

Original article

Gas cooking, kitchen ventilation, and asthma, allergic symptoms and sensitization in young children – the PIAMA study

Background: Several studies reported inconsistent associations between using gas for cooking and respiratory symptoms or lung function in children. Kitchen ventilation characteristics may modify the relationship between gas cooking and respiratory health. The aim of this study was to investigate the effect of kitchen ventilation (while cooking) on the relationship between gas cooking, combustion product dispersal, and respiratory and allergic outcomes in children.

Methods: Data on respiratory and allergic symptoms and diagnoses were collected by yearly questionnaires in a population of over 3000 children participating in a birth cohort study on development of allergy and asthma. At 4 years of age, a sub-sample of 647 children provided blood samples for antibody testing. Data on gas cooking and kitchen ventilation were collected when the children were 5 years old. Based on these data a model was constructed to determine the chance of accumulation of combustion products (CACP) in the kitchen.

Results: No relationship was found between gas cooking and any of the respiratory or allergy outcomes except nasal symptoms. The overall results did not change when the 'CACP' was used as exposure variable instead, while the association for nasal symptoms decreased to borderline significance.

Conclusion: Our results suggest that gas cooking *per se* is associated with nasal symptoms in young children and not with the other respiratory symptoms that were investigated. Taking kitchen ventilation characteristics into account did not lead to different conclusions in this population where, according to the classification system, the majority of households using gas for cooking have insufficient kitchen ventilation.

S. M. Willers¹, B. Brunekreef¹,
M. Oldenwening¹, H. A. Smit²,
M. Kerkhof³, H. De Vries⁴,
J. Gerritsen⁵, J. C. De Jongste⁶

¹Institute for Risk Assessment Sciences, Universiteit Utrecht, Utrecht; ²National Institute of Public Health and the Environment (RIVM), Bilthoven;

³Department of Epidemiology & Statistics, Groningen University; ⁴Gasunie Engineering & Technology, Groningen; ⁵Beatrix Children's Hospital, University Medical Center Groningen, Groningen;

⁶Erasmus University Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands

Key words: allergy; gas cooking; kitchen ventilation; nitrogen dioxide; respiratory symptoms.

B. Brunekreef
Institute for Risk Assessment Sciences
Universiteit Utrecht
PO Box 80178
3508 TD
Utrecht
The Netherlands

Accepted for publication 17 November 2005

The contribution of indoor air pollution to the development of childhood respiratory and allergic symptoms has attracted much attention. The use of gas stoves and other combustion appliances can lead to higher indoor concentrations of NO₂, which is potentially harmful to health (1, 2). High concentrations of NO₂ can cause pulmonary oedema or even death (3), but the effects of exposure to short-term peak- or continuous low concentrations of NO₂ are less clear (4, 5). The results of studies on the effect of indoor NO₂ or the use of domestic gas appliances on respiratory health are inconsistent. Several studies have reported that the use of domestic gas appliances or exposure to NO₂ indoors is associated with respiratory symptoms or a diminished lung function in children (6–10) and adults (11). Some studies found significant associations only in girls or women. Studies under laboratory conditions have indicated a relationship between NO₂ exposure and an enhanced bronchial responsiveness or inflammatory reaction to inhaled allergens (12–15). Other studies have found no evidence that using gas for cooking or NO₂-exposure is associated with

respiratory symptoms or a diminished lung function (16–21).

Most studies have relied on NO₂ measurements or on the presence of sources of combustion products in the home. Often, kitchen ventilation characteristics are ignored, leading to a simplification of the exposure situation. We developed a model that combined the presence of sources of combustion products and the ventilation characteristics in the kitchen, thereby aiming at reducing the misclassification of exposure. This model determined the chance of accumulation of combustion products (CACP) and was used besides the distinction between using gas or electricity for cooking. In the separate part of the study, the CACP model was validated by measurements in the kitchen. Details of this measurement study will be published elsewhere (22).

The purpose of the present study was to determine the relationship between using gas for cooking, the CACP and the prevalence of asthma, allergic symptoms and sensitization in 4-year-old children.

Methods

Study population and study design

In the Netherlands, a multi-centre birth cohort study is being conducted on prevention and incidence of asthma and mite allergy (PIAMA) in more than 4000 children, recruited from the general population through prenatal care clinics. Children with an atopic mother were defined as high-risk ($n = 1327$), while children with a nonatopic mother were defined as low-risk ($n = 2819$). Part of the high-risk children participated in the intervention part of the PIAMA study ($n = 855$) in which the effectiveness of mite-impermeable mattress and pillow covers was evaluated; the remaining high-risk children ($n = 472$) and all low-risk children ($n = 2819$) participated in the natural history part.

At the start of the study, all high-risk children and a random sample of low-risk children ($n = 663$) were selected for close follow-up, including a home visit at 3 months of age and a medical examination at 4 years of age. During this medical examination, blood samples were drawn to determine specific IgE levels to inhalant allergens. The primary aim of the PIAMA study is to investigate the incidence of allergic disease in childhood in the Netherlands and to evaluate the role of environmental and dietary risk factors for the development of allergic disease. The participating children were born between July 1996 and October 1997 and are being followed until they are 8 years old. Details of the study design have been published previously (23).

Data on the prevalence of asthma and allergic symptoms were derived from the PIAMA-questionnaire at age 4 and information on specific IgE levels to inhalant allergens came from the medical examination at age 4. Information on gas cooking and kitchen ventilation provisions was collected when the children were 5 years old. The situation in the house in which the children live was assumed to be the same at age 4 and age 5. Children who had moved between their fourth and fifth birthday were excluded from the analysis. After exclusions, information of health effects at age 4 and home characteristics at age 5 was available for 3148 children. Information on specific IgE was available for 647 children.

Prevalence of respiratory and allergic outcomes

Some of the health outcome variables were derived from the ISAAC core questions on symptoms of asthma, allergic rhinitis and atopic eczema included in the 4-year questionnaire. These questions have been reported elsewhere (24, 25). Other outcome variables were the wheezing phenotypes according to Martinez at age 4 (26) and for a sub-sample of 647 children information on sensitization to inhalation allergens was available [house dust mite, cat, dog, birch pollen (*Betula verrucosa*), grass pollen Cocksfoot (*Dactylis glomerata*) and *Alternaria alternata*]. Children with the symptoms current (defined as having the symptoms in the last 12 months) eczema, nasal symptoms (having a runny or stuffy nose without having a cold or flu), asthma or wheezing were compared with children who never had these symptoms. Children who ever had these symptoms but not at age 4 were not included in the analyses. In addition, three categories of wheezing were defined: 'transient early wheeze' (wheezing during the first 3 years of life, but no wheezing at 4 years of age), 'late-onset wheeze' (no wheezing during the first 3 years of life, but wheezing at 4 years of age), and 'persistent wheeze' (wheezing in the first 3 years of life and wheezing at 4 years of age) (26). Children with these symptoms were compared with children who were 'never wheezers'. Children were classified as sensitized when specific IgE against one or more of the tested inhalation allergens was ≥ 35 IU/ml. Sensitized children

were compared with children who were not sensitized according to the antibody tests.

Kitchen situation

The questionnaire administered at age 5 contained questions about cooking and ventilation habits to evaluate the relationships between indoor air pollution, asthma and allergic diseases. By asking detailed questions about the ventilation situation in the kitchen during cooking, it is assumed that a realistic impression can be obtained concerning the effect of cooking on indoor air quality in the kitchen in the homes of the children studied.

A series of variables was defined for the source and ventilation provisions, based upon considerations as published elsewhere (22):

- Using gas for cooking (yes/no),
- Effectiveness of the extractor fan (defined as 'favourable' if it is often or always used during cooking and has an outlet to the outside, and defined as 'unfavourable' if there is no extractor fan, or the extractor fan is never or seldom in use, or the extractor does not have an outlet to outside),
- Kitchen volume ('large' when the kitchen is integrated in the living room or when the kitchen has a volume of 25 m³ or more; 'small' when the kitchen is separate from the living room and has a volume < 25 m³),
- Air supply in the kitchen ['insufficient' when there is no door to outside, no window that can be opened, no duct through the wall or ceiling to outside and when no ventilation holes in the doors are present in the kitchen, and when there is a door to outside or a window that can be opened but these are normally never opened during cooking; 'sufficient' when there is a door to outside or a window that can be opened and these are regularly opened during cooking or when there is a duct (without a fan) through the wall or ceiling to outside or if there are ventilation holes in the doors],
- The use of other ventilation in the kitchen (fan in the window used during cooking, duct through the wall or ceiling with a fan or mechanical ventilation system) and
- The presence of other sources of combustion products (oven heated with gas, small oil stove, hot-water heater with an outlet to outside, gas heater, gas dryer or gas boiler).

Children living in homes with a hot-water heater without an outlet to outside, a fireplace, or a woodstove in the kitchen were excluded from the analyses. These sources can have a major effect on the accumulation of combustion products and therefore could seriously disturb the relationship between using gas for cooking and the health outcome variables. We designed a model based on possible combinations of values of the source and ventilation parameters. The outcome of the model is the binary parameter 'CACP' with possible values 'high' or 'low'. Figure 1 shows the structure of the CACP model reflecting the interdependence between the different source and ventilation parameters.

Statistical methods

The relationships between using gas for cooking, a high 'CACP' and the different health outcome variables were analysed using logistic regression analysis. Crude odds ratios (OR) were estimated as well as ORs adjusted for gender, smoking in the home, dampness in the home, allergy or asthma in the parents, presence of older siblings, pets, pregnancy duration, education level of the mother, breast-feeding and study arm (intervention or natural history).

All the analyses were performed using SAS for Windows version 8.2 (SAS Institute, Cary, NC, USA).

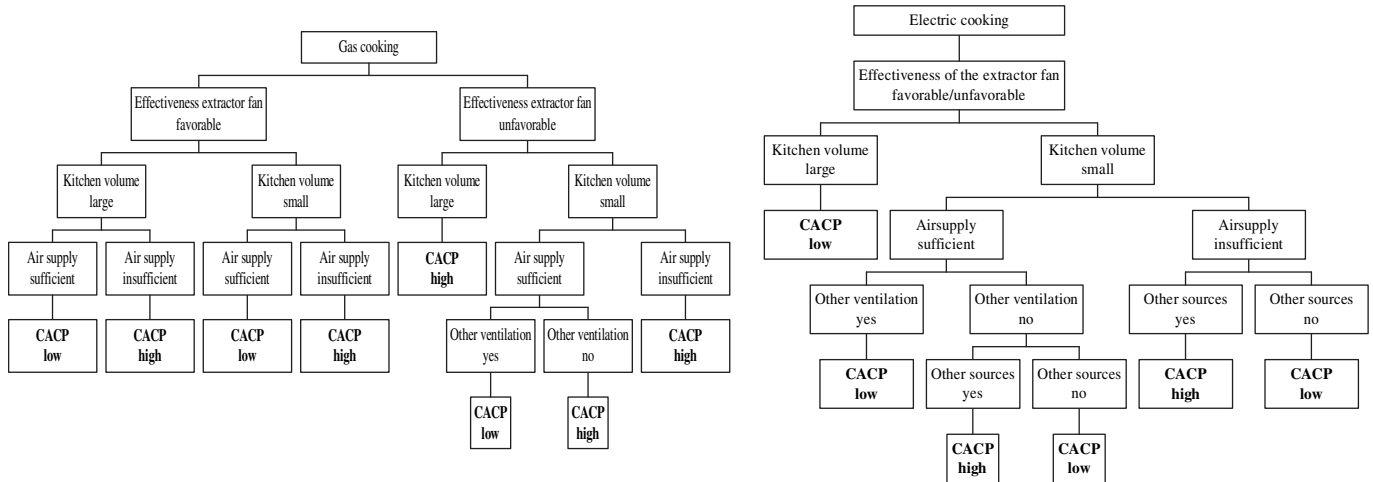


Figure 1. Stratification schemes according to the chance of accumulation of combustion products model.

Results

Study population and prevalence of the health outcome variables

The total population consisted of 3148 children. These are the children from whom we had information on the 5-year questionnaire, who had not moved in the last 12 months, and who had no additional combustion sources as defined above in the kitchen. Out of this population, data on allergic sensitization were present for 647 children. Health outcome variables were derived from the 4-year questionnaire. The prevalence of health outcomes is shown in Table 1. Table 1 shows that the most common health outcomes were ‘transient early wheezing’ (28.5%), nasal symptoms (22.1%) and eczema (18.3%).

Prevalence of the exposure variables and the chance of accumulation of combustion products

Data on cooking and ventilation habits were extracted from the 5-year questionnaire. Table 2 shows the prevalence of the different kitchen characteristics. Almost 80% of the households used gas for cooking. Most households

had an effective extractor fan and a large kitchen volume. However, more than 80% of the households had insufficient air supply in the kitchen. Table 3 shows the difference between gas and electric cooking as affecting the CACP. Using gas for cooking did not automatically lead to a high CACP. About 87% of the households using gas for cooking had a high CACP according to the CACP model and about 98% of the households using electricity for cooking had a low CACP. The agreement between gas cooking (yes/no) and CACP (high/low) expressed as the Kappa coefficient was 0.75. The majority of households using gas for cooking showed insufficient kitchen ventilation situations, taking into account the ‘high’/‘low’ assignments for the parameter combinations in the CACP model.

Table 1. Prevalence of health outcomes

Variable	Frequency n/N (%)
Eczema	447/2438 (18.3)
Nasal symptoms	648/2929 (22.1)
Wheezing	373/2574 (14.5)
Asthma	125/2955 (4.2)
Transient early wheeze*	733/2569 (28.5)
Late-onset wheeze*	63/1899 (3.3)
Persistent wheeze*	290/2126 (13.6)
Sensitization	135/618 (21.8)

*Wheezing phenotypes according to Martinez (26).

Table 2. Prevalence of the exposure variables

Variable	Frequency n/N (%)*
Gas cooking	2445/3138 (77.9)
Effectiveness of the extractor fan unfavourable	823/3130 (26.3)
Kitchen volume is small	414/3137 (13.2)
Air supply is insufficient	2575/3148 (81.1)
No use of other ventilation	1263/3148 (40.1)
Presence of other sources of combustion products	414/3148 (13.2)
High chance of accumulation of combustion products	2146/3122 (68.7)

*Differences in N related to varying numbers of missing values.

Table 3. Difference in CACP between gas cooking and electric cooking

Housing characteristic n/N (%)	Gas cooking n/N (%)	Electric cooking n/N (%)
High CACP	2136/2431 (87.87)	10/691 (1.45)
Low CACP	295/2431 (12.13)	681/691 (98.55)

CACP, chance of accumulation of combustion products; $\kappa = 0.75$.

Table 4. Relationships between using gas for cooking, respiratory and atopic outcomes

Outcome	N	Crude OR (95% CI)	Adjusted OR (95% CI)
Eczema	2146	0.91 (0.70–1.18)	0.97 (0.74–1.26)
Nasal symptoms	2591	1.23 (0.98–1.55)	1.34 (1.06–1.71)*
Asthma	2611	1.43 (0.87–2.37)	1.50 (0.90–2.49)
Wheezing	2276	0.97 (0.74–1.28)	0.99 (0.74–1.32)
Transient early wheeze	2311	0.87 (0.70–1.08)	0.91 (0.73–1.14)
Late-onset wheeze	1718	0.88 (0.48–1.63)	0.89 (0.48–1.67)
Persistent wheeze	1923	0.96 (0.70–1.31)	1.06 (0.76–1.47)
Sensitization	541	1.02 (0.62–1.68)	1.06 (0.63–1.79)

ORs adjusted for gender, smoking in the home, dampness in the home, allergy or asthma in the parents, presence of older siblings, pets, pregnancy duration, education level of the mother, breastfeeding and study (intervention or natural history). OR, odds ratio; CI, confidence interval.
* $P < 0.05$.

Table 5. Relationships between a high ‘CACP’, respiratory and atopic outcomes

Outcome	N	Crude OR (95% CI)	Adjusted OR (95% CI)
Eczema	2140	0.88 (0.70–1.11)	0.94 (0.74–1.19)
Nasal symptoms	2582	1.10 (0.90–1.35)	1.22 (0.99–1.51)
Asthma	2601	1.37 (0.88–2.12)	1.40 (0.90–2.18)
Wheezing	2267	0.98 (0.76–1.26)	1.03 (0.79–1.33)
Transient early wheeze	2308	0.88 (0.73–1.07)	0.92 (0.75–1.12)
Late-onset wheeze	1711	0.80 (0.46–1.38)	0.84 (0.48–1.47)
Persistent wheeze	1914	1.04 (0.78–1.38)	1.13 (0.84–1.53)
Sensitization	539	0.82 (0.53–1.26)	0.89 (0.56–1.41)

ORs adjusted for gender, smoking in the home, dampness in the home, allergy or asthma in the parents, presence of older siblings, pets, pregnancy duration, education level of the mother, breastfeeding and study (intervention or natural history). OR, odds ratio; CI, confidence interval.

Association between the exposure variables and respiratory and allergic symptoms

Gas cooking and the CACP were used as exposure variables in a logistic regression model. Table 4 shows the relationships between gas cooking, and the different health outcomes. Only nasal symptoms (OR1.34) were significantly associated ($P = 0.02$) with gas cooking. Table 5 shows the relationships between the CACP and the different health outcomes. The association with nasal symptoms (OR 1.22) was the only one reaching borderline ($P < 0.10$) significance. There were no significant relationships between gas cooking, CACP, and sensitization or any of the other health outcome variables.

Discussion

Our study provides only limited evidence that combustion products from gas cooking are associated with increased reporting of respiratory and allergic symptoms in young children. Only the association between gas cooking and

nasal symptoms reached statistical significance ($P < 0.05$). As is usually found, children with nasal symptoms were more often allergic (sensitized against one or more inhalant allergens) than children without these symptoms, and children in the subgroup with information on specific IgE reported more symptoms than children in the subgroup without this information. However, the crude associations between nasal symptoms and gas cooking/high CACP in the subgroup of sensitized children ($n = 135$) and in the subgroup of nonsensitized children ($n = 481$) were similar. The crude associations between gas cooking or a high CACP and the different symptoms, in the subpopulation with information on specific IgE ($n = 647$) and in the overall population ($n = 3148$) were also similar. Thus, it is unlikely that this has biased our results.

As the narrow confidence intervals for symptoms in Tables 4 and 5 show, our study had sufficient statistical power to detect effects of modest magnitude (ORs of < 2). The power to detect effects on allergic sensitization was less, but the estimated ORs for sensitization were close to unity and far from statistical significance so that it seems unlikely that we have missed an effect that was actually present.

The overall results based on gas cooking and on the CACP show similar outcomes (Tables 4 and 5). This was to be expected, as the majority of households using gas for cooking show the high CACP value, while about 98% of the households using electricity for cooking have a low CACP value (Table 3).

The population in our study in the Netherlands turned out to be representative for the overall population in the country as far as the way of cooking is concerned. The ratio of the number of households using gas for cooking vs the number using electricity for cooking in 1999 as well as in 2000 amounted to 83:17. In newly built houses the portion of electric cooking is increasing: in the year 2000 for houses built after 1996 the gas/electric ratio was 63/37 (27). In the present study Table 2 shows this ratio to be 77.9/22.1. This means that in the Netherlands a certain minimum study population number is required to have the number of households using electricity for cooking sufficiently large. In our study this number amounted to 693.

The results of studies on the effect of indoor NO_2 or the use of domestic gas appliances on respiratory health are inconsistent. These inconsistencies may be due to low statistical power, effect modification by other pollutants, misclassification of exposure or the use of insensitive measures of health outcome (5, 8, 20, 28, 29). The classification of exposure by questionnaires can be influenced by recall-bias and nondifferential misclassification (7). Classification of exposure by measurements can also be different because in some studies passive samplers are used while in other studies concentrations are measured real-time. Passive sampling does not show exposure to peak concentrations of combustion products.

A previous study showed that passive sampling of weekly indoor NO₂ concentrations produced no better predictor of lung function in children from 6 to 12 years of age than the report of combustion sources indoors by questionnaires (30). Hasselblad et al. performed a meta-analysis on studies where NO₂ levels were deducted from passive sampling or from the presence of a gas cooker. They concluded that an increase of 15 ppb in long-term NO₂ exposure would result in an increase of about 20% in respiratory illness and that the estimated effect is likely to be an underestimate, given the problems of misclassification of exposures and health outcomes (10).

To imply comparisons between subpopulations with really distinct levels of accumulation of cooking pollutants and to limit misclassification of exposure to a more acceptable level we took the kitchen ventilation situation (especially while cooking) into account. This was performed using the CACP model. However, in our study population, the agreement between the simple variable 'gas cooking' and CACP was so high ($\kappa = 0.75$) that detailed classification of the kitchen ventilation did not result in improved accuracy and precision of the estimated exposure-response relationship.

In a companion study we have performed a validation of the CACP model. Concentration measurements for a number of combustion products were performed in a number of kitchens. The measured NO₂ and CO concentrations were generally lower compared with previous studies in the Netherlands. This may have contributed to the poor performance of the CACP model because the

range of the measured pollutants was not large enough to see which parameters are most important to determine the pollutant concentrations. This work has been published elsewhere (22).

Often, the kitchen ventilation characteristics are ignored, leading to potential misclassification of exposure to possibly relevant pollutants. Of course, if no relationship exists between cooking on gas and a certain outcome that misclassification should not make a difference. However, it could be of importance for other outcomes and it may depend on the country considered, the cooking fuel used, the cooking habits and local kitchen situations. In such cases, associations with medical endpoints derived while ignoring the ventilation characteristics can easily lead to incomplete and misleading advice considering the kitchen situation.

Our results suggest that gas cooking *per se* is associated with nasal symptoms in young children and not with the other respiratory symptoms that were investigated. Taking kitchen ventilation characteristics into account did not lead to different conclusions in this population where, according to the classification system, kitchen ventilation was not optimal.

Acknowledgments

This study was supported by a grant from Gasunie Trade & Supply. Constructive discussions with P.H.J. Bartholomeus and H.B. Levinsky are gratefully acknowledged.

References

1. Melia RJW, Chinn S, Rona RJ. Indoor levels of NO₂ associated with gas cookers and kerosene heaters in inner city areas of England. *Atmos Environ* 1990;**24B**:177–180.
2. Dennekamp M, Howarth S, Dick CA, Cherrie JW, Donaldson K, Seaton A. Ultrafine particles and nitrogen oxides generated by gas and electric cooking. *Occup Environ Med* 2001;**58**:511–516.
3. Ekwo EE, Weinberger MM, Lachenbruch PA, Huntley WH. Relationship of parental smoking and gas cooking to respiratory disease in children. *Chest* 1983;**84**:662–668.
4. Speizer FE, Ferris B, Bishop YMM, Spengler JD. Respiratory disease rates and pulmonary function in children associated with NO₂ exposure. *Am Rev Respir Dis* 1980;**121**:3–10.
5. Brunekreef B. NO₂: the gas that won't go away. *Clin Exp Allergy* 2001;**31**:1170–1172.
6. Wong TW, Yu TS, Liu HJ, Wong AHS. Household gas cooking: a risk factor for respiratory illnesses in preschool children. *Arch Dis Child* 2004;**89**:631–636.
7. Neas LM, Dockery DW, Ware JH, Spengler JD, Speizer FE, Ferris BG. Association of indoor nitrogen dioxide with respiratory symptoms and pulmonary function in children. *Am J Epidemiol* 1991;**134**:204–219.
8. Garrett MH, Hooper MA, Hooper BM, Abramson MJ. Respiratory symptoms in children and indoor exposure to nitrogen dioxide and gas stoves. *Am J Respir Crit Care Med* 1998;**158**:891–895.
9. Melia RJW, Florey C du V, Altman DG, Swan AV. Association between gas cooking and respiratory disease in children. *BMJ* 1977;**2**:149–152.
10. Hasselblad V, Eddy DM. Synthesis of environmental evidence: nitrogen dioxide epidemiology studies. *J Air Waste Manage Assoc* 1991;**42**:662–671.
11. Jarvis D, Chinn S, Luczynska C, Burney P. Association of respiratory symptoms and lung function in young adults with use of domestic gas appliances. *Lancet* 1996;**347**:426–431.
12. Strand V, Rak S, Svartengren M, Bylin G. Nitrogen dioxide exposure enhances asthmatic reaction to inhaled allergen in subjects with asthma. *Am J Respir Crit Care Med* 1997;**155**:881–887.
13. Tunnicliffe WS, Burge PS, Ayres JG. Effect of domestic concentrations of nitrogen dioxide on airway responses to inhaled allergen in asthmatic patients. *Lancet* 1994;**344**:1733–1736.
14. Barck C, Sandstrom T, Lundahl J, Hallden G, Svartengren M, Strand V et al. Ambient level of NO₂ augments the inflammatory response to inhaled allergen in asthmatics. *Respir Med* 2002;**96**:907–917.
15. Barck C, Lundahl J, Hallden G, Bylin G. Brief exposure to NO₂ augment the allergic inflammation in asthmatics. *Environ Res* 2004;**97**:58–66.

16. Dijkstra L, Houthuijs D, Brunekreef B, Akkerman I, Boleij JSM. Respiratory health effects of the indoor environment in a population of Dutch children. *Am Rev Respir Dis* 1990;**142**:1172–1178.
17. Keller MD, Lanese RR, Mitchell RI, Cote RW. Respiratory illness in households using gas and electricity for cooking I. Survey of incidence. *Environ Res* 1979;**19**:495–503.
18. Koo LC, Ho JHC, Ho CY, Matsuki H, Shimizu H, Mori T et al. Personal exposure to nitrogen dioxide and its association with respiratory illness in Hong Kong. *Am Rev Respir Dis* 1990;**141**:1119–1126.
19. Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA et al. Nitrogen dioxide and respiratory illnesses in infants. *Am Rev Respir Dis* 1993;**148**:1258–1265.
20. Sunyer J, Puig C, Torrent M, Garcia-Algar O, Calico I, Munoz-Ortiz L et al. Nitrogen dioxide is not associated with respiratory infection during the first year of life. *Int J Epidemiol* 2004;**33**:116–120.
21. Moran SE, Strachan DP, Johnston IDA, Anderson HR. Effects of exposure to gas cooking in childhood and adulthood on respiratory symptoms, allergic sensitisation and lung function in young British adults. *Clin Exp Allergy* 1999;**29**:1033–1041.
22. Willers SM, Brunekreef B, Oldenwening M, Smit HA, Kerkhof M, De Vries H. Gas cooking, kitchen ventilation, and exposure to combustion products. *Indoor Air* 2006;**16**:65–73.
23. Brunekreef B, Smit J, de Jongste J, Neijens H, Gerritsen J, Postma D et al. The prevention and incidence of asthma and mite allergy (PIAMA) birth cohort study: design and first results. *Pediatr Allergy Immunol* 2002;**13**(S15):55–60.
24. Asher MI, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8**:483–491.
25. The International Study of Asthma and Allergies in Childhood Study Group. Worldwide variations in the prevalence of atopic diseases: the International Study of Asthma and Allergies in Childhood (ISAAC). *Lancet* 1998;**351**:1225–1232.
26. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. *N Engl J Med* 1995;**332**:133–138.
27. Huiskamp GE. Basisonderzoek Aardgasverbruik Kleinverbruikers BAK 2000. Arnhem: Federatie van Energiebedrijven in Nederland EnergieNed, 2001.
28. Samet JM, Utell MJ. The risk of nitrogen dioxide: what have we learned from epidemiological and clinical studies? *Toxicol Ind Health* 1990;**6**:247–262.
29. Chauhan AJ. Gas cooking appliances and indoor pollution. *Clin Exp Allergy* 1999;**29**:1009–1013.
30. Brunekreef B, Houthuijs D, Dijkstra L, Boleij JSM. Indoor nitrogen dioxide exposure and children's pulmonary function. *J Air Waste Manage Assoc* 1990;**40**:1252–1256.