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

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Long-term exposure to household air pollution (gas, wood smoke, tobacco smoke and their combinations) is linked to adverse respiratory health in middle age, particularly for those with GST risk variants and living in poorly ventilated houses https://bit.ly/3ammfKu

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ABSTRACT

Introduction: We investigated if long-term household air pollution (HAP) is associated with asthma and lung function decline in middle-aged adults, and whether these associations were modified by glutathione *S*-transferase (GST) gene variants, ventilation and atopy.

Materials and methods: Prospective data on HAP (heating, cooking, mould and 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 characterise longitudinal patterns of exposure. Regression models assessed associations and interactions.

Results: We identified seven longitudinal HAP profiles. Of these, three were associated with persistent asthma, greater lung function decline and % reversibility by age 53 years compared with the "Least exposed" reference profile for those who used reverse-cycle air conditioning, electric cooking and no smoking. The "All gas" (OR 2.64, 95% CI 1.22–5.70), "Wood heating/smoking" (OR 2.71, 95% CI 1.21–6.05) and "Wood heating/gas cooking" (OR 2.60, 95% CI 1.11–6.11) profiles were associated with persistent asthma, as well as greater lung function decline and % reversibility. Participants with the *GSTP1* Ile/Ile genotype were at a higher risk of asthma or greater lung function decline when exposed compared with other genotypes. Exhaust fan use and opening windows frequently may reduce the adverse effects of HAP produced by combustion heating and cooking on current asthma, presumably through increasing ventilation.

Conclusions: 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.

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Introduction

Asthma is the most common chronic respiratory disease worldwide. 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 recognised as risk factors for asthma, COPD and asthma–COPD overlap only in low- and 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 and wood) are inconsistent.

A cross-sectional, population-based study in South America of 5539 subjects aged ⩾40 years found indoor wood smoke was associated with asthma and wheezing [7]. Another large cross-sectional study in China suggested a range of domestic risk factors, including gas cooking and incense burning, were associated with respiratory symptoms in adults. However, two large-scale cross-sectional surveys, *i.e.* 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 studies 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 a 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 fifth and sixth decade follow-ups from the Tasmanian Longitudinal Health Study (TAHS), we investigated the relationship between longitudinal exposure to heating/cooking facilities, smoking and mould, 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.

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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) [16]. We have recently followed participants into their fifth and sixth decades (beginning in 2002 and 2012, respectively) at ages 43 years (mean±SD 42.7±0.82 years) and 53 years (mean±SD 53.0±0.93 years), respectively (figure 1 and table 1). The mean±SD follow-up duration was 10.1±1.1 years. 5729 participants (78.4% of those traced) completed the fifth decade questionnaire and 3609 participants (42.0%) completed the sixth decade questionnaire. 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 measurements (figure 2). Additionally, 1215 subjects contributed genetic information at the fifth decade follow-up. Of these, 930 also completed the sixth decade questionnaire. More details of follow-ups have been reported elsewhere [16–18].

HAP exposures

The fifth and sixth decade questionnaires included the same items for determining HAP exposure in the previous 12 months. Details of specific questions concerning HAP exposures are given in the supplementary material.

Asthma and lung function decline

At the sixth 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 reference equations for Caucasians [19, 20]. Lung function decline was determined by reductions in lung function between follow-ups, derived from reductions in *z*-scores and % predicted. Details of asthma definitions and lung function procedures are in given in the supplementary material.

Other variables

A satellite-based land-use regression (LUR) model was used to assign mean annual exposure to nitrogen dioxide (NO_2). LUR used satellite observations of tropospheric NO_2 columns with land use, roads and

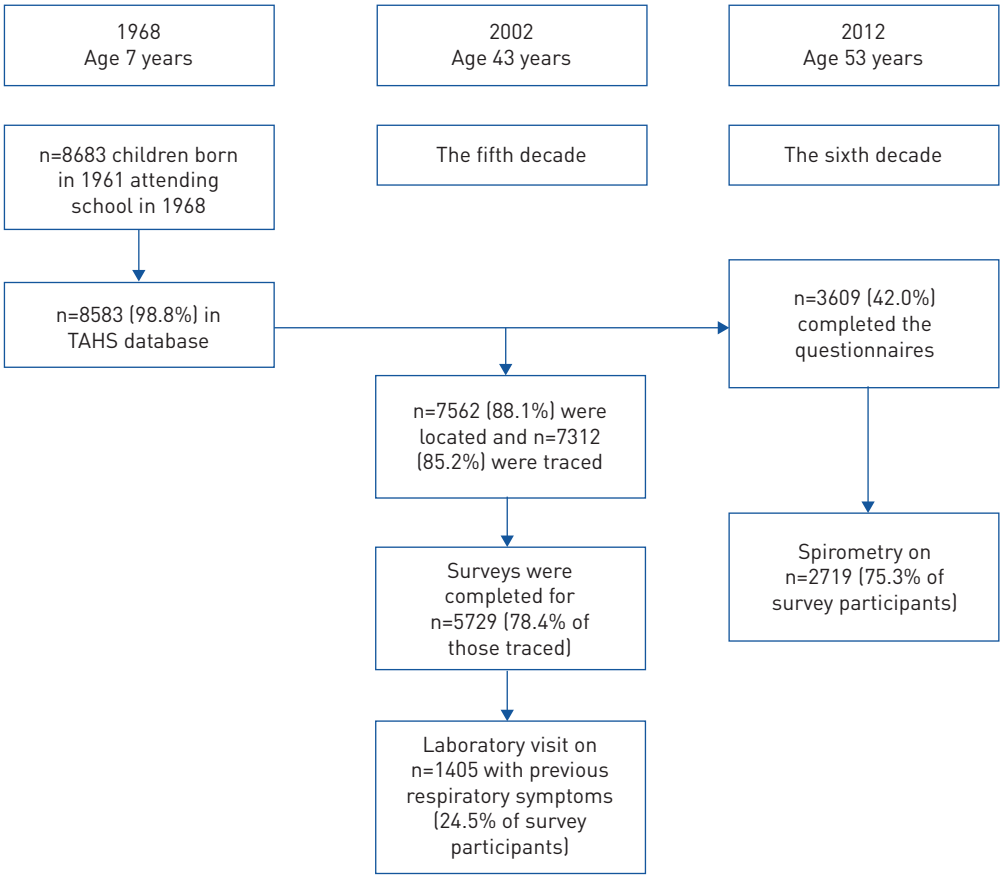

FIGURE 1 Flowchart of the Tasmanian Longitudinal Health Study (TAHS).

TABLE 1 Characteristics of the 3314 study sample participants at both follow-ups

	Fifth decade follow-up	Sixth decade follow-up
Age years	42.7±0.82	53.0±0.93
Male	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)

Data are presented as mean±SD or n (%).

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 [21]. We adjusted NO_2 at the fifth decade only as small changes between the 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 given in the supplementary material.

Genotyping of GST genes

DNA was isolated from whole-blood samples provided at the sixth decade follow-up. *GSTM1/T1* genotypes 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 given in the supplementary material.

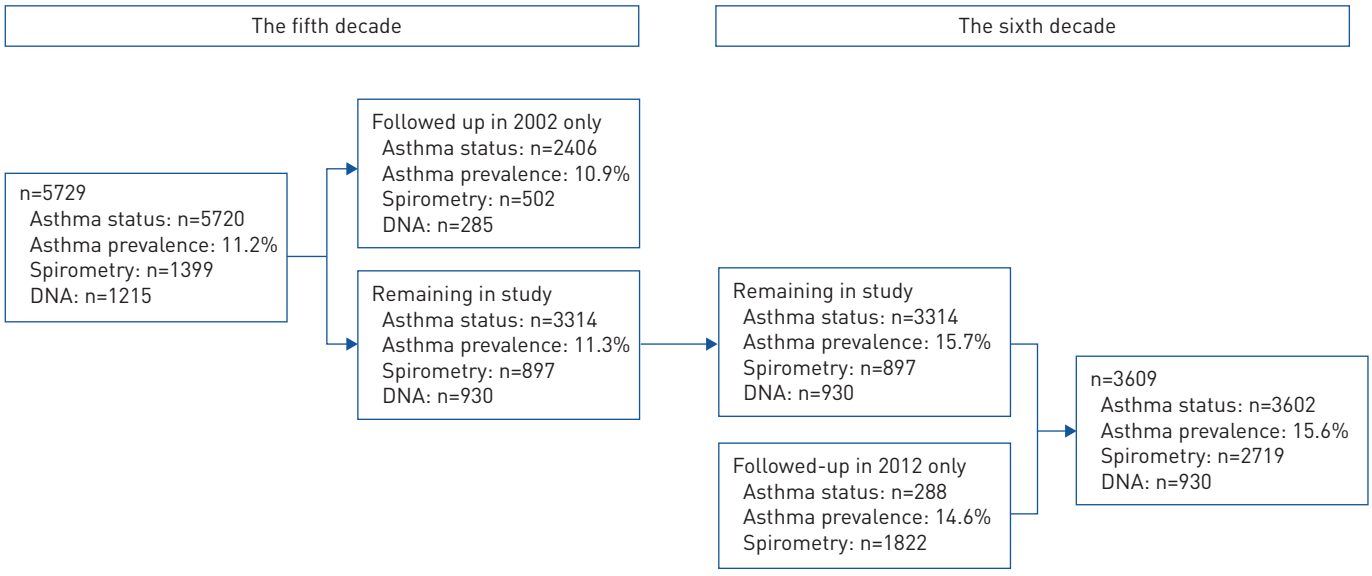

FIGURE 2 Flowchart of Tasmanian Longitudinal Health Study proband participation at the 2002 and 2012 surveys stratified by asthma status.

Statistical analysis

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. Details of LCA statistical methods are given in the supplementary material.

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 sixth decade. For lung function decline, we adjusted for change of age, change of body mass index, sex, atopy, outdoor NO_2 and occupation at the sixth 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 1) GST polymorphisms, 2) atopy and 3) ventilation parameters, including build 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 and then the stratified analyses were presented. Stata version 14.2 (StataCorp, College Station, TX, USA) was used for all analyses.

Results

The characteristics of the TAHS participants who participated in the fifth and sixth 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 fifth decade characteristics for the remaining participants with those lost to follow-up for lung function and survey is presented in supplementary tables S1 and S2.

Latent class exposure profiles

The Bayesian information criterion for the LCA model with seven classes was found to be the best fit (supplementary table S3). There was no substantial improvement in models with more than seven classes. The seven latent classes were labelled as "Least exposed", "Wood heating", "All gas", "Wood heating/smoking", "All electric", "Wood and 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 and 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 persistent asthma/symptoms was seen for the "Wood heating/smoking" profile (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) profiles. The "All electric" profile did not demonstrate evidence for this clinical association.

The "Wood and gas heating/gas cooking/smoking" and "Wood heating/smoking" profiles were associated with new-onset asthma/symptoms (OR 2.52, 95% CI 1.06–5.99 and OR 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, 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 fifth and sixth decades (n=181). Associations found were largely unchanged and similar to those using self-reported asthma outcomes (supplementary table S4).

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

The "Wood heating", "All gas", "Wood heating/smoking" and "Wood heating/gas cooking" profiles were associated with increased lung function decline for forced expiratory volume in 1 s (FEV_1) and/or forced vital capacity (FVC) (table 4). Participants who were exposed to the "Wood heating/smoking" profile had the most lung function decline for pre-bronchodilator FEV_1 (β-coefficient 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 of follow-up compared with the reference profile. We present absolute values for lung function decline for each profile in supplementary table S5. Participants in the "Wood heating/smoking" and "Wood and gas heating/gas

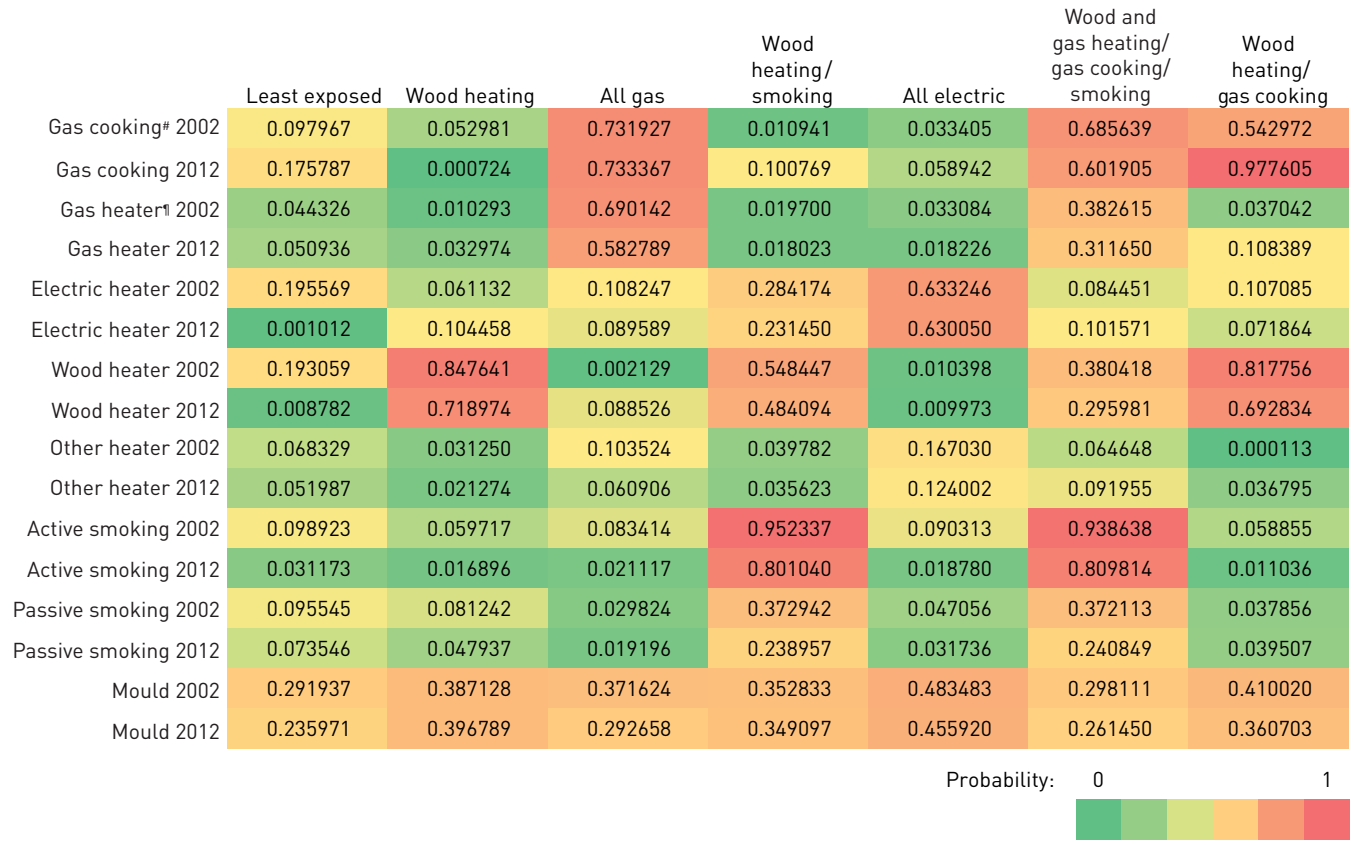

FIGURE 3 Heatmap of probability of having each risk factor for seven household air pollution risk profiles estimated from the latent class analysis model. Intensity of colour indicates probability of each risk factor in each latent class (from 0 to 1 or 100%). #: for cooking choices, >98% of participants 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 cooking as reference, thus only gas appears in the heatmap. ¶: combined gas heater and ducted gas heating.

cooking/smoking" profiles had increased FEV_1 % reversibility compared with 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 are given in supplementary table S6.

TABLE 2 Prevalence and characteristics of household air pollution profiles identified by latent class analysis

Series number	Profile name	n (%)	Description
1	Least exposed	453 (13.7)	Highest probability of reverse-cycle air conditioning and 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; the 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 and lowest probability of gas cooking indicating higher probability of electric cooking; the probability of other risk factors was similar to "Least exposed"
6	Wood and gas heating/gas cooking/smoking	157 (4.7)	Highest probability of current smoking at both surveys, and 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 household air pollution profiles and asthma outcomes by the sixth decade

	Exposed n	New-onset asthma/symptoms			Persistent asthma/symptoms		
		n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
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/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 and 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*

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 sixth decade. [#]: adjusted for age, sex, atopy, nitrogen dioxide and occupation at the sixth decade; [¶]: reference group included people who used electric cooking, air conditioning for heating and no smoking. *: p<0.05.

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 (supplementary tables S7 and S8).

Interactions by GST genotype, ventilation and atopy

We used current asthma/symptoms at the sixth 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 (supplementary tables S9 and S10). However, we found evidence of interactions between GST genotypes and HAP profiles and asthma and lung function decline (supplementary tables S11–S14). The "All gas" and "Wood heating/smoking" profiles were associated with increased risks of current asthma symptoms for participants with the *GSTP1* Ile/Ile genotype, but this association was not seen for participants with Ile/Val and Val/Val genotypes (interaction p-value 0.04 and 0.01, respectively) (table 5). Exposure to the "Wood heating/gas cooking" profile was associated with greater post-bronchodilator FEV_1 and FVC decline for those with the *GSTP1* Ile/Ile genotype (table 6). The "Wood and gas heating/gas cooking/smoking" profile was associated with greater FEV_1/FVC ratio decline for people with the *GSTM1* null genotype compared with those with the

TABLE 4 Associations[#] between household air pollution profiles and lung function decline between the two follow-ups

	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/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 and 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)

Data are presented as β-coefficient (95% CI) from linear regression, representing change in *z*-scores. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity. [#]: adjusted for sex, change of age, change of body mass index, atopy, nitrogen dioxide and occupation at the sixth decade; [¶]: reference group included people who used electric cooking, air conditioning for heating and no smoking. *: p<0.05.

TABLE 5 Associations[#] between longitudinal household air pollution profiles and current asthma at the sixth decade stratified by *GSTP1*

	Current asthma/symptoms OR (95% CI)		
	***GSTP1* Ile/Val and Val/Val**	***GSTP1* Ile/Ile**	**$p_{interaction}$-value**
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/smoking	1.06 (0.36–3.09)	19.57 (2.34–163.94)*	0.01*
All electric	1.63 (0.62–4.33)	2.11 (0.16–27.91)	1.00
Wood and gas heating/gas cooking/ smoking	2.15 (0.44–10.60)	NA	0.70
Wood heating/gas cooking	1.08 (0.33–3.49)	3.28 (0.22–49.09)	0.73

NA: not available (the number was too small to generate a result in this cell). [#]: adjusted for age, sex, occupation, atopy at the sixth decade, nitrogen dioxide and asthma status at the fifth decade; [¶]: reference group included people who used electric cooking, air conditioning for heating and no smoking. *: p<0.05.

GSTM1 present genotype (interaction p-value <0.01). We did not observe evidence of interaction for *GSTT1* genotypes (supplementary table S11).

Participants who did not use cooking exhaust fans or were living in newer buildings had increased risk of asthma when exposed to "All electric", 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.

TABLE 6 Associations[#] between household air pollution profiles and lung function decline by glutathione *S*-transferase genotype

	Pre- or post-BD	**Parameter**	**Change of lung function**		**$p_{interaction}$-value**
			***GSTM1* present**	***GSTM1* null**	
Wood heating/smoking	Post-BD	FEV_1/FVC	−0.30 (−0.75–0.16)	0.22 (−0.40–0.83)	0.09
Wood and 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

Data are presented as β-coefficient (95% CI) representing change in *z*-scores, unless otherwise stated. BD: bronchodilator; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity. [#]: adjusted for sex, change of age, change of body mass index, nitrogen dioxide, atopy and occupation at the sixth decade; [¶]: significant interactions (criteria for interaction: interaction p<0.1 and p-value for stratified association <0.05). *: p<0.05.

TABLE 7 Associations[#] between longitudinal household air pollution profiles and respiratory outcomes stratified by ventilation parameters

	Current asthma OR (95% CI)		$p_{interaction}$-value
	Exhaust fan in use	**Exhaust fan not in use**	
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/smoking	1.51 (0.83–2.75)	10.53 (1.92–57.65)*	0.01
Wood and gas heating/gas cooking/smoking	1.41–0.61–3.23)	20.11 (1.64–246.12)*	0.06
	Build year before 1990	**Build year after 1990**	
All electric	0.74 (0.31–1.73)	7.77 (1.40–42.98)*	0.01

[#]: adjusted for age, sex, atopy, nitrogen dioxide and occupation at the sixth decade; [¶]: reference group included people who used electric cooking, air conditioning for heating and no smoking. *: p<0.05.

Discussion

Using comprehensive data from the 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 the *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 the prevention of asthma and COPD are poorly identified in current guidelines [4–6]. While the Global Initiative for Asthma guidelines recognise 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 considers complex interplays in the home environment, rather than isolated contributions from each specific source of HAP. Our results support potential asthma prevention strategies, which may inform asthma guidelines and prevention of future COPD burden related to accelerated lung function decline.

The "Wood heating", "All gas", "Wood heating/smoking" and "Wood heating/gas cooking" exposure profiles were associated with increased risk of persistent asthma/symptoms and accelerated FEV_1 and FVC decline over 10 years of follow-up. These findings are consistent with results from previous studies for a range of household risk factors and adverse respiratory health [14, 22–26]. 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 the effects of reactive oxygen species on alveolar epithelial cells [27]. In this way, long-term HAP exposure may be involved in the development and progression of obstructive respiratory diseases and lung function deficits [28–30]. Further analysis found that the associations between HAP profiles and lung function decline remained after excluding participants with asthma and COPD (supplementary table S15), indicating lung function decline found in our study may be independent of such disease status.

Consistent with previous studies, our reference profile ("Least exposed": reverse-cycle air conditioning, electric cooking and a nonsmoking environment) and the "All electric" profile were associated with lower risks for asthma symptoms and lung function decline compared with other categories [31, 32]. Although cooking itself can generate particulates, compared with other cooking methods, using electric technologies can reduce the release of particulates from combustion in the home. Reduced particulate levels in indoor air may also be due to the associated air filtration in reverse-cycle air conditioning removing airborne particulate material [33]. Absence of smoking could also reduce the risk of airway inflammation and enhance the responsiveness of asthma treatment [34].

Three multiple exposure profiles ("Wood heating/smoking", "Wood and 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 individually. 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, which reported that adults exposed to both smoking and wood burning were at a far higher risk than those with single exposures to HAP in relation to asthma severity and reduced lung function [35].

We found a moderately reduced risk of new-onset asthma/symptoms in those in the "Wood heating/gas cooking" profile (p=0.08), which contrasted with the increased risk from all other multiple exposure smoking groups. We hypothesise 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, similar behaviour was not seen for the "Wood and 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 [36–38]. It is particularly important to ventilate houses when using home heating and cooking systems that can generate high levels of pollutants.

Strengths and 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 [39, 40]. 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 modelling is 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 more traditional 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 nondifferential. 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 (supplementary tables S16 and S17). Our proxy measures for home ventilation, *i.e.* 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, *i.e.* 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, although 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 ECRHS, Respiratory Health in Northern Europe (RHINE) and Italian Study on Asthma in Young Adults (ISAYA) [41], 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 this 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 [42] 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 [43, 44]. HAP profiles may be associated with the 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 and 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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