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Early View

Original article

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Exposure to household air pollution over 10 years is related to asthma and lung function decline

Short running head: household air pollution, GST and lung health

Xin Dai[1], Dinh Bui[1], Jennifer L Perret[1], Adrian Lowe[1], Peter A Frith[2,3], Gayan Bowatte[1,4], Paul Thomas[5], Graham G Giles[1,6,7], Garun S Hamilton[8,9], Helen Tsimiklis[10], Jennie Hui[11], John Burgess[1], Aung K Win[1], Michael J Abramson[6], E. Haydn Walters[1,12], Shyamali Dharmage[1*], Caroline Lodge[1*].

1. Allergy and Lung Health Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Parkville, VIC, Australia.
2. College of Medicine and Public Health, Flinders University, Adelaide, SA, Australia.
3. Faculty of Health Sciences, University of South Australia, Adelaide, SA, Australia.
4. Natioanl Institute of Fundamental Studies, Kandy, Sri Lanka.
5. Inflammation and Infection Research, Faculty of Medicine, University of New South Wales, New South Wales, Australia.
6. School of Public Health & Preventive Medicine, Monash University, Melbourne, Vic, Australia
7. Cancer Epidemiology Division, Cancer Council Victoria, Melbourne, VIC, Australia.
8. Department of Lung and Sleep Medicine, Monash Health, Melbourne, Vic, Australia
9. School of Clinical Sciences, Monash University, Vic, Australia
10. Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia
11. The PathWest Laboratory Medicine of West Australia, Perth, WA, Australia.
12. School of Medicine, University of Tasmania, Tasmania, Australia.

* Equal senior authors

Corresponding author:

Prof. Shyamali Dharmage

Allergy and Lung Health Unit

Centre for Epidemiology and biostatistics

School of Population and Global Health

Level 3 207 Bouverie Street

University of Melbourne

3010

Email: s.dharmage@unimelb.edu.au

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Abstract 234 word count

The question addressed by the study: Are long-term Household Air Pollutions (HAPs) associated with asthma and lung function decline in middle-aged adults, and whether these associations were modified by GST gene variants, ventilation and atopy.

Materials and Methods: Prospective data on HAPs (heating, cooking, mould, smoking) and asthma were collected in the Tasmanian Longitudinal Health Study (TAHS) at mean ages 43 and 53 years (n=3314). Subsamples had data on lung function (n=897) and GST gene polymorphisms (n=928). Latent class analysis was used to characterize longitudinal patterns of exposure. Regression models assessed associations and interactions.

Results: We identified seven longitudinal HAP profiles. Of these, 3 were associated with persistent asthma, greater lung function decline and %reversibility by age 53 years, compared to "least exposed" profile, for who used reverse cycle air conditioning, electric cooking and without smoking. "All gas"(OR:2.64, 95%CI 1.22-5.70), "wood heating/smoking" (2.71, 1.21-6.05) and "wood heating/gas cooking" (2.60, 1.11-6.11) were associated with persistent asthma, greater lung function decline and %reversibility. Participants with GSTP1 Ile/Ile genotypes were at a higher risk of asthma or greater lung function decline when exposed compared to other genotypes. Exhaust fan use and opening windows frequently could reduce the adverse effects of HAP produced by combustion heating and cooking on current asthma presumably through increasing ventilation.

Answer to the question: Exposures to wood heating, gas cooking and heating, and tobacco smoke over 10 years increased the risks of persistent asthma, lung function decline and %reversibility, with evidence of interaction by GST genes and ventilation.

Key words: asthma, respiratory function tests, indoor air pollution, glutathione transferase, cohort studies

Take Home message: Long-term exposure to household air pollution (gas, wood smoke, tobacco smoke and their combinations) is linked to adverse respiratory health in mid-age, particularly for those with GST risk variants and living in poorly ventilated houses.

Introduction

Asthma is the most common chronic respiratory disease across the world. Persistent asthma and excess lung function decline are risk factors for chronic obstructive pulmonary disease (COPD)[1]. Household air pollution (HAP) has been implicated in asthma causation and persistence, including specifically tobacco smoke, heating/cooking emissions and surface mould [2]. Tobacco smoke has been implicated as a respiratory risk factor worldwide. However, heating and cooking exposures have been recognized as risk factors for asthma, COPD and asthma-COPD overlap only in low-middle income countries through exposure to biomass fuels [3, 4]. Current asthma and COPD guidelines rarely mention specific sources of HAP in developed countries as potentially modifiable risk factors [3, 5, 6]. Lack of guidance on these exposures is because it is currently unclear from the existing literature whether HAP is associated with an increased risk of asthma, COPD and reduced lung function in such settings. Although several studies have found various types of specific short-term HAP to be associated with adverse respiratory health in adults [2, 7, 8], the findings for longer term exposures due to common indoor cooking and heating methods (gas, electric, wood) are inconsistent.

A cross-sectional, population-based study in South America of 5539 subjects over 40 years found indoor wood smoke was associated with asthma and wheezing [7]. Another large cross-section study in China suggested a range of domestic risk factors including gas cooking and incense burring were associated with respiratory symptoms on adults. However, two large scale cross-sectional surveys - The European Community Respiratory Health Survey (ECRHS) [2] and The International Study of Asthma and Allergy in Childhood (ISAAC) in Germany [9] did not find significant associations between heating/cooking methods and asthma symptoms [8]. There were no previous study investigating household exposures longitudinally.

There may be several reasons for the inconsistent evidence concerning relationships between HAP and respiratory health. The impact of different mixtures of pollutants may vary with particular

mixtures of exposures compounding effects either in additive or synergistic ways. Another reason may be that some pollutants show effects only after a long latent period and cross-sectional studies do not have the ability to investigate such relationship. Finally, inconsistency in the reported associations may also reflect that effect-modifiers have not been taken into account, including variables that directly measure or act as proxies for home ventilation, and gene-environment interactions. Glutathione S-Transferase (GST) genes regulate the response to oxidative stress, which is induced by HAP. GST polymorphisms variably act as modifiers of the effects of outdoor air pollution on respiratory health [10, 11]. Some studies have found venting of cooking gases outdoors to be an important modifier of short-term effects of HAP [12, 13]. Atopy has also been investigated as a potential modifier of short-term effects of HAP due to its close relationship with air pollution and respiratory health [14, 15]. However, interactions with long-term exposures to HAP have not been explored longitudinally.

There is a need to provide high quality evidence to incorporate strategies addressing HAP into clinical and public health guidelines for better management and prevention of obstructive respiratory diseases. Using the 5^{th} and 6^{th} decade follow-ups from the Tasmanian Longitudinal Health Study (TAHS), we investigated the relationship between longitudinal exposure to heating/cooking facilities, smoking and moulds, including their potential interactions, and respiratory health in middle-aged adults. We also investigated the potential interactions between HAP and respiratory health. Specifically, we investigated: 1) distinct longitudinal patterns of HAP exposure; 2) whether these patterns were associated with risks of asthma and/or accelerated lung function decline between ages 43 and 53 years; and 3) whether these associations were modified by GST genotypes, household ventilation or atopic status.

Methods

Study design and data collection

TAHS is a population-based prospective cohort study, which commenced in 1968, including 8583 children at the age of 7 years (98.8% of the entire Tasmanian population at that age) [17]. We have recently followed participants into their 5th and 6th decades (beginning in 2002 and 2012, respectively) when they were aged on average, 43 years (Standard Deviation [SD]: 0.82) and 53 years (SD: 0.93) (Figure 1) . The mean follow-up duration was 10.1 years (SD: 1.1). A total of 5729 (78.4%) participants completed 5th decade, and 3609 (41.9%) completed 6th decade questionnaires. Of these, 3314 participated at both follow-ups with complete information, and 897 had spirometry at both follow-ups, with both pre- and post-inhaled bronchodilator (Pre- and post-BD) measurements (Figure 2). Additionally, 1215 subjects contributed genetic information at the 5th decade follow-up. Of these, 930 also completed the 6th decade questionnaire. More details of follow-ups were reported somewhere else [17-19].

Household air pollution exposures

The 5th and 6th decade questionnaires included the same items for determining HAP exposure in the last 12 months. The details of specific questions concerning HAP exposures are in the Supplement.

Asthma and lung function decline

At the 6th decade we defined new-onset or persistent asthma/symptoms depending on previous status. Z-scores for lung function indices were calculated from the Global Lung Initiative (GLI) reference equations for Caucasians [20, 21]. Lung function decline was determined by reductions in lung function between follow-ups, derived from reductions in z-scores and %predicted. The details of asthma definition and lung function procedure are in the supplement.

Other variables

A satellite-based land-use regression (LUR) model was used to assign mean annual exposure to NO_2. LUR used satellite observations of tropospheric NO_2 columns with land use, roads and other predictors to estimate ground-level NO_2 across Australia. Mean annual residential exposures to

outdoor NO_2 were estimated on the basis of participants' geocoded addresses [22]. We adjusted NO_2 at 5th decade only as small changes between two follow-ups were unlikely to influence respiratory health.

Details of atopy, occupation, definitions of COPD, duration of follow-up and outdoor NO_2 measurement are in the Supplement.

Genotyping of GST genes

DNA was isolated from whole blood samples provided at the 6th decade follow-up. *GSTM1/T1* genotype were classified as either present or null genotypes. Individuals were categorised by *GSTP1* genotypes as Val/Val, Ile/Ile or Val/Ile. More details of *GST* genotyping are in the Supplement.

Statistical analysis

Identification of HAP profiles

The following HAP exposures were included in the Latent Class Analysis (LCA): heating method (wood or coal fire, gas heaters, electric heater and reverse-cycle air conditioning); cooking method (gas or electric); visible mould; and smoking (passive and/or active). Participants were assigned to the class for which they had the highest probability of membership. The details of LCA statistical methods are in the Supplement.

The associations between LCA profiles and risk of asthma/lung function decline were determined using multivariable regression. Potential confounders, chosen with reference to the literature and causal modelling theory, were included in the final model. For asthma, we adjusted for age, sex, occupation and atopy at the 6th decade. For lung function decline, we adjusted for change of age, change of BMI, sex, atopy, outdoor NO_2 and occupation at the 6th decade. We also performed a standard multivariable regression analysis, to compare the results with those found from the LCA model.

Two-way interactions between LCA defined exposure classes and a) GST polymorphisms, b) atopy and c) ventilation parameters including building year, window opening frequency, and cooking exhaust fan use were assessed using likelihood ratio tests. P-values ≤0.1 were considered as evidence of interaction, then the stratified analyses were presented. Stata® 14.2 (2015 Stata Corp, College Station, TX) was used for all analyses.

Results

Characteristics of those who participated in the 5th and 6th decade follow-ups are presented in Table 1. There were changes in asthma status between the two follow-ups, defined as new-onset asthma in 283 (8.6%) participants and remitted asthma in 139 (4.2%) participants. A comparison of 5th decade characteristics for the remaining participants with those lost to follow-up for lung function and survey are presented in Table S1 and S2.

Latent class exposure profiles

The Bayesian Information Criterion (BIC) for LCA with 7 classes model was found to be the best fit (Table S3). There was no substantial improvement in models with >7 classes. The 7 latent classes were labelled as “least exposed”, “wood heating”, “all gas”, “wood heating/smoking”, “all electric”, “wood & gas heating/gas cooking/smoking” and “wood heating/gas cooking” (Figure 3). The prevalence and characteristics of household profiles are shown in Table 2. The “least exposed” profile was chosen as the reference group as low possibilities for all exposures. The prevalence of mould exposure was similar for all profiles thus we were unable to determine the influence of mould exposure by using LCA .

Main associations of HAP profiles with asthma/symptoms

Several profiles were associated with increased risk of persistent asthma/symptoms, compared with the reference profile (Table 3). The highest risk of <u>persistent</u> asthma/sym[ptoms was seen for the “wood heating/smoking” (OR: 2.71, 95%CI 1.21, 6.05), followed by the “all gas” (OR: 2.64, 95%CI

1.22, 5.70), “wood heating/gas cooking” (OR: 2.60, 95%CI 1.11, 6.11) and “wood heating” (OR: 1.77, 95%CI 0.92, 3.38). The “all electric” profile did not demonstrate evidence for this clinical association.

The profiles of “wood & gas heating/gas cooking/smoking” and “wood heating/smoking” were associated with new-onset asthma/symptoms (OR: 2.52, 95%CI 1.06, 5.99; and 2.02, 95%CI 1.09, 3.73, respectively). In contrast, adults in the “wood heating/gas cooking” profile had a moderately decreased risk of new-onset asthma/symptoms (OR 0.41, 95%CI 0.15, 1.12). We found, in this profile, that people who developed new-onset asthma/symptoms were more likely to stop using gas cooking to switching to other cooking methods (44.4%), compared with those who did not develop asthma symptoms (23.1%).

As a sensitivity analysis, we repeated the investigation after exclusion of those with fixed airway obstruction at the 5^{th} and 6^{th} decades (n=181) . Associations found were largely unchanged and similar to those using self-reported asthma outcomes (Table S4).

Main associations of HAP profiles with lung function decline/% reversibility

The profiles of “wood heating”, “all gas”, “wood heating/smoking”, and “wood heating/gas cooking” were associated with increased lung function decline for FEV_1 and/or FVC (Table 4). Participants who were exposed to the “Wood heating/smoking” profile had the most lung function decline for pre-BD FEV_1 (β-coef representing change in z score: -0.35, 95%CI -0.63, -0.07) and FVC (-0.52 95%CI -0.81, -0.24) over 10 years follow-up, compared with reference. We have also presented absolute values for lung function decline for each profile in Table S5. People in the “wood heating and smoking” and “wood & gas heating/gas cooking/smoking” profiles had increased FEV_1 %reversibility compared to the reference profile (1.25, 95% CI 0.24, 2.25 and 1.47, 95% CI -0.05, 2.99, respectively) (Table 4). Lung function results for %predicted can be seen in Table S6.

Individual household exposures

Traditional logistic regression to assess associations between individual household exposures and asthma/symptoms and lung function decline showed similarities with the LCA profile analysis. Ducted gas heating and smoking were associated with increased risk of asthma and increased lung function decline (Tables S7 and S8).

Interactions by GST genotype/ventilation/atopy

We used current asthma/symptoms at the 6th decade for the *GST* genotype interaction analyses, due to limited power to stratify by persistent and new-onset asthma/symptoms. There was no evidence of main associations between *GST* genes and asthma or lung function decline (Tables S9 and S10). However, we found evidence of interactions between *GST* genotypes and HAP profiles and asthma and lung function decline (Table S11-14). The profiles "All gas" and "Wood heating/smoking" were associated with increased risks of current asthma symptoms for participants with *GSTP1* Ile/Ile genotypes, but this association was not seen for participants with Ile/Val and Val/Val genotypes (interaction p= 0.04 and 0.01, respectively) (Table 5). Exposure to the "wood heating/gas cooking" profile was associated with greater post-BD FEV_1 and FVC decline for those with GSTP1 Ile/Ile genotype (Table 6). The profile "wood & gas heating/gas cooking/smoking" was associated with greater FEV_1/FVC ratio decline for people with *GSTM1* null genotypes, compared with those with *GSTM1* present genotypes (interaction p value<0.01). We did not observe evidence of interaction for *GSTT1* genotypes (Table S11).

Participants who did not use cooking exhaust fans or were living in newer buildings had increased risk of asthma when exposed to "electric heater", but we did not observe consistent results for exhaust fan use or building year on lung function decline (data not shown) (Table 7). We did not observe any significant interaction for window opening frequency on asthma and lung function outcomes. We found no evidence of interaction by atopy, and there was no interaction on %reversibility seen for GST, ventilation or atopy.

Discussion

Using comprehensive data from TAHS participants studied for a decade during middle-age, we found that HAP was a significant contributor to both asthma symptoms and accelerated lung function decline in middle age. Notably, we also found that GSTP gene genotypes modified this relationship; participants with *GSTP1* Ile/Ile genotype were more predisposed to asthma and worsening lung function. We also found evidence that better house ventilation may reduce the influence of HAP.

Risk reduction measures related to the indoor environment in developed countries for prevention of asthma and COPD are poorly identified in current guidelines [4-6]. While the GINA guidelines recognize HAP as a modifiable risk factor, they do not specify what adverse household sources may need to be addressed, especially in a more technologically advanced country. Our study provides high quality evidence based on long-term exposures and consideres complex interplays in the home environment, rather than isolated contributions from each specific source of HAP. Our resutls support potential asthma prevention strategies, which may inform asthma guidelines and prevention of future COPD burden related to accelerated lung function decline.

The exposure profiles “wood heating”, “all gas”, “wood heating/smoking” and wood heating/gas cooking” were associated with increased risk of persistent asthma/symptoms and accelerated FEV_1 and FVC decline over ten years’ follow-up. These findings are consistent with results from previous studies for a range of household risk factors and adverse respiratory health [14, 23-27]. Inefficient combustion of solid fuels (including wood) generates a complex mixture of carbon-based particles and gases that may cause health effects in humans. Cigarette smoke may induce an inflammatory response through effects of ROS on alveolar epithelial cells [28]. In this way long-term HAP exposure may be involved in the development and progression of obstructive respiratory diseases and lung function deficits [29-31]. Further analysis found that the associations between HAP profiles and lung function decline remain after excluding participants with asthma and COPD (Table S15), indicating lung function decline found in our study may be independent of such disease status.

Consistent with previous studies [32, 33], our reference profile “reverse-cycle air conditioning, electric cooking and a non-smoking environment” and the “all electric” profile were associated with the lower risks for asthma symptoms and lung function decline compared to other categories. Although cooking itself can generate particulates, compared to other cooking methods, using electric technologies can reduce the release of particulates from combustion in the home. They may also be due to the associated air filtration in reverse cycle air conditioning removing airborne PM [34]. Absence of smoking could also reduce the risk of airway inflammation and enhance the responsiveness of asthma treatment [35].

Three multiple exposure profiles (“wood heating/smoking”, “wood & gas heating/gas cooking/smoking” and “wood heating/gas cooking”) were associated with higher respiratory health risk than the sum of the individual values for wood and smoking obtained from our traditional regression analysis, suggesting there may be a synergistic effect which is not captured when investigating these exposures singly. More severe lung function decline was also seen when compared with the individual exposures. This observation was consistent with the findings of a cross-sectional study in Brazil. This study reported that adults exposed to both smoking and wood burning were at a far higher risk than those with single exposures to household air pollution in relation to asthma severity and reduced lung function [36].

We found a moderately reduced risk of new-onset asthma/symptoms in those belonging to the “wood heating/gas cooking” profile ($p=0.08$), that contrasted with the increased risk from all other multiple exposure smoking groups. We hypothesize that symptomatic people who do not smoke may be more concerned about their health and more inclined to change heating/cooking methods. These changes may have resulted in apparent reductions in asthma risk for those remaining in this profile. However, a similar behaviour was not seen for the “wood & gas heating/cooking/smoking” profile (data not shown). Another possible reason is that smokers may be more likely to attribute

symptoms to smoking, and other environmental exposures may be "hidden" from epidemiological measures of association due to this reverse-causation.

We found some evidence that the effects of HAP profiles were modified by *GST* gene polymorphisms. Although we found no good evidence for interaction by *GSTT1* polymorphisms, there was little power to robustly investigate this association. Our findings suggesting that better indoor ventilation may modify the adverse effects of HAP on respiratory health are consistent with previous literature [37-39]. It is particularly important to ventilate house when using home heating and cooking systems, that can generate high levels of pollutants.

Strengths & Limitations

Our study identified longitudinal HAP profiles using LCA, which considers multiple exposures together. HAP profiles can more comprehensively capture the complexities of HAP and may help identify a "lower exposed" category.

As TAHS is a large whole-of-population birth-cohort study, it would have been difficult and expensive to directly measure household air quality to capture differences in toxicity and concentrations of the indoor pollutants, especially over time. Our exposure was assessed by questionnaires. Although this approach may be imprecise concerning exact levels of exposure, there is evidence that survey-based answers, can be predictive of objective measurements of pollutants in household settings [40, 41]. As we measured exposures and outcomes across the same time period, we were unable to conclude that the relationships were temporally related. Most participants used the same methods of heating and cooking at both surveys for all profiles. LCA modellingis unable to account fully for participant-initiated lifestyle changes in exposures across a long time period due to the low prevalence of such changes, , and this may have introduced a degree of misclassification. However we found similar associations using moretraditional logistic regression analysis that included these changes. Any misclassification in the LCA models was unlikely to affect our conclusions as it was most likely to be non-differential. We also performed further sensitivity analysis for those participants who lived at

the same address for both follow-ups. The associations remained similar and did not change our conclusions (Tables S16 and S17). Our proxy measures for home ventilation, interventions which would have been intended to increase ventilation, have not been validated by home air exchange measurements. However, the observed modifying effect of these proxies, exhaust fan use and window opening frequency lend support to some simple specific interventions that may be useful in mitigating poor respiratory health when exposed to HAP. Also, sample sizes were small for considering interactions for GST genotypes, reducing the power to find statistically significant differences between GST polymorphisms.

We did not perform correction for multiple comparisons. However, it should be noted that the associations were based on pre-established hypotheses. All point estimates for associations were consistent. We cannot definitively rule out the possibility of attrition bias, however we think that the risk is low. There was a loss to follow-up for active smokers, however previous respiratory cohorts with similar or greater attrition rates, including European Community Respiratory Health Survey (ECRHS), Respiratory Health in Northern Europe (RHINE) and Italian Study on Asthma in Young Adults (ISAYA) [42], have shown that associations between smoking and asthma remain unbiased over 10 and 20 years of follow-up. The prevalence of our exposure profiles may differ marginally from the general population, but it should not make our internal associations less valid.

We recognise that asthma symptoms defined from questionnaires in this age group may actually represent fixed airway obstruction or COPD [43], and some of these participants may have had COPD without asthma. We therefore performed a sensitivity analysis after removal of participants with known COPD. We found most COPD cases in the “wood heating/smoking” profile. This finding is consistent with previous evidence that smoking history and biomass exposure are key risk factors for COPD [44, 45]. HAP profiles may be associated with development of COPD, but we were unable to robustly investigate this relationship in the TAHS due to the small numbers with COPD.

Conclusions

We identified longitudinal HAP profiles associated with the risk of obstructive lung diseases and greater lung function decline in middle-age, including “wood heating”, “all gas”, “wood heating/smoking”, “wood & gas heating/gas cooking/smoking” and “wood heating/gas cooking”. Our findings also support a synergistic effect of multiple exposures on respiratory health compared with single exposures. We found some evidence of increased risk for individuals with specific GST genotypes. Our findings provide further evidence that long-term HAP exposure may impair respiratory health and also point to the importance of good indoor ventilation, particularly for those who are at high individual risk. Our study has the potential to improve evidence-based preventive strategies in asthma and COPD clinical guidelines.

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Figure 1 Flowchart for TAHS

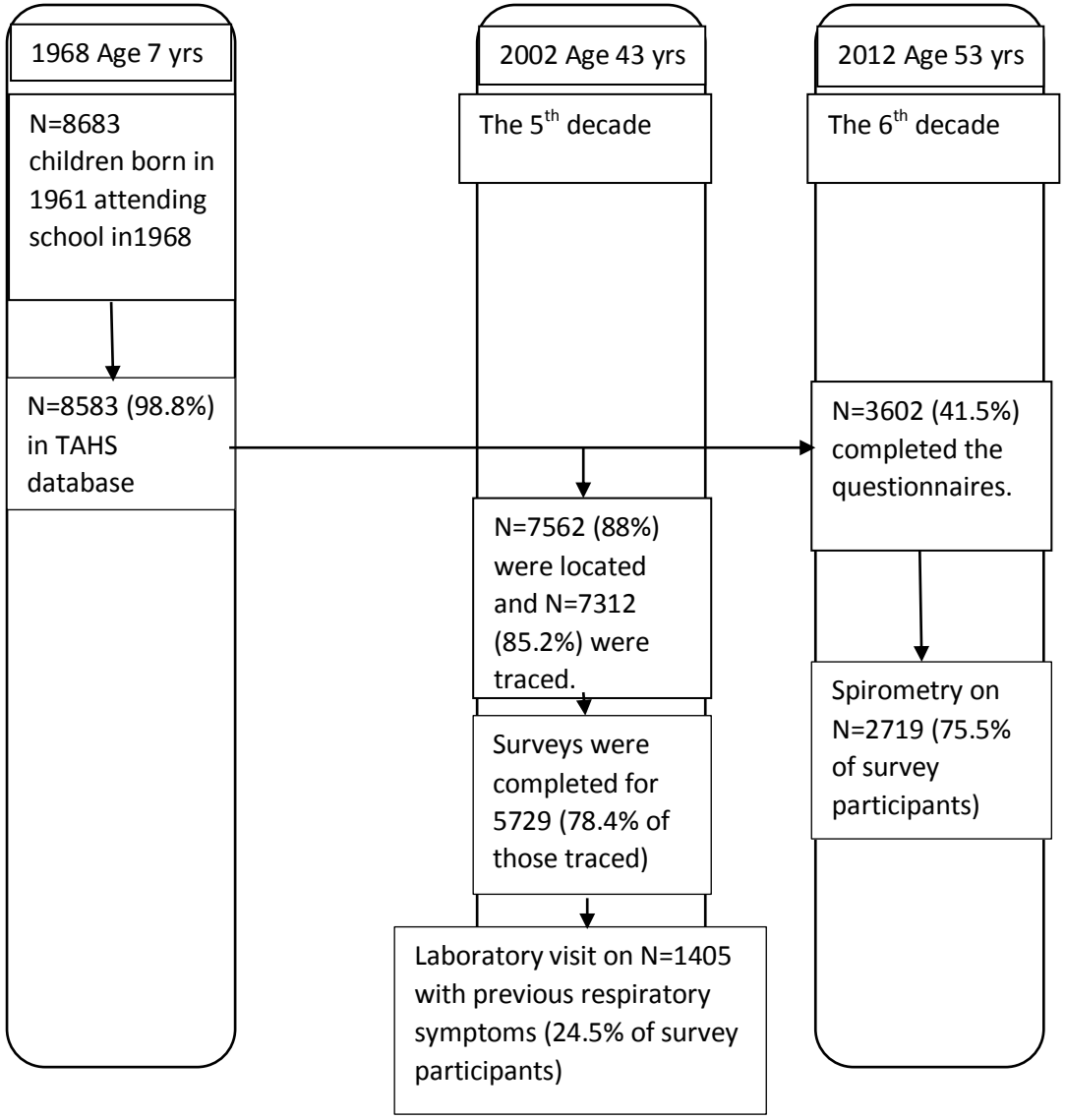


Figure 2 Flowchart for TAHS Proband participation at 2002 and 2012 surveys stratified by asthma status.

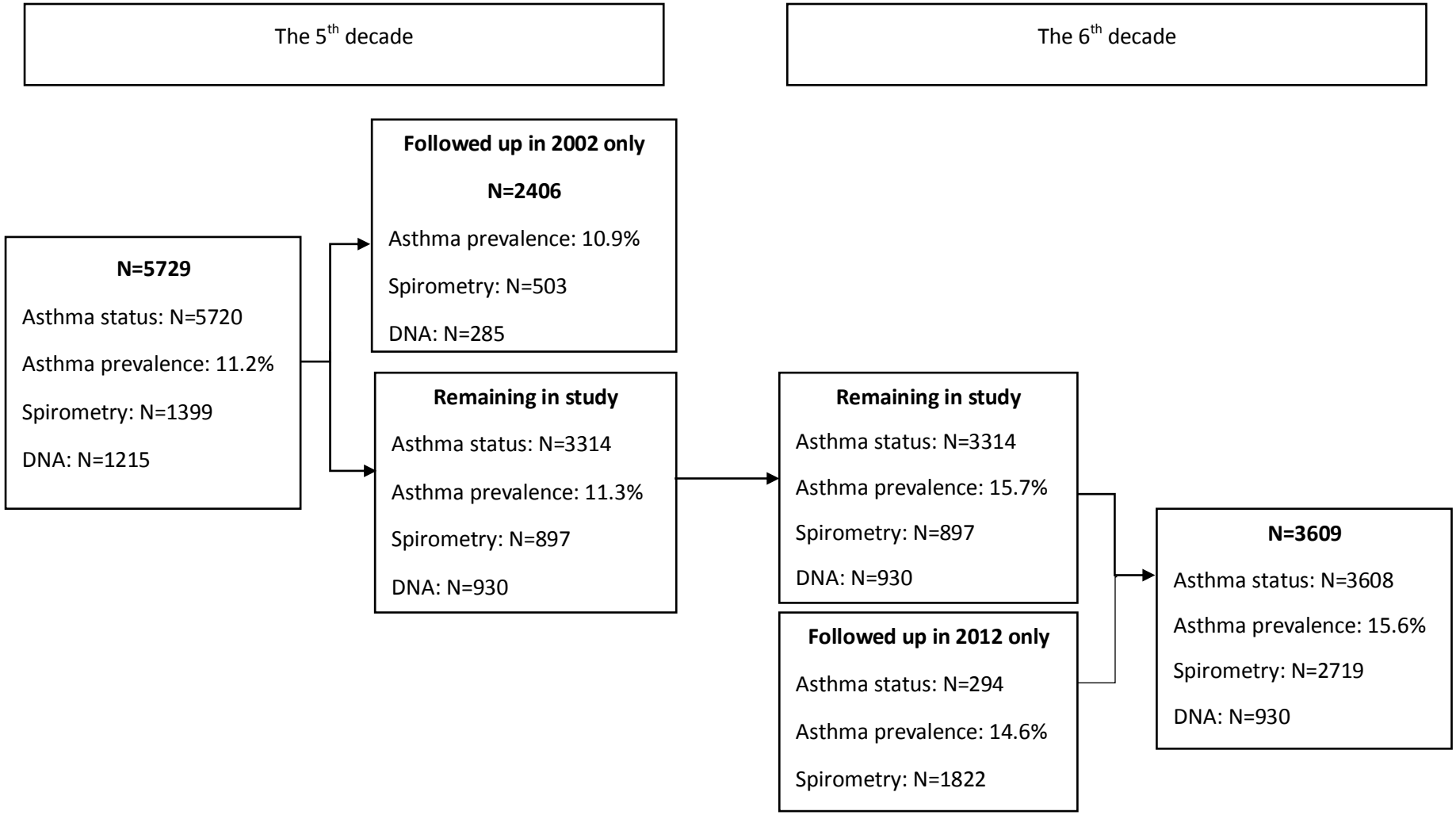
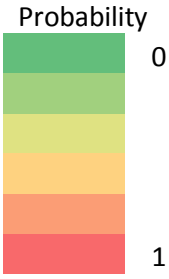


Figure 3 Heat map of probability of having each risk factor for seven HAP risk profiles estimated from the latent class analysis model.

	Reference	Wood heating	Gas cooking and heater	Wood heating and smoking	Electric heater	Gas heating, cooking and smoking	Gas cooking and wood heating
Gas cooking†2002	0.097967	0.052981	0.731927	0.010941	0.033405	0.685639	0.542972
Gas cooking2012	0.175787	0.000724	0.733367	0.100769	0.058942	0.601905	0.977605
Gas heater*2002	0.044326	0.010293	0.690142	0.019700	0.033084	0.382615	0.037042
Gas heater2012	0.050936	0.032974	0.582789	0.018023	0.018226	0.311650	0.108389
Elect. heater2002	0.195569	0.061132	0.108247	0.284174	0.633246	0.084451	0.107085
Elect. heater2012	0.001012	0.104458	0.089589	0.231450	0.630050	0.101571	0.071864
Wood heater2002	0.193059	0.847641	0.002129	0.548447	0.010398	0.380418	0.817756
Wood heater2012	0.008782	0.718974	0.088526	0.484094	0.009973	0.295981	0.692834
Other heater2002	0.068329	0.031250	0.103524	0.039782	0.167030	0.064648	0.000113
Other heater2012	0.051987	0.021274	0.060906	0.035623	0.124002	0.091955	0.036795
current smoke2002	0.098923	0.059717	0.083414	0.952337	0.090313	0.938638	0.058855
current smoke2012	0.031173	0.016896	0.021117	0.801040	0.018780	0.809814	0.011036
Passmoke2002	0.095545	0.081242	0.029824	0.372942	0.047056	0.372113	0.037856
Passmoke2012	0.073546	0.047937	0.019196	0.238957	0.031736	0.240849	0.039507
Mould2002	0.291937	0.387128	0.371624	0.352833	0.483483	0.298111	0.410020
Mould2012	0.235971	0.396789	0.292658	0.349097	0.455920	0.261450	0.360703



Intensity of colour indicates probability of each risk factor in each latent class (from 0 to 1 or 100%)

*Gas heater combined gas heater and ducted gas heating.

†For cooking choices, over 98% of participants used gas or electric cooking at both surveys. The choices were mutually exclusive with participants indicating which form of energy was predominantly used. We modelled with gas cooking as the exposure group and electric as reference, thus only gas appears in heat map.

Table 1 Characteristics of study sample

	Participants at both follow-ups (N=3314)	
	5th decade follow-up (average age 43 years)	6th decade follow-up (average age 53 years)
Age (SD)	42.7 (0.82)	53.0 (0.93)
Men (%)	1630 (49.2)	1630 (49.2)
Tertiary education (%)	1790 (53.9)	1872 (59.4)
GSTM1 null (%)	500 (53.8)	500 (53.8)
GSTT1 null (%)	158 (17.0)	158 (17.0)
GSTP1 Ile/Ile alleles (%)	372 (40.1)	372 (40.1)
Current asthma (%)	376 (11.3)	520 (15.7)
Ducted gas central heating (%)	215 (6.5)	261 (7.9)
Wood or coal fire (%)	1461 (44.1)	1216 (36.7)
Gas room heater (%)	386(11.6)	314 (9.7)
Electric heater (%)	1279 (38.6)	990 (30.6)
Reverse cycle air conditioning (%)	715 (21.6)	1578 (47.6)
Gas cooking (%)	783 (23.6)	927 (28.0)
Electric cooking (%)	2507 (75.6)	2276 (68.7)
Mould in last 12 months (%)	1250 (37.7)	1135 (34.9)
Active smoking (%)	793 (24.0)	545 (16.6)
Passive smoking (%)	391 (10.5)	261 (8.0)

Table 2 Prevalence and characteristics of Household Air Pollution (HAP) profiles identified by Latent Class Analysis (LCA).

Series number	Profile name	N (Prevalence)	Description
1	Least exposed	453 (13.7%)	Highest probability of reverse cycle air conditioning, electric cooking, and lowest probability of smoking and other risk factors.
2	Wood heating	952 (28.7%)	Highest probability of coal or wood fire for heating at both surveys, but probability of other risk factors was similar to “least exposed”.
3	All gas	538 (16.2%)	Higher probability of gas used for heating and cooking at both surveys, the probability of other risk factors was similar to “least exposed”.
4	Wood heating/smoking	446 (13.4%)	Highest probability of current smoking at both surveys, moderate probability of coal or wood fire for heating at both surveys. The probability of other risk factors was similar to “least exposed”.
5	All electric	450 (13.6%)	Highest probability of electric heating, lowest probability of gas cooking indicating higher probability of electric cooking. The probability of other risk factors was similar to “least exposed”.
6	Wood & gas heating/gas cooking/smoking	157 (4.7%)	Highest probability of current smoking at both surveys, moderate probability of gas cooking and wood heating. The probability of other risk factors was similar to “least exposed”.
7	Wood heating/gas cooking	323 (9.7%)	Higher probability of wood heating and moderate probability of gas cooking at both surveys. The probability of other risk factors was similar to “least exposed”.

Table 3 Associations between longitudinal indoor exposure profiles and asthma outcomes by the 6th decade

HAP exposure profiles	N of exposed	New Onset asthma/symptoms			Persistent asthma/symptoms		
		N	ORs+	P	N	ORs+	P
Least exposed (Reference*)	453	29	1		26	1	
Wood heating	952	50	0.95 (0.53, 1.70)	0.86	91	1.77 (0.92, 3.38)	0.09
All gas	538	37	1.15 (0.59, 2.21)	0.69	56	**2.64 (1.22, 5.70)**	**0.01**
Wood heating and smoking	446	45	**2.02 (1.09, 3.73)**	**0.03**	48	**2.71 (1.21, 6.05)**	**0.02**
All electric	450	38	1.61 (0.87, 2.96)	0.13	34	1.16 (0.54, 2.47)	0.70
Wood & gas heating/gas cooking/smoking	157	13	**2.52 (1.06, 5.99)**	**0.04**	17	1.37 (0.46, 4.10)	0.58
Wood heating/gas cooking	323	10	0.41 (0.15, 1.12)	0.08	28	**2.60 (1.11, 6.11)**	**0.03**

*Reference group included people used electric cooking, air conditioning for heating, and no smoking

+ All ORs were adjusted for age, sex, atopy, NO_2 and occupation at the 6th decade.

Baseline outcome for new onset asthma was participants who had never reported asthma in previous surveys, baseline outcome for persistent asthma was participants who had remitted asthma at the 6th decade.

Table 4 Associations* between HAP profiles and lung function decline (Beta coefficients from linear regression, representing change in z scores) between the two follow-ups.

HAP exposure profiles	**Pre-bronchodilator**			**Post-bronchodilator**			**% reversibility in FEV_1**
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC	
Least exposed (reference)	0	0	0	0	0	0	0
Wood heating	-0.12 (-0.32, 0.09)	**-0.26 (-0.46, -0.05)**	0.20 (-0.03, 0.43)	**-0.28 (-0.49, -0.08)**	**-0.27 (-0.48, -0.06)**	0.02 (-0.20, 0.24)	0.43 (-0.40, 1.25)
All gas	-0.18 (-0.43, 0.06)	**-0.31 (-0.56, -0.06)**	0.17 (-0.11, 0.44)	-0.23 (-0.48, 0.02)	**-0.34 (-0.59, -0.08)**	0.17 (-0.10, 0.44)	0.48 (-0.50, 1.46)
Wood heating and smoking	**-0.35 (-0.63, -0.07)**	**-0.52 (-0.81, -0.24)**	0.20 (-0.11, 0.52)	**-0.35 (-0.63, -0.07)**	**-0.31 (-0.59, -0.02)**	0 (-0.31, 0.30)	**1.25 (0.24, 2.25)**
All electric	-0.03 (-0.27, 0.21)	-0.12 (-0.36, 0.13)	0.12 (-0.15, 0.39)	-0.10 (-0.34, 0.14)	-0.11 (-0.35, 0.13)	-0.01 (-0.26, 0.25)	0.44 (-0.51, 1.39)
Wood & gas heating/gas cooking/smoking	-0.38 (-0.82, 0.06)	-0.42 (-0.87, 0.03)	-0.03 (-0.53, 0.48)	-0.33 (-0.81, 0.14)	-0.45 (-0.93, 0.04)	0.22 (-0.30, 0.73)	1.47 (-0.05, 2.99)
Wood heating/gas cooking	-0.21 (0.46, 0.05)	**-0.32 (-0.59, -0.06)**	0.17 (-0.13, 0.46)	**-0.28 (-0.53, -0.02)**	**-0.32 (-0.58, -0.05)**	0.07 (-0.22, 0.35)	0.39 (-0.68, 1.47)

*Adjusted for sex, change of age, change of BMI, atopy, NO_2 and occupation at the 6^{th} decade.

Table 5 Associations between longitudinal HAP profiles and current asthma at the 6th decade stratified by GSTP1.

HAP exposure profiles	**Current asthma/symptoms, OR (95%CI)**		
	GSTP1 Ile/Val and Val/Val	GSTP1 Ile/Ile	Interaction p values
Least exposed (Reference*)	1	1	
Wood heating	1.42 (0.58, 3.48)	4.48 (0.85, 23.53)	0.12
All gas	0.93 (0.28, 3.07)	**6.03 (1.03, 35.24)**	**0.04**
Wood heating and smoking	1.06 (0.36, 3.09)	**19.57 (2.34, 163.94)**	**0.01**
Electric heating	1.63 (0.62, 4.33)	2.11 (0.16, 27.91)	1.00
Wood & gas heating/gas cooking/smoking	2.15 (0.44, 10.60)	-	0.70
Wood heating/gas cooking	1.08 (0.33, 3.49)	3.28 (0.22, 49.09)	0.73

*Adjusted for age, sex, occupation, atopy at the 6th decade, NO_2 and asthma status at the 5th decade.

Table 6 Associations between HAP profiles and lung function decline by GST genotype (β coefficients representing change in z scores)

			Change of lung function		P interaction
			GSTM1 present	**GSTM1 null**	
Wood heating and smoking	Post-BD	FEV_1/FVC	-0.30 (-0.75, 0.16)	0.22 (-0.40, 0.83)	0.09
Wood & gas heating/gas cooking/smoking	Pre-BD	FEV_1/FVC†	**1.18 (0.17, 2.19)**	-0.50 (-1.30, 0.29)	<0.01
			GSTT1 present	**GSTT1 null**	
Wood heating/smoking	Pre-BD	FEV_1	-0.17 (-0.55, 0.21)	-1.06 (-2.78, 0.66)	0.05
		FVC	-0.20 (-0.56, 0.15)	-2.53 (-7.14, 2.07)	<0.01
		FEV_1/FVC	-0.02 (-0.44, 0.40)	2.28 (-3.02, 7.57)	<0.01
	Post-BD	FVC	-0.12 (-0.46, 0.22)	-0.43 (-2.82, 1.95)	0.03
		FEV_1/FVC	-0.11 (-0.47, 0.24)	1.07 (-3.41, 5.55)	0.03
Wood heating/gas cooking	Pre-BD	FVC	-0.21 (-0.51, 0.09)	-0.62 (-2.85, 1.61)	0.08
			GSTP1 Ile/Val and Val/Val	**GSTP1 Ile/Ile**	
All gas	Post-BD	FEV_1/FVC	0.12 (-0.19, 0.42)	**0.91 (0.27, 1.56)**	0.01
All electric	Pre-BD	FVC	0.03 (-0.29, 0.35)	-0.11 (-0.68, 0.15)	0.09
	Post-BD	FEV_1	0.17 (-0.11, 0.44)	0.04 (-0.44, 0.52)	0.05
		FVC	0.24 (-0.05, 0.52)	-0.11 (-0.72, 0.49)	<0.01
		FEV_1/FVC	-0.19 (-0.56, 0.18)	0.33 (-0.48, 1.14)	0.09
Wood heating/gas cooking	Pre-BD	FEV_1†	-0.01 (-0.37, 0.35)	**-0.62 (-1.07, -0.16)**	0.04
	Post-BD	FEV_1†	-0.06 (-0.41, 0.28)	**-0.53 (-0.97, -0.09)**	0.04
		FVC†	-0.03 (-0.38, 0.32)	**-0.71 (-1.12, -0.30)**	<0.01

*Adjusted for sex, change of age, change of BMI, NO_2, atopy and occupation at the 6^{th} decade.

†Significant interactions (Criteria for interaction: 1. Interaction p<0.1; 2. P value for stratified association<0.05)

Table 7 Associations between longitudinal HAP profiles and respiratory outcomes stratified by ventilation parameters

HAP exposure profiles	**Current asthma*, OR (95% CI)**		
	exhaust fan in use	exhaust fan not in use	Interaction p values
Least exposed (Reference)**	1	1	
Wood heating	1.21 (0.73, 2.02)	**5.47 (1.06, 28.28)**	0.03
All gas	1.33 (0.70, 2.53)	**6.77 (1.25, 36.56)**	0.02
Wood heating and smoking	1.51 (0.83, 2.75)	**10.53 (1.92, 57.65)**	0.01
Wood & gas heating/gas cooking/smoking	1.41, 0.61, 3.23)	**20.11 (1.64, 246.12)**	0.06
	Build year early than 1990	Build year later than 1990	
Electric heater	0.74 (0.31, 1.73)	**7.77 (1.40, 42.98)**	0.01

*Adjusted for age, sex, atopy, NO_2 and occupation at the 6^{th} decade.

†Adjusted for sex, change of age, change of BMI, atopy, NO_2 and occupation at the 6^{th} decade.

**Reference group included people used electric cooking, air conditioning for heating, and no smoking

Exposure to household air pollution over 10 years is related to asthma and lung function decline

Short running head: household air pollution, GST and lung health

Xin Dai[1], Dinh Bui[1], Jennifer L Perret[1], Adrian Lowe[1], Peter A Frith[2,3], Gayan Bowatte[1,4], Paul Thomas[5], Graham G Giles[1,6,7], Garun S Hamilton[8,9], Helen Tsimiklis[10], Jennie Hui[11], John Burgess[1], Aung K Win[1], Michael J Abramson[6], E. Haydn Walters[1,12], Shyamali Dharmage[1*], Caroline Lodge[1*].

1. Allergy and Lung Health Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Parkville, VIC, Australia.
2. College of Medicine and Public Health, Flinders University, Adelaide, SA, Australia.
3. Faculty of Health Sciences, University of South Australia, Adelaide, SA, Australia.
4. Natioanl Institute of Fundamental Studies, Kandy, Sri Lanka.
5. Inflammation and Infection Research, Faculty of Medicine, University of New South Wales, New South Wales, Australia.
6. School of Public Health & Preventive Medicine, Monash University, Melbourne, Vic, Australia
7. Cancer Epidemiology Division, Cancer Council Victoria, Melbourne, VIC, Australia.
8. Department of Lung and Sleep Medicine, Monash Health, Melbourne, Vic, Australia
9. School of Clinical Sciences, Monash University, Vic, Australia
10. Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia
11. The PathWest Laboratory Medicine of West Australia, Perth, WA, Australia.
12. School of Medicine, University of Tasmania, Tasmania, Australia.

*** Equal senior authors**

Corresponding author:

Prof. Shyamali Dharmage

Allergy and Lung Health Unit

Centre for Epidemiology and biostatistics

School of Population and Global Health

Level 3 207 Bouverie Street

University of Melbourne

3010

Email: s.dharmage@unimelb.edu.au

Section 1- Variables from questionnaires

Heating exposures were defined by selection of one or more of the following categories: "Gas ducted central heating", "Coal or wood fire", "Gas room heater", "Electric heater (eg. Radiator, fan or Dimplex-type)", "other central heating (eg. Electric hydronic, slab floor heating)", "Reverse cycle air conditioning", and "Other";

Cooking exposures were defined by the question "What kind of stove do you mostly use for cooking": "Gas", "Electric", "Coal, coke or wood", or "Other";

Mould exposure was defined from the question "Has there been mould or mildew on any surface, other than food, in your home in the last 12 months?";

Active current smoking was identified by any smoking within the last 4 weeks; passive smoking was identified by any currently active smoking inside the house but not counting yourself.

Exposure status was categorized as consistent exposure and no exposure. Consistent exposure to any category was defined by a positive answer for that category on both the 5th and 6th decade questionnaires. No exposure was defined as a negative answer at both time points.

Current asthma: Current asthma/symptoms was defined by any episode of asthma in the past 12 months or any asthma medication taken within the past 3 months (5th decade) or 12 months (6th decade).

New onset asthma: Participants were determined to have new-onset asthma if they had never reported asthma previously but reported current asthma at the 6th decade.

Persistent asthma: Participants were determined to have persistent asthma if they had reported asthma during the study up until the 5th decade and also reported current asthma at the 6th decade.

Lung function

Lung function at the 5th and 6th decade was measured with an EasyOne ultrasonic spirometer (NDD Medizintechnik AG, Zürich, Switzerland). Participants were asked not to smoke for 4-6 hours prior to testing. Spirometry was repeated 10 minutes after 200 µg of salbutamol was administered via a spacer. Forced expiratory volume (FEV_1) and Forced vital capacity (FVC) were recorded as the best of three manoeuvres.

Other variables

As a proxy for **socioeconomic status (SES),** occupation recorded at the 6th decade and coded according to the International Standard Classification of Occupations (ISCO-88) four-digit classification. Participants were grouped into five categories including "managers, administrators, professionals, and associated professionals"; "tradespersons and related workers, advanced clerical and service workers"; "intermediate clerical, sales and service workers, intermediate production and transport workers"; "elementary clerical, sales and service workers" and "labourers and related workers".

Atopy was defined as an average Skin Prick Tests (SPTs) wheal diameter of 3mm or greater for 1 or more of the allergens tested at the 6th decade survey. Skin Prick Tests (SPTs) were performed at the TAHS 6th decade of follow-up by using a standard technique (ref). In total, 10 allergens were included in the testing: *house dust mite, cat, hormodendrum, alternaria, penicillium, aspergillus, rye grass, mixed grasses, egg white, peanut, shellfish and cow's milk.* Histamine was used as a positive control in SPTs. Saline was used as the negative control. Trained research scientists performed all the SPTs and a wheal size of $\geqslant$3 mm or more than the negative control was regarded as an indication of atopy.

COPD was defined as post-BD FEV1/FVC< lower limit of normal (LLN) derived from Global Lung Initiative (GLI) reference equations for Caucasian ethnicity, plus at least one of the key indicators (shortness of breath at rest or after exercise, chronic cough or chronic sputum production; a history of smoking $\geqslant$10 packyears; occupational exposure to vapour/gas/dust/fumes; a family history of COPD) (1).

Building year was defined by the decade in which the home was built. We dichotomized this variable, based on the literature for housing design in Australia, into houses built before and after 1990.

We defined types of **building base structures** as: stumps and wooden flooring, concrete slab, or a combination of both.

Window open was defined by the bedroom airing frequency. This was a binary variable: more than once per week vs. once or less than once per week.

Exhaust fan was defined by positive answers to the following questions "Do you have an exhaust fan over the stove?" and "Does the fan take the fumes outside the house?", and answers to the question: "When cooking how often do you use the fan": ("All of time", "some of time")

e-methods

Genotypes of GSTM1 null and GSTT1 null were detected using a multiplex polymerase chain reaction (PCR) technique as described previously(17) , and for all experiments positive primers for β-globin were included as a positive PCR control. A customised GoldenGate genotyping assay (Illumina, San Diego, CA, USA) was used to genotype the GSTP1 (resulting in Ile105Val at codon 105) polymorphism.

LCA methods: The Latent Class Analysis aimed to classify participants into mutually exclusively sub-groups of an unobserved latent profile, based on the similarity of their patterns of HAP exposures. The number of latent classes were examined sequentially starting at a 2-class model. The final number of latent classes was determined by model fit criteria (AIC, BIC and log-likelihood) by comparing models from 2 classes to 9 classes. This process identifies a best fit model which maximizes between-class and minimizes within-class variance, resulting in participants assigned to the class for which they had the highest probability of membership. Identified HAP features can then be related to the individual level behaviours of interest.

Table S1. Comparison of 5th decade exposures in participants with lung function at both 5th and 6th decades and those lost to follow-up (5th decade only)

	Participants followed–up to the 6th decade for lung function [N (%)]	**Participants at 5th decade for lung function only [N (%)]**	**Comparison P values**
N	897	502	
Ducted gas central heating	47 (5.2)	22 (4.4)	0.48
Wood or coal fire	438 (48.8)	229 (45.6)	0.25
Gas room heater	70 (7.8)	45 (9.0)	0.45
Electric heater	390 (43.5)	191 (38.1)	0.05
Reverse cycle air conditioning	198 (22.1)	98 (19.5)	0.26
Gas cooking	188 (21.0)	61 (12.2)	<0.01
Electric cooking	706 (78.9)	437 (87.1)	<0.01
Mould in last 12 months	361 (40.3)	184 (37.0)	0.22
Active smoking*	211 (34.2)	174 (48.6)	<0.01
Passive smoking	103 (11.6)	83 (17.0)	0.01

* Participants who attended both follow-ups for lung function were more likely to be exposed to electric heater (p=0.05) and gas cooking (p<0.01); less likely to use electric cooking (p<0.01), be smoker (p<0.01) or be exposed to passive smoking (p<0.01)

Table S2 Characteristic at the 5th decade for participants followed to the 6th decade and those not followed

Participants at 5th decade (N=5720)		
	Participants followed–up to the 6th decade	**Participants lost to follow up**
N	3314	2406
Age	42.7 (41-44)	43.0 (42-44)
Men	1630 (49.2)	1318 (54.8)
Tertiary education	1790 (53.9)	975 (40.6)
GSTM1 null	481 (53.7)	165 (57.7)
GSTT1 null	150 (16.8)	40 (14.0)
GSTP1 Ile/Ile alleles	352 (39.4)	116 (40.3)
Current asthma	376 (11.3)	262 (10.9)
***Ducted gas central heating**	215 (6.5)	124 (5.2)
Wood or coal fire	1461 (44.1)	1012 (42.1)
Gas room heater	386(11.6)	246 (10.2)
Electric heater	1279 (38.6)	908 (37.7)
***Reverse cycle air conditioning**	715 (21.6)	426 (17.7)
***Gas cooking**	783 (23.6)	487 (20.2)
***Electric cooking**	2507 (75.6)	1889 (78.5)
***Mould in last 12 months**	1250 (37.7)	735 (30.8)
***Active smoking**	793 (24.0)	908 (38.0)
***Passive smoking**	391 (10.5)	447 (19.3)

*factors significantly differed between those lost and not lost to follow-up. Participants who attended both follow-ups were more likely to: use gas ducted central heating (p=0.04), reverse cycle air-conditioning (p<0.001), gas cooking (p=0.01), and report visible mould (p<0.001); and less likely to: use electric cooking (p=0.004), be smokers (p<0.001) or be exposed to passive smoking (p<0.001).

Table S3 Model fit characteristics for 3-8 class models.

No of class	**Fit criteria**					**Class size**							
	Entropy	BIC	AIC	Adjusted BIC	Log-likelihood	1	2	3	4	5	6	7	8
3	0.81	4714	4408	4555	-21357	1944	578	797					
4	0.78	4208	3799	3995	-21035	644	1246	867	562				
5	0.79	4077	3564	3810	-20901	524	1275	394	537	589			
6	0.82	4005	3388	3684	-20795	441	975	866	337	163	537		
7	0.8	**3969**	3259	**3540**	**-20640**	453	952	538	446	450	157	323	
8	0.79	3980	3145	3605	-20714	532	887	435	518	324	282	224	117

Table S4 Associations between longitudinal indoor exposure profiles and asthma outcomes at the 6th decade (excluding COPD).

Grouped environment exposures	**N of exposed**	**New Onset asthma**			**Persistent asthma**		
		N	ORs+	P	N	ORs+	P
Least exposed (Reference*)	440	29	1		20	1	
Wood heating	919	47	0.89 (0.49, 1.61)	0.70	77	1.84 (0.90, 3.74)	0.09
All gas	527	36	1.15 (0.59, 2.26)	0.68	49	**2.45 (1.07, 5.60)**	**0.03**
Wood heating and smoking	375	32	1.54 (0.79, 3.01)	0.21	29	1.57 (0.58, 4.26)	0.37
All electric	436	35	1.45 (0.78, 2.70)	0.24	31	1.26 (0.56, 2.85)	0.58
Wood & gas heating/gas cooking/smoking	142	11	**2.49 (1.01, 6.16)**	**0.05**	12	0.68 (0.16, 2.85)	0.60
Wood heating/gas cooking	314	7	**0.24 (0.07, 0.85)**	**0.03**	26	**3.02 (1.23, 7.41)**	**0.02**

*Reference group included people used electric cooking, air conditioning for heating and no smoking

ORs were adjusted for sex, age, NO_2, atopy, and occupation at 6th decade survey

Table S5 The associations between HAP profiles and lung function decline (absolute raw values in each profile) between the two follow-ups.

HAP exposure profiles	**Pre-bronchodilator**			**Post-bronchodilator**		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
Least exposed (reference)	-0.13 (-0.20, -0.06)	-0.05 (-0.15, 0.05)	-2.11 (-3.36, -0.86)	-0.11 (-0.18, -0.04)	-0.08 (-0.18, 0.02)	-1.05 (-2.62, 0.53)
Wood heating	-0.21 (-0.26, -0.15)	-0.22 (-0.29, -0.15)	-0.87 (-1.75, -0.01)	-0.24 (-0.30, -0.19)	-0.24 (-0.31, -0.17)	-1.65 (-2.76, -0.54)
All gas	-0.25 (-0.32, -0.18)	-0.31 (-0.41, -0.21)	-0.21 (-1.45, 1.02)	-0.23 (-0.30, -0.16)	-0.29 (-0.39, -0.20)	0.11 (-1.49, 1.70)
Wood heating and smoking	-0.35 (-0.45, -0.25)	-0.43 (-0.56, -0.29)	-0.96 (-2.67, 0.75)	-0.30 (-0.40, -0.20)	-0.30 (-0.43, -0.16)	-1.34 (-3.49, 0.82)
All electric	-0.19 (-0.26, -0.11)	-0.17 (-0.56, -0.29)	-1.41 (-2.69, -0.13)	-0.18 (-0.25, -0.10)	-0.18 (-0.28, -0.08)	-1.04 (-2.66, 0.57)
Wood & gas heating/gas cooking/smoking	-0.28 (-0.46, -0.09)	-0.30 (-0.55, -0.05)	-2.19 (-5.29, 0.91)	-0.21 (-0.41, -0.02)	-0.27 (-0.53, -0.02)	0.06 (-4.17, 4.28)
Wood heating/gas cooking	-0.24 (-0.33, -0.16)	-0.26 (-0.37, -0.14)	-0.99 (-2.48, 0.51)	-0.22 (-0.31, -0.13)	-0.24(-0.36, -0.13)	-0.61 (-2.50, 1.28)

*Adjusted for sex, change of age, change of BMI, atopy, NO_2, and occupation at the 6^{th} decade.

Table S6 the associations* between HAP profiles and lung function decline (change in %predicted) between the two follow-ups.

HAP exposure profiles	**Pre-bronchodilator**			**Post-bronchodilator**		
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
Least exposed (reference)	0	0	0	0	0	0
Wood heating	-2.16 (-4.98, 0.66)	-4.29 (-7.20, -1.39)	1.72 (-1.30, 4.73)	-3.48 (-8.04, 1.09)	**-3.91 (-6.75, -1.06)**	0.62 (-2.25, 3.49)
All gas	-3.31 (-6.70, 0.07)	**-4.97 (-8.46, -1.48)**	2.88 (-0.74, 6.50)	-0.48 (-6.05, 5.08)	**-4.74 (-8.21, -1.27)**	2.35 (-1.15, 5.85)
Wood heating and smoking	**-6.03 (-9.95, -2.11)**	**-7.62 (-11.66, -3.57)**	**4.24 (0.05, 8.43)**	2.01 (-4.32, 8.34)	**-4.14 (-8.08, -0.19)**	3.24 (-0.73, 7.22)
All electric	-1.19 (-4.47, 2.09)	-2.02 (-5.41, 1.36)	1.45 (-2.06, 4.96)	0.07 (-5.23, 5.36)	-1.76 (-5.06, 1.55)	0.46 (-2.87, 3.80)
Wood & gas heating/gas cooking/smoking	-5.86 (-12.04, 0.32)	**-7.21 (-13.58, -0.83)**	-0.74 (-0.73, 5.87)	1.55 (-9.11, 12.22)	-7.04 (-13.68, -0.39)	-0.04 (-6.75, 6.66)
Wood heating/gas cooking	-3.68 (-7.29, -0.07)	**-5.13 (-8.85, -1.40)**	3.77 (-0.09, 7.63)	-2.56 (-9.10, 12.22)	**-4.41 (-8.04, -0.78)**	1.85 (-1.81, 5.52)

*Adjusted for sex, change of age, change of BMI, atopy, NO_2, and occupation at the 6^{th} decade.

Table S7 Adjusted ORs* for indoor environmental exposures in the 5th to the 6th decade for participants with and without asthma at the 5th decade and asthma outcomes at the 6th decade

Consistent household exposures	N of exposed	New onset asthma		Persistent asthma	
		ORs	P	ORs	P
Ducted gas central heating	140	0.88 (0.32, 2.44)	0.81	**2.17 (1.07, 4.38)**	**0.03**
Never (ref)	2983	1		1	
Wood or coal fire	967	**0.60 (0.37, 0.99)**	**0.04**	1.29 (0.85, 1.97)	0.24
Never (ref)	4306	1		1	
Gas room heater	166	1.27 (0.61, 2.63)	0.53	0.90 (0.42, 1.93)	0.78
Never (ref)	2787	1		1	
Electric heater	590	1.35 (0.82, 2.22)	0.24	1.08 (0.70, 1.66)	0.73
Never (ref)	1636	1		1	
Reverse cycle air conditioning	553	1.32 (0.76, 2.29)	0.32	1.34 (0.83, 2.16)	0.23
Never (ref)	1578	1		1	
Gas cooking	547	0.60 (0.34, 1.05)	0.08	1.01 (0.65, 1.58)	0.95
Never (ref)	2106	**1**		1	
Electric cooking	2069	1.49 (0.87, 2.56)	0.14	0.96 (0.62, 1.49)	0.85
Never (ref)	575	1		1	
Mould exposure	619	1.09 (0.69, 1.71)	0.93	1.19 (0.79, 1.81)	0.40
Never	1512	1		1	
Active smoking	477	**2.43 (1.47, 4.03)**	**<0.01**	0.98 (0.58, 1.65)	0.95
Never	1450	1		1	
Passive smoking	117	1.62 (0.66, 3.98)	0.29	1.10 (0.39, 3.07)	0.86
Never	2694	1		1	

*All exposures were adjusted for age, sex, atopy, NO_2 and occupation, heating appliances were adjusted for other heating appliance use, active smoking was adjusted for passive smoking at home; passive smoking was adjusted for active smoking.

Table S8 Adjusted coefficients[+] for consistent household exposures and lung function decline between the 5th and 6th decade follow-ups.

Consistent household exposures	**Pre-Bronchodilator**			**Post-bronchodilator**		
	FEV1	FVC	FEV1/FVC	FEV1	FVC	FEV1/FVC
Ducted gas central heating	-0.37 (-0.78, 0.04)	-0.41 (-0.84, 0.01)	0 (-0.48, 0.47)	-0.34 (-0.75, 0.08)	**-0.60 (-1.02, -0.18)**	0.37 (-0.08, 0.81)
Never (ref)	0	0	0	0	0	0
Wood or coal fire	0.01 (-0.15, 0.16)	-0.08 (-0.25, 0.09)	0.12 (-0.06, 0.31)	-0.11 (-0.26, 0.04)	-0.08 (-0.25, 0.09)	-0.05 (-0.24, 0.14)
Never (ref)	0	0	0	0	0	0
Gas room heater	-0.19 (-0.53, 0.16)	-0.31 (-0.67, 0.04)	0.26 (-0.13, 0.65)	-0.21 (--0.56, 0.13)	-0.27 (-0.61, 0.08)	0.10 (-0.26, 0.47)
Never (ref)	0	0	0	0	0	0
Electric heater	-0.08 (-0.27, 0.10)	-0.07 (-0.26, 0.11)	-0.02 (-0.22, 0.18)	-0.14 (-0.33, 0.04)	-0.13 (-0.33, 0.07)	0.01 (-0.19, 0.20)
Never (ref)	0	0	0	0	0	0
Reverse cycle air conditioning	0.05 (-0.14, 0.23)	0 (-0.15, 0.22)	0.08 (-0.14, 0.30)	0.04 (-0.15, 0.23)	-0.05 (-0.26, 0.17)	0.18 (-0.04, 0.39)
Never (ref)	0	0	0	0	0	0
Gas cooking	0.23 (-0.18, 0.23)	0.02 (-0.19, 0.23)	0.01 (-0.24, 0.21)	0.06 (-0.15, 0.27)	-0.01 (-0.23, 0.20)	0.08 (-0.15, 0.30)
Never (ref)	0	0	0	0	0	0
Electric cooking	0.02 (-0.18, 0.23)	0 (-0.20, 0.21)	-0.07 (-0.15, 0.30)	0.01 (-0.19, 0.22)	0.10 (-0.12, 0.31)	-0.08 (-0.30, 0.14)
Never (ref)	0	0	0	0	0	0
Mould exposure	-0.02 (-0.21, 0.16)	-0.11 (-0.30, 0.08)	0.09 (-0.13, 0.30)	0.15 (-0.33, 0.04)	0.14 (-0.34, 0.06)	0.03 (-0.16, 0.22)
Never	0	0	0	0	0	0
Active smoking	**-0.35 (-0.61, -0.10)**	**-0.33 (-0.61, -0.06)**	-0.15 (-0.41, 0.20)	-0.26 (-0.52, 0.01)	-0.14 (-0.40, 0.13)	-0.11 (-0.42, 0.20)
Never	0	0	0	0	0	0
Passive smoking	-0.61 (-1.16, -0.06)	-0.14 (-0.73, 0.45)	**-0.85 (-1.48, -0.23)**	**-0.78 (-1.35, -0.22)**	-0.54 (-1.15, 0.06)	-0.36 (-0.91, 0.20)
Never	0	0	0	0	0	0

*All associations were adjusted for sex, change of age, change of BMI, NO_2, and occupation, heating appliances were adjusted for other heating appliance use, cooking appliances were adjusted for exhaust fan use, active smoking was adjusted for passive smoking at home; passive smoking was adjusted for active smoking.

Table S9 the associations between GST genes and lung function decline (beta coef for change in z-score) between the 5th and 6th decades.

	Pre-Bronchodilator			Post-bronchodilator		
	FEV1	FVC	FEV1/FVC	FEV1	FVC	FEV1/FVC
GSTM1	0 (-0.13, 0.13)	-0.02 (-0.16, 0.12)	0.04 (-0.11, 0.19)	0.08 (-0.06, 0.21)	0.09 (-0.04, 0.23)	-0.04 (-0.19, 0.10)
GSTT1	0.14 (-0.05, 0.32)	0.13 (-0.07, 0.33)	0.04 (-0.18, 0.25)	0.07 (-0.12, 0.26)	0.16 (-0.04, 0.35)	-0.03 (-0.24, 0.17)
GSTP1	0 (-0.13, 0.13)	-0.04 (-0.18, 0.10)	0.03 (-0.12, 0.19)	0.06 (-0.08, 0.20)	0.05 (-0.10, 0.19)	0.01 (-0.14, 0.16)

*Coefficients were adjusted for sex, change of age, change of BMI and occupation at 6th decade.

Table S10 the associations between GST genes and current asthma/wheeze outcomes at the 6th decade

	Current asthma		Current wheeze	
	OR	P	OR	P
GSTM1	0.90 (0.66, 1.23)	0.49	0.88 (0.65, 1.18)	0.39
GSTT1	0.71 (0.46, 1.11)	0.14	0.91 (0.61, 1.36)	0.66
GSTP1	0.87 (0.63, 1.20)	0.41	1.82 (0.60, 1.11)	0.19

*ORs were adjusted for sex, age, and occupation at 6th decade survey.

Table S11 Interaction P values on associations between longitudinal HAP profiles and current asthma at the 6th decade.

Grouped environmental exposures	**Current asthma**		
	GSTM1	GSTT1	GSTP1
Wood heating only	0.78	0.47	0.12
Gas cooking and heater	0.65	0.70	**0.04**
Wood heating and smoking	0.75	0.27	**0.01**
Electric heater	0.73	0.42	1.00
Gas heating, cooking and smoking	0.17	-	0.70
Gas cooking and wood heating	0.87	0.70	0.73

*Adjusted for age, sex, occupation and atopy at the 6th decade, NO_2, and asthma status at the 5th decade.

Table S12 Interaction P values for associations between longitudinal HAP profiles and lung function decline for GSTM1.

Grouped environment exposures	Pre-bronchodilator			Post-bronchodilator		
	FEV1	FVC	FEV1/FVC	FEV1	FVC	FEV1/FVC
Least exposed (reference)	1	1	1	1	1	1
Wood heating	0.77	0.86	0.57	0.63	0.83	0.47
All gas	0.64	0.62	0.55	0.95	0.66	0.15
Wood heating and smoking	0.98	0.68	0.58	0.15	0.76	**0.09**
All electric	0.52	0.96	0.46	0.49	0.13	0.26
Wood & gas heating/gas cooking/smoking	0.18	0.71	**<0.01**	0.58	0.84	0.45
Wood heating/gas cooking	0.91	0.66	0.61	0.21	0.21	0.95

*Adjusted for sex, change of age, change of BMI, NO_2, atopy and occupation at the 6^{th} decade.

Table S13 Interaction P values for associations between HAP profiles and lung function decline for GSTT1.

Grouped environment exposures	**Pre-bronchodilator**			**Post-bronchodilator**		
	FEV1	FVC	FEV1/FVC	FEV1	FVC	FEV1/FVC
Least exposed (reference)	1	1	1	1	1	1
Wood heating	0.79	0.82	0.88	0.62	0.87	0.46
All gas	0.43	0.20	0.44	0.33	0.12	0.40
Wood heating and smoking	**0.05**	**<0.01**	**<0.01**	0.40	**0.03**	**0.03**
All electric	0.47	0.24	0.51	0.37	0.59	0.82
Wood & gas heating/gas cooking/smoking	-	-	-	-	-	-
Wood heating/gas cooking	0.16	**0.08**	0.27	0.575	0.63	0.56

*Adjusted for sex, change of age, change of BMI, NO_2, atopy and occupation at the 6^{th} decade.

Table S14 Interaction P values for associations between HAP profiles and lung function decline for GSTP1.

Grouped environment exposures	**Pre-bronchodilator**			**Post-bronchodilator**		
	FEV1	FVC	FEV1/FVC	FEV1	FVC	FEV1/FVC
Least exposed (reference)	1	1	1	1	1	1
Wood heating	0.37	0.23	0.99	0.88	0.56	0.38
All gas	0.56	0.47	0.89	0.80	0.18	**0.01**
Wood heating and smoking	0.55	0.61	0.65	0.71	0.69	0.95
All electric	0.15	**0.09**	0.71	**0.05**	**<0.01**	**0.09**
Wood & gas heating/gas cooking/smoking	0.77	0.96	0.56	0.40	0.96	0.11
Wood heating/gas cooking	**0.04**	0.11	0.34	**0.04**	**<0.01**	0.13

*Adjusted for sex, change of age, change of BMI, NO_2, atopy and occupation at the 6^{th} decade.

Table S15 Associations between longitudinal indoor exposure profiles and lung function decline (excluding asthma and COPD).

HAP exposure profiles	**Pre-bronchodilator**			**Post-bronchodilator**			**% reversibility in FEV_1**
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC	
Least exposed (reference)	0	0	0	0	0	0	0
Wood heating	-0.20 (-0.46, 0.05)	**-0.29 (-0.56, -0.03)**	0.14 (-0.14, 0.41)	**-0.29 (-0.55, -0.03)**	-0.23 (-0.49, 0.03)	-0.07 (-0.34, 0.20)	0.27 (-0.41, 0.96)
All gas	-0.35 (-0.68, -0.03)	**-0.38 (-0.71, -0.04)**	0.03 (-0.32, 0.37)	-0.16 (-0.49, 0.18)	-0.27 (-0.60, 0.06)	0.12 (-0.23, 0.47)	0.10 (-0.71, 0.92)
Wood heating and smoking	**-0.43 (-0.79, -0.07)**	**-0.65 (-1.02, -0.28)**	0.36 (-0.02, 0.74)	**-0.40 (-0.77, -0.04)**	**-0.40 (-0.76, -0.04)**	0.09 (-0.29, 0.47)	0.10 (-0.79, 1.00)
All electric	-0.04 (-0.34, 0.25)	-0.13 (-0.43, 0.18)	0.14 (-0.18, 0.46)	-0.11 (-0.41, 0.18)	-0.05 (-0.34, 0.25)	-0.13 (-0.45, 0.18)	-0.37 (-1.56, 0.42)
Wood & gas heating/gas cooking/smoking	-0.30 (-0.89, 0.29)	-0.40 (-1.01, 0.21)	0.21 (-0.42, 0.85)	-0.11 (-0.80, 0.57)	-0.11 (-0.79, 0.57)	0.14 (-0.58, 0.86)	0.87 (-0.49, 2.23)
Wood heating/gas cooking	-0.28 (0.61, 0.05)	**-0.35 (-0.69, -0.01)**	0.15 (-0.20, 0.50)	-0.16 (-0.50, 0.17)	-0.18 (-0.51, 0.15)	0.04 (-0.31, 0.39)	0.20 (-0.69, 1.08)

*Reference group included people used electric cooking, air conditioning for heating and no smoking

ORs were adjusted for sex, age, NO_2, atopy, and occupation at 6^{th} decade survey

Table S16 the associations between LCA profiles and asthma outcomes for those who did not move their home during 10 years' follow-up.

HAP exposure profiles	N of exposed	New Onset asthma/symptoms			Persistent asthma/symptoms		
		N	ORs[+]	P	N	ORs[+]	P
Least exposed (Reference*)	256	18	1		8	1	
Wood heating	593	30	0.78 (0.32, 1.42)	0.30	57	**2.85 (1.31, 7.17)**	**0.03**
All gas	304	22	1.29 (0.57, 2.91)	0.55	33	**4.08 (1.41, 11.80)**	**0.01**
Wood heating and smoking	242	23	1.69 (0.79, 3.61)	0.18	31	**4.12 (1.39, 12.15)**	**0.01**
All electric	307	34	1.88 (0.92, 2.83)	0.08	20	1.28 (0.45, 3.66)	0.64
Wood & gas heating/gas cooking/smoking	81	6	2.08 (0.68, 6.36)	0.20	7	1.21 (0.25, 5.84)	0.81
Wood heating/gas cooking	177	2	**0.21 (0.05, 0.96)**	**0.04**	17	**3.31 (1.08, 10.15)**	**0.04**

+ All ORs were adjusted for age, sex, atopy, NO_2 and occupation at the 6^{th} decade.

Table S17 the associations between LCA profiles and lung function decline for those who did not move their home during 10 years' follow-up.

HAP exposure profiles	**Pre-bronchodilator**			**Post-bronchodilator**			**% reversibility in FEV_1**
	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC	
Least exposed (reference)	-	-	-	-	-	-	-
Wood heating	-0.11 (-0.34, 0.13)	-0.23 (-0.48, 0.02)	0.18 (-0.10, 0.46)	**-0.29 (-0.54, -0.05)**	**-0.26 (-0.51, -0.02)**	0.01 (-0.26, 0.29)	0.05 (-1.31, 1.42)
All gas	-0.15 (-0.43, 0.13)	**-0.28 (-0.57, 0.01)**	0.18 (-0.15, 0.51)	-0.26 (-0.55, 0.03)	**-0.40 (-0.69, -0.11)**	0.19 (-0.14, 0.53)	0.57 (-1.13, 2.67)
Wood heating and smoking	**-0.48 (-0.82, -0.14)**	**-0.66 (-1.01, -0.30)**	0.23 (-0.17, 0.62)	**-0.46 (-0.82, -0.11)**	**-0.41 (-0.76, -0.06)**	0 (-0.40, 0.40)	**2.19 (0.53, 3.85)**
All electric	-0.02 (-0.29, 0.26)	-0.03 (-0.31, 0.26)	-0.01 (-0.33, 0.31)	-0.12 (-0.40, 0.16)	-0.11 (-0.39, 0.17)	-0.07 (-0.39, 0.25)	0.10 (-1.45, 1.64)
Wood & gas heating/gas cooking/smoking	**-0.90 (-1.46, -0.35)**	-0.66 (-1.25, -0.08)	**-0.65 (-1.30, 0)**	-1.15 (-1.80, 0.50)	-1.09 (-1.74, -0.44)	-0.16 (-0.90, 0.58)	1.58 (-1.51, 4.67)
Wood heating/gas cooking	-0.15 (0.46, 0.16)	**-0.34 (-0.67, -0.02)**	0.27 (-0.10, 0.63)	**-0.17 (-0.49, 0.15)**	**-0.20 (-0.52, 0.12)**	0.03 (-0.33, 0.40)	0.37 (-1.42, 2.15)

*Adjusted for sex, change of age, change of BMI, atopy, NO_2 and occupation at the 6^{th} decade.

1. Global initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis Management of prevention of COPD. 2017 04/06/2019]. Available from: http://goldcopd.org.