.71 to 1.43)
Number of people in the household (per unit increase)	1.09 (1.00 to 1.19)	0.96 (0.88 to 1.05)	1.09 (0.99 to 1.19)	0.95 (0.87 to 1.04)

Association presented as relative risk ratio and their 95% CI; 1=reference value.
 The reference group for the trajectory group is 'no/low asthma symptom trajectory group'.
 Bold numbers represent statistically significant values after 'Dunn-Šidák test' for p values (p<0.008 was considered statistically significant in the unadjusted model and p<0.003 in the adjusted model).
 *Adjusted for sex, indigenous status, SEIFA economic resources, any medical condition, birth weight, preterm birth and asthma medication of the mother during pregnancy.
 SEIFA, Socio-Economic Indexes for Areas.

groups. We did not find any previous study in Australia that showed the trajectories of asthma symptoms in children; however, there are several studies reported earlier from the UK, Canada and Sweden.^{24 25 28 51} One Canadian birth cohort study where they followed children from birth to 10 years showed three to four distinct trajectories, including transient, early-onset chronic and late-onset chronic asthma.²⁸ Another large study from Canada showed the trajectory followed low progressive, early transient and early persistent patterns,²⁴ which were much similar to our findings. We also found a similarity of the results of our study to a large birth cohort from Sweden, where they showed the trajectories followed transient and persistent patterns when this developed from the first year of life.⁵¹ Our study has identified two distinct trajectory groups where children had asthma symptom over their first 14/15 years of life. One is the persistent or chronic pattern of asthma symptom and the other is the transient type. Considering the cumulative number of children belonging to these two groups, they had a higher prevalence of asthma symptom in the first 6/7 years of life than in the rest of their childhood. It seems that the period from 2/3 years to 6/7 years is the most vulnerable period for asthma symptom in this cohort. A large cross-sectional study in China also reported that the prevalence of asthma in children was high (60%–70%) within 3–7 years of their

childhood.⁵² As children have smaller airways relative to lung size in early life, they are more prone to asthma symptoms when confronted with environmental challenges.⁵³ The likelihood of asthma symptoms decreases with age as the airway grows. Although lung development begins around the fifth gestational week and continues in stages into early adulthood when lung function peaks, early childhood is crucial for lung structural and functional development.^{26 54} During this period, environmental insult can influence the lung's functional growth and development and may cause wheezing.^{22 26}

This study has also identified the trajectories of some family environmental factors over time, including the external condition of the dwelling, cluttered home condition, current maternal cigarette smoking and the number of people who smoke inside the house. One group of the external condition of the dwelling trajectories showed the condition was persistently bad, and this prevalence was slightly increasing (30%–40%) throughout the assessment. In terms of the internal environment of the household, two trajectory groups showed cluttered household condition. About 8% of the population showed persistently and slightly increasing prevalence of cluttered homes. A previous study from a nationwide representative sample in Australia showed that about 5% of people lived in dwellings classified as being in poor/derelict

Table 4 Multivariable model 2: association of different family environmental factors (exposed over the age of 0/1–4/5 years) with asthma symptom trajectories

Variables	Unadjusted (n=3846)		Adjusted* (n=3846)	
	Transient high	Persistent high	Transient high	Persistent high
External condition of dwelling, bad				
Never	1	1	1	1
1–2 time points	0.71 (0.33 to 1.50)	0.41 (0.16 to 1.04)	0.65 (0.30 to 1.38)	0.54 (0.20 to 1.41)
3 time points	1.39 (1.20 to 1.60)	1.38 (1.21 to 1.58)	1.31 (1.13 to 1.52)	1.27 (1.09 to 1.49)
Cluttered home				
Never	1	1	1	1
1–2 time points	1.06 (0.96 to 1.19)	1.32 (1.20 to 1.46)	1.09 (0.98 to 1.22)	1.37 (1.23 to 1.53)
3 time points	2.63 (1.76 to 3.92)	2.81 (1.91 to 4.14)	2.49 (1.64 to 3.77)	1.95 (1.22 to 3.10)
Current cigarette smoking, mother				
Never	1	1	1	1
1–2 time points	1.53 (1.38 to 1.69)	1.02 (0.92 to 1.13)	1.49 (1.34 to 1.66)	0.99 (0.88 to 1.12)
3 time points	2.28 (2.01 to 2.59)	1.49 (1.31 to 1.70)	2.31 (1.94 to 2.53)	1.58 (1.36 to 1.83)
Number of people in the household (per unit increase)	1.03 (0.99 to 1.06)	0.96 (0.93 to 1.00)	1.01 (0.97 to 1.04)	0.92 (0.89 to 1.01)

Association presented as relative risk ratio and their 95% CI; 1=reference value.

The reference group for the trajectory group is 'no/low asthma symptom trajectory group'.

Bold numbers represent statistically significant values after 'Dunn-Sidak test' for p values ($p < 0.012$ was considered statistically significant in the unadjusted model and $p < 0.004$ in the adjusted model).

*Adjusted for sex, indigenous status, SEIFA economic resources, any medical condition, current asthma medication, birth weight, preterm birth and asthma medication of the mother during pregnancy.

SEIFA, Socio-Economic Indexes for Areas.

condition in 2011.⁵⁵ The actual prevalence in our study measured at different time points was less than 5% for the bad external dwelling condition and more than 5% for cluttered home. However, the trajectories showed that 7%–8% of people belonged to a group with a persistently moderate prevalence of bad external dwelling condition and/or cluttered home condition. Of the children, 12% belonged to a group where there is a high prevalence of mothers being a smoker throughout childhood. The prevalence of tobacco smoking among women in Australia was about 13% in 2015.⁵⁶ There was a slight reduction in smoking prevalence over the last 12 years (15% in 2003), and the prevalence was found to decline in our study. However, 12% of the mothers of our studied children had a persistently high prevalence of smoking. There were also remarkable percentages in the prevalence of current paternal smoking in our study; however, we could not analyse the trajectory due to the 30%–40% missing responses at different time points. Looking at all persons smoking inside the house, a relatively high and increasing average number of people smoking inside the house was identified in 12% of children.

Association of asthma symptom trajectories and family environmental exposures

Compared with the 'low/no' asthma symptom trajectory group, both 'transient high' and 'persistent high' asthma trajectory groups had a significant association with several

family environmental factors. Among them, maternal current smoking was found to be the factor most associated with these two unfavourable asthma symptom trajectories. Although the trend in the overall prevalence of current maternal tobacco smoking was seen to be declining in our study, it was significantly associated with these two asthma symptom trajectories at all time points individually.

The association between household secondhand tobacco smoke (SHS) exposure and childhood asthma is well evident.⁵⁷ Among all the potential sources of SHS, maternal smoking is the most detrimental for children developing asthma symptoms.^{58,59} Although most of these previous studies described the current risk of childhood asthma due to maternal smoking, limited reports are available regarding the trajectories of maternal smoking and their associations with the trajectories of asthma symptoms among children during their childhood. Our study is the first study in Australia to assess the trajectories of this crucial environmental exposure and its association with asthma symptom trajectories. The study found two bad trajectories of maternal smoking were significantly associated with two bad trajectories of asthma symptom throughout childhood. This may imply a temporal relationship between maternal smoking and asthma symptom.

Besides the persistent exposure to maternal smoking, early life exposure (exposed in the first year of life)

Table 5 Multivariable model 3: association of different family environmental factors (exposed over the age of 0/1–14/15 years) with asthma symptom trajectories

Variables	Unadjusted (n=3846)		Adjusted* (n=3846)	
	Transient high	Persistent high	Transient high	Persistent high
External condition of the dwelling (trajectory groups)				
Persistently good	1	1	1	1
Persistently bad	1.38 (1.16 to 1.63)	1.28 (1.09 to 1.50)	1.27 (1.07 to 1.51)	1.17 (0.97 to 1.40)
Home condition (trajectory groups)				
Uncluttered	1	1	1	1
Cluttered, moderate and decreasing	1.11 (0.33 to 1.27)	1.34 (1.16 to 1.54)	1.15 (0.98 to 1.34)	1.11 (0.94 to 1.31)
Cluttered, moderate and increasing	1.20 (1.03 to 1.40)	1.34 (1.19 to 1.50)	1.14 (1.00 to 1.30)	1.37 (1.20 to 1.56)
Current cigarette smoking, mother (trajectory groups)				
Non-smoker	1	1	1	1
Moderate and declining	2.26 (1.98 to 2.58)	1.23 (1.07 to 1.41)	2.22 (1.94 to 2.54)	1.26 (1.08 to 1.46)
High and persistent	1.45 (1.27 to 1.64)	1.29 (1.14 to 1.45)	1.41 (1.23 to 1.60)	1.26 (1.10 to 1.44)
Number of residents who smoke inside the house (trajectory groups)				
None	1	1	1	1
Moderate and declining	0.99 (0.85 to 1.14)	1.01 (0.88 to 1.16)	1.02 (0.88 to 1.18)	1.04 (0.89 to 1.22)
High and increasing	0.88 (0.76 to 1.01)	1.22 (1.08 to 1.39)	0.88 (0.76 to 1.01)	1.30 (1.12 to 1.50)

Association presented as relative risk ratio and their 95% CI; 1=reference value.

The reference group for the trajectory group is 'no/low asthma symptom trajectory group'.

Bold numbers represent statistically significant values after 'Dunn-Sidak test' for p values (p<0.012 was considered statistically significant in the unadjusted model and p<0.004 in the adjusted model).

*Adjusted for sex, indigenous status, SEIFA economic resources, any medical condition, current asthma medication, birth weight, preterm birth and asthma medication of the mother during pregnancy.

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was also associated with the 'transient high' asthma symptom trajectory group. When the exposure happened persistently in the first 5 years, it could lead the children to belong to the 'persistent high' asthma symptom trajectory group for their whole childhood. The detrimental effect of maternal smoking can begin in utero if the mother smokes during pregnancy, and it can increase the prevalence of childhood wheezing and asthma by altering the functional and structural development of the child's lungs.^{41 60} In our study population, 20%–22% of the mothers from 'transient high' and 'persistent high' asthma symptom trajectory groups smoked during pregnancy. Thus, for these children, the detrimental effects of passive smoking⁶⁰ might have started from their intrauterine life. Nicotine exposure during pregnancy damages fetal lung development, modulates airway hyper-reactivity, reduces lung function and eventually increases asthma morbidity.⁴¹ Exposure to passive smoking in infancy, early childhood or late childhood may boost the condition as infants' lungs continue to develop both structurally and functionally up to early adulthood.^{26 54} Systematic reviews also revealed that passive smoking in the postnatal period significantly increased the risk of asthma symptoms in childhood.^{20 61} After birth, infants and children tend to spend most of the time with their mother, so exposure from the mother would be the most potent source of SHS compared with any other source in

the household. Our study shows that the risk of asthma symptom can increase with the number of people who smoke inside the house. An American study reported that children's urinary cotinine to creatinine ratios increased with the number of smokers at home.⁶² Thus, SHS is a risk factor for asthma symptom, and the risk can increase depending on the extent of exposure.

Some household environmental conditions were found to be significantly associated with unfavourable trajectories of asthma symptom. A persistently unfavourable trajectory of the external dwelling condition and a high and increasing trajectory of cluttered homes were significantly associated with both unfavourable trajectories of asthma symptom. Living in substandard housing may lead to exposure to asthma triggers and may exacerbate symptoms.⁶³ Holt *et al*¹⁶ reported that poor exterior housing conditions are significantly associated with higher odds of development of asthma symptoms in children. In a previous study, disarray of the internal environment, such as clutters, showed a significant association with asthma symptoms.¹⁹ Specific interventions to reduce exposure to this condition could reduce asthma morbidity.⁶⁴ These unfavourable home environmental conditions (bad external dwelling conditions and cluttered homes) are potential sources of dust, mould, mites and other allergens that can eventually trigger asthma symptoms.^{65–67} Dilapidated cluttered house may also have an impact on

child's psychological stress,⁶⁸ which eventually triggers asthma symptoms.⁶⁹ Early life exposure to furry pets at home was also associated with the 'transient high' trajectory of asthma symptom in our study. The association between early childhood exposure to cats or dogs and the development of asthma symptoms was controversial in systematic reviews.^{70 71} Exposure to cat allergens leads to a higher risk of developing cat sensitisation in children. Conversely, exposure to dogs protects children from developing sensitisation against aeroallergens which would be associated with wheezing symptoms later in life.⁷⁰ Due to lack of data, we could not elucidate the trajectory and the effect of long-time exposure to furry pets in our study.

Strengths and limitations

The main strength of our study is that it is based on a nationally representative sample of Australian children, with longitudinal follow-up for asthma symptom and presence of family environmental factors. We also used pragmatic and well-accepted analytical techniques to validate the results of our study.

However, the study has several limitations. The main limitations were the missing values and participant attrition. Thus, we could not include all participants in our study due to lack of information on our outcome variables.

In our study, in terms of some baseline characteristics, the analytical sample was significantly different from the participants who could not be included in the longitudinal analyses. There was a higher proportion of participants from lower socioeconomic and indigenous backgrounds, with lower mean birth weight, presence of medical condition and maternal smoking during pregnancy in non-included participants. Although this was not under our control, it was anticipated as these characteristics were found in a higher proportion of lower socioeconomic status and indigenous people.⁷²⁻⁷⁴ Therefore, our analytical sample was likely to lose participants with these conditions, which might create selection bias and affect estimates of associations. Thus, we conducted the sensitivity analyses of all our regression models after incorporating the IPW technique⁴⁸ to control selection bias.⁴⁹ Moreover, for missing values on the baseline characteristics of our analytical sample, we used MI.

In this study, we could not perform trajectory analysis of some important environmental factors such as paternal smoking and furry pets at home due to a large number of missing values. We also could not assess other important family environmental factors^{67 75 76} reported in earlier literature due to the unavailability of these data in the LSAC study.

Another limitation is that, being a population-based study, asthma symptom was recorded as per the caregiver's response and so there are some limitations with regard to the precision of diagnosis. There is a chance of underestimating or overestimating this symptom if the caregiver failed to identify wheezing correctly. However, in this study, we tried to assess the overall condition of the

most common asthma symptom such as 'wheeze' among the children in their childhood, so our findings may not reflect the trajectories and associations of confirmed 'asthma' cases in this population.

CONCLUSION

In conclusion, although a national report in Australia stated that only 10% of children have asthma symptoms, our study found that about one-third of the children belonged to the 'transient high' or 'persistent high' prevalence asthma symptom trajectories in their childhood. The prevalence of several potential home environmental factors has decreased over the last 15 years. However, a significant proportion of children are exposed to relatively bad trajectories of these environmental factors. Our study also found that bad trajectories of several home environmental factors were significantly associated with two bad asthma symptom trajectories in children. Both early transient and persistent maternal smoking were the most significant exposures associated with bad asthma symptom trajectories. Other exposures including bad external housing condition, cluttered home and increased number of people who smoke inside the house were found to be associated with bad asthma symptom trajectories in children. Our study evaluated that these potential family environmental factors are not only associated with asthma symptom in children, but their sustained exposure, especially in the first few years of life, can lead to a persistently high prevalence of asthma symptom during the whole period of childhood. These findings would provide substantial scientific evidence with policy and practice implications for reducing asthma morbidity in children in Australia by taking adequate actions to reduce exposures to these family environmental factors during childhood.

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