

A prospective study of the association between home gas appliance use during infancy and subsequent dust mite sensitization and lung function in childhood

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Summary

Background Home gas appliance use has been associated with child respiratory illness but prospective data on the relationship between infant exposure and the development of child allergic disease has not been readily available.

Objectives (a) To determine if home gas appliance use is associated with increased risk of house dust mite (HDM) sensitization. (b) To examine whether any association between current home gas use and airway obstruction is influenced by HDM sensitization.

Methods Design: an 8-year follow-up birth cohort study of children born during 1988 and 1989. Participants: a population-based sample ($n = 498$) of children who participated in the Tasmanian Infant Health Survey (TIHS) and resided in Northern Tasmania in 1997 (84% of eligible children). Main outcome measures: (a) Skin prick test reaction to nine allergens, including *Dermatophagoides pteronyssinus* (Der p 1) and *Dermatophagoides farinae* (Der f 1). (b) Spirometric lung function indices, including forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC).

Results The relative risk for home gas appliance use at 1 month of age and HDM sensitization was 1.98 (1.04, 3.79) in a cohort analysis with confounder matching. Current home gas use was also associated with HDM sensitization (ARR 1.73 (1.43, 2.76)). Current home gas use was related to a stronger ($P = 0.006$) reduction in the FEV₁ : FVC ratio among HDM-sensitive children (adjusted difference -6.2% (-10.0 to -2.4)) than non-HDM-sensitive children (adjusted difference -0.3% (-2.5 to 1.8)).

Conclusion Indoor pollutants from gas combustion may increase the likelihood of initial sensitization to HDM and play a role in the development of atopic asthma. HDM-sensitized children may be more vulnerable to indoor pollutant-induced airway obstruction. The ability of this study to detect such effects may partly reflect unflued gas appliance use among this sample.

Keywords: infant cohort, indoor air pollution, allergic sensitization, lung function, asthma

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Introduction

Evidence of the capacity of air pollutants to influence immune responses in airway epithelium is accumulating [1]. Nitrogen dioxide (NO₂), a common indoor pollutant

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produced by fossil fuel combustion such as gas cookers or heaters [2], has been shown to exert several effects on mucosal epithelium, including oxidative damage with the release of cytokines TNF- α , IL-8 and GM-CSF and other proinflammatory mediators, leading to a priming of eosinophils such as eosinophil cationic protein (ECP), an effect which is blocked by fluticasone propionate and beclomethasone dipropionate [1,3]. In addition, NO₂ exposure can induce ciliary dyskinesia, increase epithelial permeability and contribute to increased allergen penetration into submucosal sites [1]. In a review of air pollution and allergic disease, Wardlaw and Burge [4] highlighted two areas for special attention: whether air pollutant exposure (a) increased the risk of atopic sensitization and (b) enhanced allergen responsiveness among atopic individuals [4].

Animal studies have provided some support that gaseous pollutants may promote sensitization but the data are inconclusive [4]. NO₂ exposure has been shown to up-regulate the immune responses to HDM allergen and the subsequent immune-mediated pulmonary inflammation in rats [5]. Occupational asthma, as a model of human adult sensitization, suggests that cigarette smoking is an adjuvant for specific IgE production [4]. There has been a lack of prospective studies with regard to air pollutants and child sensitization. Progress in this area has been hampered by a paucity of infant exposure data, difficulty of measuring long-term pollutant exposure in a population-based setting and disease misclassification, resulting from the use of respiratory symptom report rather than biological measurements of lung function, and a direct measurement of sensitization to classify affected children.

The question of enhanced allergen responses in established sensitization has been partially addressed by experimental studies in patients with established asthma. Among 10 adult asthmatics with house dust mite (HDM) sensitization, exposure to NO₂ (400 ppb) and sulphur dioxide (SO₂) (200 ppb) reduced the *Dermatophagoides pteronyssinus* (Der p 1) allergen load required to induce a specified level of airway obstruction by 61% [6] and exposure to NO₂ (400 ppb) resulted in a greater drop in forced expiratory volume in 1 s (FEV₁) after exposure to a fixed dose HDM challenge among adults with HDM-sensitive asthma [7]. Similarly, concomitant exposure to diesel exhaust particles (DEP) has been shown to potentiate the nasal allergic response to ragweed pollen among ragweed-sensitive subjects [8] and allergen challenge increased ECP, particularly after NO₂ exposure in seasonal allergic rhinitis [9]. These studies demonstrate symptom exacerbations due to air pollutants in individuals with established allergic disease but the role of gaseous pollutants in the initiation of allergen sensitization remains to be elucidated.

In a birth cohort study in Tasmania, we have recently

reported that living room gas heater use in infancy was associated with subsequent child asthma [10]. We present here a 1997 follow-up study which examines the relationship between domestic gas appliance use during infancy and childhood and the development of HDM sensitization and child lung function.

Methods

The Tasmanian Infant Health Survey (TIHS)

This birth cohort study operated from hospitals where approximately 93% of births in Tasmania, Australia, occurred [11]. The sample of eligible infants represented approximately one-fifth of live births in the state from 1988 to 1995, with an overall state-wide response rate during this period of 89% [10]. Infants born were scored to assess the risk of sudden infant death syndrome (SIDS) using a local predictive model based on maternal age, birthweight, infant sex, breastfeeding, season of birth and duration of second stage of labour [12]. Multiple births were automatically included. The eligibility criteria and study methods are discussed in more detail elsewhere [11,13]. Research assistants obtained data on three occasions. The first interview was conducted in hospital on the fourth day of life. A home interview was conducted during the fifth postnatal week. The third interview was conducted by phone when the infant was approximately 10 weeks postnatal age. Biological validation of questionnaire data on infant exposure to tobacco smoke was provided by a 1995 sub-study using infant urinary cotinine levels [13]. Home gas appliance use is defined as the positive report of gas cooking or gas heater use in the living room. A 1985–1986 survey reported that 86% of the gas-heated Tasmanian homes used bottled gas for heaters of portable or fixed type [14]. Thus these results pertain to gas combustion heaters rather than modern ducted gas central heating. In 1988/1989, 609 (88% of eligible) infants had a TIHS interview at 1 month of age in Northern Tasmania.

The 1997 Childhood Allergy and Respiratory Health Study (CARHS)

A follow-up study of cohort participants was conducted in Northern Tasmania in 1997 through school records. Eligible children and their parents were asked to attend the Launceston General Hospital for a parental interview and child assessment. The parental questionnaire included eight questions on asthma and wheeze from the International Study of Asthma and Allergy in Childhood (ISAAC) [15] and also questions on cooking fuel, home heating and other factors.

Baseline lung function measures were obtained as follows: the children were asked to perform forced expiratory manoeuvres standing without a nose clip, following a standard protocol [16], using an Alpha compact spirometer which was calibrated at the beginning of every session. Skin prick testing (SPT) was used to assess the cutaneous reaction to exposure to the house dust mites *Dermatophagoides pteronyssinus* (Der p 1) and *Dermatophagoides farinae* (Der f 1), cat, dog, alternaria, ryegrass, cow's milk, egg and peanut (Hollister-Stier purified allergen extracts supplied by Bayer, Sydney, Australia) and positive (histamine 10 mg/mL and 1 mg/mL) and negative (glycerine) controls. Weal allergen reactions of 3 mm or greater at 15 min were classified as positive [17]. In 1997, 596 children who had participated in the TIHS in 1988 or 1989 were identified as residing in the northern region of Tasmania (excluding offshore islands) during 1997. Of these, 499 (84%) agreed to participate in the 1997 CARHS study but SPTs were not carried out on one autistic child. For these 498 children, 456 had prospective data on home gas use in infancy available. For the 18 children with exposure to home gas use in infancy, nine were exposed to gas cooking only, eight to gas heaters only and one to both. For the 60 children exposed to home gas use in 1997, the number of children was 25, 31 and 4, respectively. A high proportion of the gas heaters in infancy or 1997 were unflued. In 1997, of the 35 children with home gas heaters, 20 were of the unflued type. During infancy, six of the nine infants who lived in a home with a gas heater were exposed to an unflued gas heater. The mean age at follow-up testing was 8.71 (SD = 0.59) years. The proportion of 1988–1989 TIHS infants with home interview data who were followed-up did not differ by whether home gas was used in infancy.

Statistical methods

Relative risks were calculated with test-based 95% confidence intervals [18]. The effect of individual confounders was assessed by stratified analysis. The Breslow-Day test was used to examine differences between stratum-specific risk estimates [18]. To control simultaneously for multiple confounders and to obtain confidence intervals for relative risk estimates, a generalized linear model with a log link function and binomial error structure was used [19]. A matched cohort analysis was used to further assess the effect of home gas appliance use in infancy on HDM (either Der p 1 or Der f 1) sensitization [20]. Multiple linear regression models were used to examine the effect of exposure on continuous outcomes, such as the lung function measures of FEV₁, forced vital capacity (FVC) and the ratio of FEV₁ to FVC with adjustment for relevant covariates (Table 3). We conducted the analyses using SAS version 6.12 [21].

Results

Home gas appliance use and HDM sensitization

Exposure to domestic gas appliance during infancy was prospectively associated with an increased risk of sensitization to several predominantly indoor aeroallergens, including HDM allergens, but not to the predominantly outdoor allergen ryegrass (Table 1). Examining by type of appliance, the relative risk for HDM sensitization for home gas cooking during infancy was 2.21 (1.02, 4.76) and for gas heaters was 1.43 (0.53, 3.89). Home gas appliance use in infancy was not strongly related to subsequent asthma (RR 1.30 (0.74, 2.29)). HDM sensitization was related to asthma (RR 1.65 (1.32, 2.06)). The absolute risk difference was an

Table 1. The prospective relation between home gas appliance use in infancy and child sensitization to common allergens

Outcome	Proportion (%) of children with home gas with outcome (n/total n)	Proportion (%) of children without home gas with outcome (n/total n)	Univariate relative risk (95%CL)	P value
Dust mite Der p 1 sensitization	44.4% (8/18)	21.5% (94/438)	2.07 (1.11, 3.86)	0.022
Dust mite Der f 1 sensitization	33.3% (6/18)	10.3% (45/438)	3.25 (1.52, 6.94)	0.002
House dust mite sensitization*	44.4% (8/18)	22.4% (98/438)	1.99 (1.07, 3.69)	0.030
Alternaria sensitization	16.7% (3/18)	3.7% (16/438)	4.57 (1.52, 13.70)	0.007
Cat sensitization	11.1% (2/18)	2.5% (11/438)	4.42 (10.6, 18.51)	0.032
Dog sensitization	5.6% (1/18)	0.0% (0/438)		0.039†
Ryegrass sensitization	22.2% (4/18)	17.1% (75/438)	1.30 (0.52, 3.24)	0.575
Food sensitization**	0.0% (0/18)	0.0% (0/438)		–

*Skin prick reaction of greater than or equal to 3 mm to either mite allergen. **Skin prick reaction of greater than or equal to 3 mm to cow's milk, egg or peanut. †Fisher exact two-tailed *P*-value.

Table 2. Confounder identification: the univariate relative risk for home gas use in infancy and child house dust mite sensitization by selected infant characteristics

Infant variables	RR (95% CL)		RR (95% CL)	
	Home gas in infancy	<i>P</i> -value	HDM sensitization	<i>P</i> -value
Private health insurance at birth	1.84 (0.72, 4.67)	0.200	1.48 (1.08, 2.04)	0.015
Use of a plastic mattress liner	0.30 (0.12, 0.79)	0.015	1.43 (1.01, 2.03)	0.039
Solid food introduced by phone interview at 10 weeks	0.79 (0.29, 2.16)	0.643	1.44 (1.04, 2.01)	0.030
Sheepskin used at 1 month interview or parent stated that would be used in cold winter weather	0.71 (0.21, 2.39)	0.582	1.34 (0.94, 1.92)	0.110
More than six residents in household at birth	1.50 (0.51, 4.44)	0.461	1.28 (0.84, 1.93)	0.250
Family history of asthma at birth	0.66 (0.24, 1.80)	0.413	1.16 (0.84, 1.61)	0.360
Carpet use in infant bedroom	0.37 (0.13, 1.06)	0.063	1.09 (0.61, 1.93)	0.779
Infant bedroom relative humidity > 75% at home interview	0.71 (0.10, 5.05)	0.730	1.00 (0.53, 1.89)	0.989
Infant exclusively breast-fed at home interview	0.89 (0.34, 2.34)	0.818	0.93 (0.66, 1.32)	0.690
Infant exposed to active smoking in same room	0.79 (0.32, 1.96)	0.617	0.92 (0.66, 1.27)	0.600
Mother smoked during pregnancy	1.01 (0.41, 2.52)	0.981	0.86 (0.62, 1.20)	0.373

excess of 22 HDM-sensitized children per 100 children exposed to home gas in infancy (Table 1).

To prepare for the selection of confounders for the multivariate analyses, we examined more than 40 other factors, to see how they each related to both home gas use in infancy and HDM sensitization. The infant factors of most relevance are summarized in Table 2. Private health insurance, plastic mattress liner use, sheepskin use and early solid food introduction were associated with a higher risk of HDM sensitization and differences in home gas use (Table 2). The following infant factors had little association with HDM sensitization: teenage motherhood, male sex, multiple birth, premature birth, head circumference at birth > 37 cm, use of a pillow or natural fibre mattress or any quilt at 1 month of age, postnatal smoking by other household residents (excluding mother), history of a cold by 1 month of age, more than 3 siblings in 1997 or low maternal education in 1997, with relative risk estimates between 0.80 and 1.25 for HDM sensitization. Among the child factors examined, the current use of a feather quilt was inversely associated with mite sensitization. We then examined the effect of confounding factors or effect modifiers on the association between gas use in infancy and HDM sensitization using stratification. Individual adjustment for the factors listed above, in Table 2, or season of birth, multiple birth or duration of second stage of labour, 1997 feather quilt use, child's fish consumption frequency, or child exposure to active smoking in the same

room, did not alter the point estimate for the gas-HDM association by 10% or more, except for the following factors: adjustment for the confounding effect of use of a plastic mattress liner at 1 month or family history of asthma, which each increased the risk estimate to 2.27. The stratification procedure revealed two factors that were possible modifiers of the gas-HDM association. The magnitude of the association was greater ($P = 0.042$) in homes where the infant's bedroom windows were always closed at night (RR 3.76 (1.64, 8.62)) compared with homes where they were sometimes or always open (RR 1.23 (0.50, 3.03)). Similarly, the strength of association was greater ($P = 0.038$) for infants who slept in rooms which were painted within the last year (RR 4.27 (1.88, 9.71)) compared with other infants (RR 1.16 (0.43, 3.13)).

Each of the 18 children with infant home gas exposure was then matched with unexposed children in relation to plastic mattress liner use, sheepskin use, early introduction of solid food and private health insurance. For one exposed child, health insurance data were not available, so this child was matched with two unexposed children with the same confounder profile who also had missing insurance data. The matched estimate was obtained using data on 360 children in 11 matched sets. The relative risk for home gas appliance use in infancy and subsequent HDM sensitization in this matched analysis was 1.91 (1.05, 3.56). Further adjustment for the confounding effect of 1997 feather quilt use increased this home gas-HDM estimate (ARR 1.98

Table 3. Adjusted difference in mean spirometric values between children with and without home gas appliances in infancy, ETS exposure, HDM sensitization or asthma ever

	Adjusted difference in mean FEV ₁ (mL) with 95% confidence interval between children with and without the variable	<i>P</i> -value	Adjusted difference in mean FVC (mL) with 95% confidence interval between children with and without the variable	<i>P</i> -value	Adjusted difference in FEV ₁ /FVC (%) (with 95% confidence interval) between children with and without the variable	<i>P</i> -value
Home gas appliance use during infancy (1988 to 89)	-116.1 (-213.1 to -19.1)	0.019	-61.3 (-185.0 to 62.4)	0.332	-3.2 (-6.5 to 0.1)	0.060
Home gas use during childhood (1997)	-25.5 (-79.8 to -2.9)	0.036	-13.2 (-83.5 to 57.1)	0.713	-2.0 (-3.9 to -0.2)	0.034
House dust mite sensitization	-26.1 (-67.1 to 14.9)	0.213	1.4 (-39.5 to 66.7)	0.616	-2.0 (-3.44 to -0.65)	0.004
Child exposed to indoor smoking	-46.6 (-83.6 to -9.7)	0.014	155.2 (-68.3 to 178.8)	0.492	-1.6 (-2.8 to -0.4)	0.017
Asthma ever	-3.2 (-39.7 to 33.3)	0.864	132.3 (-14.8 to 79.5)	0.180	-1.7 (-2.9 to -0.3)	0.008

All estimates adjusted for child height (cm), child age (years), child sex, season of lung function (3-month periods) and technician.

(1.04, 3.79)). Examining weal size as a continuous outcome, after adjustment for the matching variables and feather quilt use, the adjusted difference in mean weal size between children with home gas use in infancy compared with those without was 1.21 (0.18, 2.25) mm greater for Der p 1 ($P = 0.023$) and 1.39 (0.66, 2.10) mm greater for Der f 1 ($P = 0.0002$).

The cross-sectional association between child home gas use and HDM sensitization (unadjusted relative risk 1.53 (1.01, 2.33)) increased after adjustment for infant plastic mattress liner use, sheepskin use, early introduction of solid food, private health insurance, family history of asthma, resident number in 1997, exposure to active smoking in same room in 1997 and 1997 feather quilt use (ARR 1.73 (1.43, 2.76)).

The association between current home gas use and mite sensitization was stronger ($P = 0.016$) among children who lived in the same postcode address as their birth address. Among the 128 children who had not changed residence since birth, the risk estimates of gas appliance use and mite sensitization were: 1997 home gas use ARR 2.83 (1.62, 4.95); 1997 gas cooking ARR 2.33 (1.16, 4.66); and 1997 gas heater use ARR 3.42 (1.41, 8.30). Similar results were obtained when SPT wheal size reaction to Der p 1 or Der f 1 was used as an outcome measure.

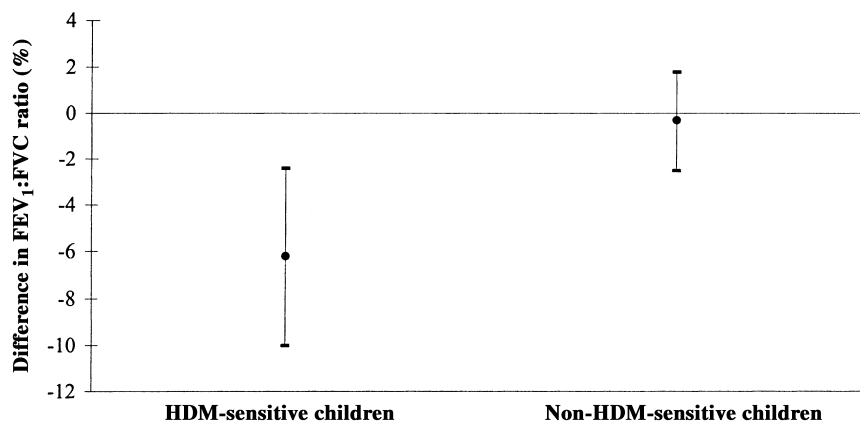
The interaction between current home gas use, HDM sensitization and lung function

The relations between home gas appliance use, HDM sensitization and lung parameters after adjustment for other

determinants of lung function are shown in Table 3. Home gas use in infancy or childhood was associated with a significant FEV₁ reduction. The effect of home gas in infancy on FEV₁ : FVC ratio was reduced after additional adjustment for HDM sensitization (mean difference -2.4% (95% CL -5.7, 0.9)) consistent with the effect on lung function mediated partly through mite sensitization. The mean difference in the FEV₁ : FVC ratio associated with the characteristics listed in Table 3 was similar among children regardless of whether or not they were sensitized to HDM, with the exception of current home gas use.

There was evidence of a strong interaction between current home gas use and HDM sensitization in relation to the mean difference in FEV₁ : FVC ratio. That is, the FEV₁ : FVC ratio was significantly ($P = 0.002$) reduced by 6.2% with current home gas exposure in HDM-sensitized children (mean difference in FEV₁ : FVC ratio -6.2% (95% CI -10.0 to -2.4)), but not significantly ($P = 0.758$) changed in children who were not sensitive to HDM (mean difference in FEV₁ : FVC ratio -0.3% (95% CI -2.5 to 1.8)). Adjustment for relevant covariates further increased the interaction between HDM sensitization, current gas use and lung function (Fig. 1). The interaction persisted after further adjustment for the factors listed in Table 2, the study entry scoring characteristics, feather quilt use in 1997, use of medications in the preceding 24 h, use of steroid, antihistamine or other medications in the preceding week, or whether beta agonists had been used in the past 24 h or past year. We then examined the effect of current home gas use among child subgroups. Among

Fig. 1. Adjusted difference (95% confidence interval) in mean FEV₁ : FVC ratio associated with current home gas appliance use in childhood among HDM-sensitized children and non-HDM-sensitized children. With adjustment for child height, age, sex, season of testing, technician, and whether child is exposed to active smoking in the same room in 1997. The difference in the effect of home gas use on lung function is significant ($P = 0.006$).



children with asthma ever, the mean difference in the FEV₁ : FVC ratio associated with current home gas was -6.5% ($P = 0.026$) among HDM-sensitive children and 1.0% ($P = 0.591$) among non-HDM-sensitive children. Among children with no asthma, the mean difference in the FEV₁ : FVC ratio associated with current home gas was -5.5% ($P = 0.051$) among HDM-sensitive children and 0.8% ($P = 0.578$) among non-HDM-sensitive children. Thus, among HDM-sensitive children, the adverse effect of current home gas use on this lung function measure was of similar magnitude among children with or without asthma ever.

Discussion

In this birth cohort, indoor gas appliance use was associated with an increased risk of allergic sensitization in children. These findings are consistent with previous animal studies showing that pollutant exposure may promote sensitization to inhaled allergens [4]. Exposure to 70 p.p.m. NO₂ promoted the sensitization of guinea-pigs to aerosolized albumen [22] and exposure of rats to 5 p.p.m. NO₂ resulted in higher levels of allergen-specific IgE and increased pulmonary inflammation following HDM immunization [5]. Intranasal DEP administration has been found to increase the IgE level of nasal washings in 11 human volunteers [23] and the specific IgE response to allergens in mice [24]. In primates, additional exposure to ozone resulted in increased positive skin pricks to platinum compared with exposure to platinum alone [25]. There is evidence that NO₂ can potentiate the early and late airway responses to inhaled allergen in sensitized asthmatics [7] and increase the inflammatory mediator (mast cell tryptase, ECP) release to inhaled allergen in allergic rhinitis [9]. Previous studies have not found gas cooking to be positively associated with atopic sensitization but exposure was measured concurrently [26] or recalled for age 11 [27] rather than measured in the postnatal period as in this study.

Here, the prospective association between home gas appliance use in infancy and subsequent HDM sensitization was based on a small number of exposed individuals and direct personal exposure measures were not available. This potentially important finding will need to be replicated in other studies which measure personal exposure to fossil fuel combustion products during early infancy on a larger number of children before a causal inference can be clearly established. However, it was noteworthy that in this study the prospective association persisted after adjustment for many possible confounding factors by individual stratification and a matched cohort analysis. In addition, a similar cross-sectional association was demonstrated based on the larger sample of 60 children with current home gas exposure. Furthermore, home gas use in infancy was also associated with increased sensitization to other indoor aeroallergens and the relation between home gas use and HDM sensitization was modified by a ventilation practice, bedroom window closure.

Strengths of this study include prospective exposure data and the availability of biological parameters to define the outcomes of atopy and airway obstruction among the child sample. The results are not likely to be influenced by differential follow-up as the proportion of TIHS children followed up from infancy did not differ by whether they were exposed to home gas. The study sample was not representative of all live births in the geographical area but the eligibility criteria were well defined and the potential effects of the scoring system components were examined in the analysis and found not to be important. Thus, the TIHS selection criteria are unlikely to affect the generalizability of these results. Other generalization issues to consider here are that the gas heaters used in 1988 were predominantly of combustion type using bottled gas [14] and that Tasmania has low levels of outdoor pollution. The gas heaters used at the time of the study may be more likely to expel fossil fuel combustion products than modern flued central heating. A 1992 Australian study reported that of 121 homes with

unflued gas appliances, 83% recorded mean daily NO₂ levels of greater than 40 ppb, with 31% greater than 120 ppb [28] using personal child exposure monitors. Thus it is likely that our findings would not be observed to the same extent in homes that used modern gas-fired central heating or pilot-light-free gas cooking with ventilation.

Another issue is that heavy outdoor pollution could potentially confound any relation between indoor pollutants and atopic disease. We would still contend that modern infants and children spend the majority of their time indoors, thus indoor exposure to pollutants would be important even in communities with greater levels of outdoor pollution, but the contribution of indoor pollutants may be more difficult to detect. The association here between home gas use and asthma (RR 1.30 (0.74, 2.29)) is of similar magnitude to that reported for gas heater use and asthma from our larger ($n = 6378$) cross-sectional study (ARR 1.33 (1.12, 1.57)) [10], and the wider confidence intervals here reflect in part the smaller study sample in this prospective study. In addition, in the 1995 follow-up study, the relation between gas appliance use in infancy and subsequent asthma was higher in certain subgroups, such as children who had not changed address since infancy or children who slept as infants with the bedroom door open [10]. Here, the association between home gas use and HDM sensitization was also more marked among children residing in the same postcode address since birth.

Exposure to home gas appliances in infancy was associated with an increased risk of being sensitized to other possible indoor aeroallergens, such as cat, dog and alternaria. This may reflect sensitization to multiple allergens among exposed children but it is interesting that home gas use in infancy was not associated with increased sensitization to ryegrass, an outdoor aeroallergen (Table 1). This may indicate that home gas appliance use in infancy is not influencing host immune function in a general way but acting at the site of the human airway and is consistent with a mechanism involving concomitant exposure to both NO₂ and indoor allergen or exposure to both over a short time period. Possible mechanisms include disorders of epithelial immune function [4] due to cytokine-induced up-regulation [1], airway epithelial damage with increased allergen presentation or decreased allergen clearance [29] or alteration of the allergenicity of indoor allergens by physical coating or submicronic ($< 0.1 \mu\text{m}$) particle formation [30]. Our study examined home gas use, an indirect measure of higher levels of indoor NO₂. Although the principle active component of gas combustion is likely to be NO₂, the finding of a residual positive relation between gas cooking and respiratory symptoms after controlling for NO₂ levels [31] suggests other combustion products, such as volatile organic compounds or particulates, may also be important.

Ventilation and air circulation practices will influence the effect of indoor pollutants from home gas appliances. The Oslo birth cohort study has recently reported findings consistent with the hypothesis that poor ventilation strengthens the effect of indoor pollutants [32]. The positive relation between home dampness or plasticizer exposure index and early bronchial obstruction were stronger in homes with lower air exchange rates, implicating volatile chemical compounds in vapour phase or adsorbed particulate matter [32]. In the 1995 asthma follow-up study, we reported that the association between gas heater use and asthma was stronger among children who, as infants, slept with the bedroom door open at night compared with those who slept with the door always closed [10]. Here, the adverse effect of home gas use was stronger if the bedroom windows were always closed at night at 1 month of age. These findings highlight the importance of air circulation and indicate that the adverse effect of gas use may operate while the child is sleeping in bed, with a concomitant high HDM exposure, rather than in other sites such as the kitchen where peak NO₂ levels would be likely to be higher. Our finding in relation to the possible enhancement of the adverse effect of gas fumes if the bedroom was recently painted could indicate a multiple pollutant effect, but this may have occurred by chance due to the large number of possible factors examined. Thus replication in other studies is required before any firm conclusions can be made.

We used the reduction in the ratio of FEV₁ to FVC as a measure of airway obstruction. The association between home gas use in infancy and a reduction in the FEV₁ : FVC ratio was partly explained by the effect of HDM sensitization on lung function. However, among HDM-sensitive children, a further drop in the FEV₁ : FVC ratio was associated with current home gas use. HDM allergen levels in Australian homes are generally found to be considerably higher than the threshold proposed for sensitization, particularly in bedding [33]. It is likely that most children in Fig. 1 had constant high HDM antigen exposure at night, providing a background for gas fumes to act as an important variable cofactor enhancing pollutant–allergen interaction. Our observation that gas cooking during infancy or childhood was associated with a reduction in FEV₁ is consistent with the report of an FEV₁ reduction associated with current gas cooking in the 1958 UK birth cohort study [27] and among women [26]. However, overall, the epidemiological data on gas cooking and lung function have been conflicting [34].

This inconsistency has also been found in the wider work on the role of nitrogen dioxide and other gaseous pollutants in the respiratory health of children [34–36]. Two cross-sectional population-based studies have found a non-significant tendency for the association between gas

cooking [26], NO₂ [31] and respiratory symptoms to be stronger among atopic individuals. The 1958 UK birth cohort study reported that the cross-sectional relation between gas cooking and FEV₁ reduction was concentrated among current asthmatics [27], a group that is likely to have an over-representation of mite-sensitized individuals. Here, the marked difference in effect of current gas use on the FEV₁ : FVC ratio depending on HDM sensitization (Fig. 1) shows that the inconsistency between previous studies may be, in part, because pollutant inhalation leads to different airway effects depending on allergen sensitivity. Although this may be of particular clinical importance for mite-sensitized asthmatics, it should be noted that the adverse effect of current home gas on the FEV₁ : FVC ratio was of similar magnitude for HDM-sensitized children with no report of asthma.

In addition to the methodological problems outlined well by Samet and Utell [35] in epidemiological studies of the health effects of poor indoor air quality, host differences in allergen sensitivity and environmental differences in allergen exposure are likely to also determine pollutant-induced respiratory effects, making this a complex issue to investigate. Here, the opportune combination of prospective postnatal exposure measurements, the use of unflued gas appliances, lack of a confounding effect of outdoor pollution, data on a range of relevant confounders or effect modifiers, and biological outcome measurements during childhood assisted our assessment. In conclusion, the findings from this birth cohort study suggest that exposure to indoor gas combustion products promotes initial HDM sensitization and also increases airway obstruction among HDM sensitized individuals. Although difficult to measure, the contribution of indoor pollutants to the increasing problem of childhood allergic disease must be better understood in view of the important potential public health implications for atopic disease prevention and management.

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