ENVIRONMENTAL EXPOSURE

Indoor nitrous acid and respiratory symptoms and lung function in adults

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Background: Nitrogen dioxide (NO_2) is an important pollutant of indoor and outdoor air, but epidemiological studies show inconsistent health effects. These inconsistencies may be due to failure to account for the health effects of nitrous acid (HONO) which is generated directly from gas combustion and indirectly from NO_2.
Methods: Two hundred and seventy six adults provided information on respiratory symptoms and lung function and had home levels of NO_2 and HONO measured as well as outdoor levels of NO_2. The association of indoor HONO levels with symptoms and lung function was examined.
Results: The median indoor HONO level was 3.10 ppb (IQR 2.05–5.09), with higher levels in homes with gas hobs, gas ovens, and in those measured during the winter months. Non-significant increases in respiratory symptoms were observed in those living in homes with higher HONO levels. An increase of 1 ppb in indoor HONO was associated with a decrease in forced expiratory volume in 1 second (FEV_1) percentage predicted (−0.96%; 95% CI −0.09 to −1.82) and a decrease in percentage FEV_1/forced vital capacity (FVC) (−0.45%; 95% CI −0.06 to −0.83) after adjustment for relevant confounders. Measures of indoor NO_2 were correlated with HONO ($r=0.77$), but no significant association of indoor NO_2 with symptoms or lung function was observed. After adjustment for NO_2 measures, the association of HONO with low lung function persisted.
Conclusion: Indoor HONO levels are associated with decrements in lung function and possibly with more respiratory symptoms. Inconsistencies between studies examining health effects of NO_2 and use of gas appliances may be related to failure to account for this association.

Nitrous acid (HONO) is present as a gas in indoor and outdoor air. In the indoor environment HONO is produced both directly by combustion processes—for example, use of unvented gas appliances—and indirectly by absorption of nitrogen dioxide (NO_2) and then release of HONO from moisture on surfaces within the home.[1] HONO levels in outdoor air are substantially lower than indoor levels[2 3] due to rapid photodissociation in sunlight. It has been established that the presence of HONO will interfere with accurate measurement of NO_2 by most commonly used methods,[4 5] and it has been proposed that adverse health outcomes that have been attributed to NO_2 (or to exposure to NO_2 producing appliances such as gas stoves) could be confounded (or explained) by exposure to HONO. It has been argued that the variations in the reported association of indoor NO_2 with respiratory health may be explained by failure to measure this co-pollutant.[6]

There are three mechanisms through which HONO may, in theory, be harmful to health. Firstly, it is an acid and may cause damage to mucous membranes and to the lung by virtue of its solubility and acidic nature. Secondly, it may combine with amines in vivo to produce carcinogenic nitrosamines. Thirdly, it may photolyse in the air to form highly oxidative free hydroxyl radicals which may in turn exacerbate or cause respiratory conditions such as chronic bronchitis or asthma. Studies linking these theoretical health risks to HONO exposure are lacking. One chamber study in healthy volunteers has shown that exercising in 650 parts per billion (ppb) HONO for 3 hours is followed by minor reductions in airway conductance,[7] and another small study in asthmatics—again conducted in a chamber—showed that similar levels of exposure are associated with minor reductions in forced vital capacity (FVC).[8]

We have previously reported a strong association of respiratory symptoms and decrements in lung function with exposure to gas appliances in young adults (particularly atopic women) living in East Anglia.[9] Although these associations were also found in other European centres, the results were not consistent between centres and these inconsistencies could not be explained.[10] The purpose of this study is to assess the association of exposure to HONO with symptoms and lung function in a subsample of individuals who took part in our earlier study and who agreed to having repeat lung function measures taken and to having indoor home measures made.

METHODS

Details of the European Community Respiratory Health Survey I (ECRHS I) and the European Community Respiratory Health Survey II (ECRHS II) have been published elsewhere.[11 12] In ECRHS I, conducted from 1991–3, a community based random sample of 20–44 year old men and women was identified and sent a postal questionnaire. A random sample of responders was invited to a local testing centre where they provided more detailed information on health status and suspected risk factors for asthma. Blood samples were taken and serum tested for specific IgE to house dust mite, cat, grass and *Cladosporium* using the Pharmacia CAP system. In addition, subjects reporting being woken by breathlessness or an asthma attack in the last 12 months or current use of asthma medication (the ''symptomatic sample'') who had not already been identified

Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HONO, nitrous acid; NO_2, nitrogen dioxide; SOB, shortness of breath

to take part in these more intensive tests as part of the random sample were also asked to provide this further information. In 1999/2001 all subjects (both random and symptomatic) who provided information at the clinic visit were contacted again and asked to take part in ECRHS II.

Information on respiratory symptoms in the last 12 months was collected. Lung function tests included measurement of forced expiratory volume in 1 second (FEV_1) and FVC using a water sealed bell spirometer (Biomedin, Italy). Subjects refrained from smoking 1 hour before the tests and those with asthma were asked to withhold treatment with inhalers for at least 4 hours before testing. Subjects were given a minimum of five and a maximum of nine attempts to produce two technically satisfactory manoeuvres.

Home visits on consenting subjects were conducted by field workers who, by direct observation, collected information on fuels used for cooking, distance of the kitchen to the nearest street, and dampness in the home.

Three passive samplers were set up—one for indoor NO_2 (Passam AG, Switzerland),[13] one for outdoor NO_2, and one for indoor HONO.[14] Indoor samplers were set up side by side in the kitchen on the opposite side to the cooking appliance and away from a window. The outdoor sampler was suspended by string attached outside the kitchen window. HONO measurements were made only in the two British centres taking part in ECRHS II (Ipswich and Norwich in East Anglia).

All samplers were left exposed for 14 days. Participants recorded use of their gas appliances and estimated frequency with which cigarettes had been smoked in the kitchen and frequency with which heavy vehicles had passed outside their home during this period.

One in 10 participants had two of each sampler installed in their homes (duplicate measurements).

Ethical approval for the study was granted from both the Ipswich Hospital and Norfolk and Norwich Hospital ethics committees.

Statistical analysis

HONO was observed to be log normally distributed. The association of indoor and outdoor factors with indoor HONO was explored by regression analyses with the log transformed values as the outcome measure, expressing the ratio of geometric means and 95% confidence intervals (95% CI). For these analyses all available measures (both symptomatic and random sample) were used. Limits of agreement between duplicate readings for the measures were assessed using the Bland-Altman method.[15]

All health outcomes were first assessed in the random sample only. HONO values were divided into quartiles and the prevalence of wheeze, wheeze with shortness of breath, waking with shortness of breath, and waking with coughing within each quartile determined. The association of these outcomes with indoor HONO as a linear variable was conducted within logistic regression analyses, with adjustment for age at questionnaire, sex, smoking status, centre in which the study was conducted, the presence of damp patches in either the lounge or bedroom, and occupational group. Occupational group was defined as (1) senior officials, managers, professionals and technicians; (2) clerks, service workers and skilled agricultural and fishery workers; (3) trade workers, plant and machine operators and elementary occupations; and (4) other, based on the ISCO-88 coding of current occupation.[16]

Lung function was considered in two ways. Firstly, the percentage predicted FEV_1 was determined using the highest recorded FEV_1 from the lung function readings and standard reference equations.[17] Secondly, the percentage airways obstruction was determined from the proportion of the

Table 1 Characteristics (as reported at clinic interview in 1999/2000) of those providing information on HONO levels and those not providing information on HONO levels (random sample subjects only shown)

	Did not provide HONO (n = 351)	Did provide HONO (n = 203)	Test for difference*
Female (%)	56.9	61.0	p = 0.34
Mean age (years)	42.6	43.5	p = 0.10
Currently living in Norwich (%)	39.3	58.1	p<0.001
Wheeze in last 12 months (%)	30.2	30.1	p = 0.97
Woken by attack of SOB in last 12 months (%)	5.4	5.9	p = 0.82
Ever asthma (%)	14.5	17.2	p = 0.39
Mostly used gas for cooking (%)	57.7	53.3	p = 0.32
Employment status (%)			
Employed/self employed	83.5	81.8	p = 0.10
Full-time houseperson	9.9	5.9	
Unemployed looking for work	1.9	2.0	
Unemployed due to poor health	4.4	6.4	
Student/retired/other	1.5	3.9	
Occupational status†			
ISCO code 1–3	34.8	43.2	p = 0.23
ISCO code 4–6	26.1	21.6	
ISCO code 7–9	21.1	16.7	
Other	18.0	18.4	
Smoking status (%)			
Lifetime non-smoker	51.4	53.2	p = 0.10
Ex-smoker	27.4	32.5	
Current smoker	21.4	14.3	
Pack years of smoking among smokers	22.6	17.9	p = 0.19
Sensitised to either house dust mite, grass, cat or *Cladosporium* (>0.35 kU/l)‡	33.9	46.3	p = 0.007

*χ^2 test for categorical variables, unpaired *t* test for continuous variables.
†ISCO code 1–3: senior officials, managers, professionals and technicians; 4–6: clerks, service workers and skilled agricultural and fishery workers; 7–9: trade workers, plant and machine operators and elementary occupations.
‡283 non-responders and 179 responders had IgE levels measured.

Table 2 Distribution of indoor HONO and indoor and outdoor NO_2 from all homes (random and symptomatic sample)

	Min	25th centile	Median	75th centile	Max	Duplicate (N)	Median (range) difference between duplicates	95% limits of agreement for duplicates
Indoor HONO (ppb) (n = 255)	0	2.05	3.10	5.09	20.55	21	0.08 (−0.72 to 0.94)	−0.80 to 0.99
Indoor NO_2 (μg/m^3)	5.40	14.55	24.55	42.00	113.70*	23	0.29 (−6.03 to 6.10)	−5.40 to 4.25
Indoor NO_2 (ppb) (n = 240)	2.80	7.57	12.76	21.84	59.12		0.15 (−3.13 to 3.17)	−2.80 to 2.21
Outdoor NO_2 (μg/m^3)	0	19.50	26.60	33.00	69.40*	21	0.30 (−3.10 to 3.80)	−3.03 to 3.52
Outdoor NO_2 (ppb) (n = 239)	0	10.14	13.83	17.16	36.09		0.16 (−1.61 to 1.97)	−1.57 to 1.83

Readings from one home with values of 393.80 (indoor) and 102.30 (outdoor) have been excluded as values appear implausibly high and it is considered likely that closing times reported are incorrect.
N.B. Not all homes with HONO measures had indoor or outdoor NO_2 measures.

highest FEV_1 to the highest FVC recorded. The association of these parameters with HONO was examined using multiple regression, controlling for age at lung function testing, sex, current smoking status and pack years of smoking, centre in which the study was conducted, presence of damp patches in the lounge, bedroom or bathroom, occupational group, season in which HONO was measured, and season in which lung function was measured. Estimates obtained for HONO were examined before and after adjustment for the other NO_2 measures by three methods: (1) adjustment for indoor NO_2 measure; (2) adjustment for the indoor NO_2 measure corrected for potential interference by HONO; and (3) correction for both the indoor and the outdoor NO_2 measure. Analyses were then repeated in the symptomatic sample.

Consistent with other published research, HONO has been analysed with results presented as parts per billion (ppb). Nitrogen dioxide is presented in the most part as μg/m^3 as this is the most widely used unit for this pollutant. However, in basic descriptive statistics and in the final analyses, NO_2 is also considered in ppb.

All analyses were conducted with Stata 7.0 (Stata Corporation, Texas, USA).

RESULTS

Response

Six hundred and ninety one subjects took part in the clinic assessment of whom 276 agreed to be visited at home. Of these, 255 (203 random and 52 symptomatic) returned an HONO sampler for analysis. The 203 subjects from the random sample who provided HONO data were similar to the 351 random sample subjects who did not provide information on indoor HONO in most respects including age, sex, smoking status, symptom status, occupational status, and use of gas for cooking as reported at the clinic visits (table 1). Non-responders who had specific IgE measured were less likely to be sensitised than responders who had specific IgE measured (33.9% and 46.3%, respectively). Response rates were higher in Norwich than in Ipswich (58.1% *v* 41.9%: $p<0.001$). The median time between health measures and indoor measures was 410 days (interquartile range (IQR) 322–512 days).

Household factors associated with indoor HONO

The distribution of values obtained for all three pollutant measures from all homes with available HONO are shown in table 2. The differences between duplicate readings and the limits of agreement are also given.

HONO levels were higher in homes with a gas hob, a gas oven, and in those measured during months other than the summer, but there was no association of HONO with reported smoking in the home, damp patches present in the lounge or bedroom, distance to the street, and reported traffic flow outside the home. These associations were not substantially altered by mutual adjustment for all factors (table 3).

HONO was associated with indoor NO_2 and weakly associated with outdoor NO_2 (HONO with indoor NO_2: $r = 0.77$, $p<0.001$; HONO with outdoor NO_2: $r = 0.38$, $p<0.001$). After further adjustment for indoor and outdoor NO_2, all previously identified risk factors for high HONO remained statistically significant although the strength of the associations diminished slightly. The proportion of variation in HONO explained by all these risk factors and the two NO_2 measures was 48% (39% without the NO_2 measures).

One hundred and forty four individuals who lived in homes with a gas hob or gas oven documented their use of gas cooking appliances during the monitoring period. Reported use varied with 39/144 (27.1%) reporting use of their gas hob for more than half an hour per day and 47/144 (32.6%) reporting use of their gas oven for more than half an hour per day. HONO increased with increasing use of the gas hob (ratio of geometric mean in HONO for each half hour use of gas hob 1.52 (95% CI 1.11 to 2.07)). This association was not apparent after adjustment for indoor NO_2 levels.

Association of HONO with symptoms and lung function

Random sample only

The prevalence of wheeze and wheeze with breathlessness was higher in individuals living in homes within the highest quartile of HONO than in those in the lowest quartile (prevalence of wheeze in lowest quartile 25.5%; prevalence of wheeze in highest quartile 33.3%), but this difference did not reach statistical significance ($p>0.05$) and there was no statistically significant trend across the groups ($p>0.05$, table 4). There was no association of HONO with any of the other symptoms suggestive of asthma, and no evidence that these associations were any different in men than in women or in those who were atopic compared with those who were non-atopic.

There was, however, an association between HONO and lung function. Subjects living in homes within the highest quartile of HONO had the lowest percentage predicted FEV_1 (p for trend across quartiles = 0.09) and had had more airway obstruction (p for trend across quartiles = 0.007). In unadjusted analyses the FEV_1/FVC% in subjects in the lowest quartile of HONO was 3.4% (95% CI 0.97 to 6.02) higher than in subjects in the highest quartile. In multivariable analyses controlling for all relevant confounders, this strong association between HONO and airway obstruction remained, an increase of 1 ppb in HONO being associated with the loss of 0.45% (95% CI 0.06 to 0.83) in this measure of lung function (table 5). With further adjustment for indoor and outdoor NO_2, the strength and direction of this association remained the same although the estimate became statistically non-significant. Negative associations of FEV_1/FVC% with indoor

Table 3 Association of household exposures with HONO levels in all homes with data

	N	Geometric mean HONO (ppb)	Unadjusted ratio of geometric mean (95% CI)	Adjusted* ratio of geometric mean (95% CI) (n = 234)	Adjusted† ratio of geometric means (95% CI) (n = 213)
Gas hob					
No	103	2.05	1 (ref)	1 (ref)	1 (ref)
Yes	149	4.05	1.97 (1.66 to 2.35)	1.37 (1.12 to 1.68)	1.26 (1.04 to 1.53)
Gas oven					
No	159	2.33	1 (ref)	1 (ref)	1 (ref)
Yes	92	5.03	2.16 (1.82 to 2.57)	1.95 (1.59 to 2.41)	1.62 (1.30 to 2.01)
Season					
Summer	57	2.20	1 (ref)	1 (ref)	1 (ref)
Autumn	86	3.15	(1.15 to 1.88)	1.55 (1.25 to 1.93)	1.44 (1.16 to 1.79)
Winter	35	4.09	(1.39 to 2.59)	2.09 (1.58 to 2.76)	1.59 (1.19 to 2.12)
Spring	74	3.42	1.58 (1.22 to 2.05)	1.89 (1.51 to 2.38)	1.65 (1.31 to 2.08)
Distance to street					
<20 m	205	3.09	1 (ref)	1 (ref)	1 (ref)
⩾20 m	42	2.94	0.94 (0.73 to 1.22)	1.01 (0.81 to 1.25)	1.00 (0.81 to 1.22)
Buses and trucks pass in front of home					
No	185	2.94	1 (ref)	1 (ref)	1 (ref)
Yes	55	3.42	1.16 (0.92 to 1.47)	1.17 (0.96 to 1.42)	1.10 (0.92 to 1.32)
Smoking in kitchen during monitoring					
No	209	3.03	1 (ref)	1 (ref)	1 (ref)
Yes	34	3.25	1.06 (0.80 to 1.41)	1.03 (0.82 to 1.30)	1.06 (0.85 to 1.31)
Damp patches observed in bedroom or lounge					
No	228	3.09	1 (ref)	1 (ref)	1 (ref)
Yes	24	2.77	0.89 (0.65 to 1.23)	0.82 (0.11 to 1.08)	0.73 (0.60 to 0.94)

*Adjusted for all other factors in table.
†Adjusted for all factors in the table plus indoor NO_2 and outdoor NO_2.

and outdoor NO_2 were observed. These associations were not as consistent as those observed with HONO and, after adjustment for HONO, the effect estimates became weaker.

These analyses were repeated with the indoor NO_2 measures corrected for potential interference by HONO levels (corrected indoor NO_2 equals indoor NO_2 minus HONO in ppb).[4] In all instances the patterns of associations presented in table 5 remained, confirming that the association between HONO and lung function was independent of any association with NO_2 and suggesting that the association between NO_2 and lung function was explained by HONO. There was no evidence that the association between HONO and lung function was different in men and women or in atopic and non-atopic subjects (interaction sex × HONO for FEV_1 percentage predicted: $p = 0.6$; interaction atopy × HONO for FEV_1 percentage predicted: $p = 0.8$).

Symptomatic sample

Fifty subjects from the symptomatic sample underwent FEV_1 and FVC and HONO measurements. In this small group, weak negative non-significant ($p>0.05$) associations which were compatible with the results from the random sample were observed (data not shown) in the unadjusted analyses. In analyses controlling for relevant confounders but not indoor and outdoor NO_2, a positive association with HONO was observed with wide confidence intervals (change in % predicted FEV_1 per 1 ppb increase in HONO 0.62 (95% CI −1.81 to 3.05); change in FEV_1/FVC % per 1 ppb increase in HONO 0.54 (95% CI −0.41 to 1.49)).

DISCUSSION

We have shown that, in adults living in two towns in East Anglia, exposure to HONO in the home is associated with decrements in lung function and with a non-significant increase in some respiratory symptoms. To our knowledge, this is the first study to examine and report this association in a community based sample of adult subjects. The level of indoor HONO was higher in homes with a gas cooker, a gas oven, and during the winter months. There was no evidence that the association with lung function was different in those with and without symptoms, in women than in men, or in those who were atopic compared with those who were non-atopic.

The subjects in this study were participants in the English part of the ECRHS II which involves the follow up of a cohort of young adults first studied in 1990. There is little evidence of substantial response bias, with those taking part in the home visits being similar in many aspects at baseline to those who did not take part. Even if response bias was present, it is

Table 4 Prevalence (%) of respiratory symptoms and mean lung function parameters by quartile of HONO (random sample only)

	Quartile 1 (n = 51) (0–2.11 ppb)	Quartile 2 (n = 50) (2.17–3.08 ppb)	Quartile 3 (n = 50) (3.09–4.80 ppb)	Quartile 4 (n = 50) (4.84–20.55 ppb)	p for trend across categories
Symptoms in last 12 months					
Wheeze	25.5	26.0	28.6	33.3	0.19
Wheeze with breathlessness	14.3	18.0	24.0	22.0	0.25
Woken by attack of SOB	7.8	2.0	8.0	6.0	0.98
Woken by coughing	31.3	22.0	32.0	24.0	0.66
FEV_1 as % predicted	110.2	106.9	106.6	105.3	0.09
FEV_1/FVC ratio (%)	79.7	79.0	78.5	76.2	0.007

SOB, shortness of breath; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 5 Change in lung function per 1 ppb increase in each pollutant showing changes in estimates with adjustment for confounders and of further adjustment for other pollutants

	N	Change in lung function per 1 ppb increase in HONO	p value	N	Change in lung function per 1 ppb (1.91 μg/m^3) increase in indoor NO_2	p value	N	Change in lung function per 1 ppb (1.91 μg/m^3) increase in outdoor NO_2	p value
FEV_1 (% predicted)									
Unadjusted	192	−0.84 (−1.60 to −0.07)	0.03	181	−0.07 (−0.18 to 0.05)	0.24	179	0.04 (−0.32 to 0.40)	0.82
Adjusted[1]	176	−0.96 (−1.82 to −0.09)	0.03	168	−0.10 (−0.23 to 0.02)	0.11	166	0.25 (−0.74 to 0.23)	0.31
Adjusted[2]	168	−1.16 (−2.65 to 0.33)	0.12	168	0.03 (−0.18 to 0.25)	0.77	162	N/A	0.84
Adjusted[3]	168	−1.13 (−2.45 to 0.19)	0.09	162	N/A	0.73		N/A	
Adjusted[4]	162	−1.13 (−2.65 to 0.39)	0.14	162	0.04 (−0.19 to 0.27)			−0.06 (−0.65 to 0.53)	
FEV_1/FVC ratio (%)									
Unadjusted	193	−0.55 (−0.91 to −0.21)	0.002	182	−0.04 (−0.09 to 0.01)	0.09	180	−0.06 (−0.23 to 0.10)	0.44
Adjusted[1]	176	−0.45 (−0.83 to −0.06)	0.02	168	−0.05 (−0.10 to 0.01)	0.11	166	−0.11 (−0.32 to 0.11)	0.34
Adjusted[2]	168	−0.57 (−1.23 to 0.09)	0.09	168	0.02 (−0.07 to 0.12)	0.67	163	N/A	0.94
Adjusted[3]	168	−0.54 (−1.13 to 0.04)	0.07	163	N/A	0.67		N/A	
Adjusted[4]	163	−0.56 (−1.25 to 0.12)	0.07	163	0.02 (−0.08 to 0.12)			−0.01 (−0.27 to 0.25)	

Adjusted[1]: model includes age, sex, smoking status, pack years of smoking, occupational group, damp observed in the home, centre in which study was conducted, season of HONO measurement, season of lung function testing. Each pollutant examined separately.
Adjusted[2]: adjusted[1] + HONO + indoor NO_2. (Estimates from this single model for HONO and indoor NO_2 shown.)
Adjusted[3]: adjusted[1] + HONO + corrected indoor NO_2. (Estimates for HONO shown.)
Adjusted[4]: adjusted[1] + HONO + indoor NO_2 + outdoor NO_2. (Estimates from this single model for HONO and indoor NO_2 and outdoor NO_2 shown.)
N/A, not applicable.

unlikely that it would produce false associations between HONO and lung function parameters.

The 2 week mean levels of HONO in the homes in this study are consistent with the levels seen in homes in the USA[2 3 18 19] and Egypt.[20] We have shown that levels of HONO were higher in homes measured during the winter months than in the summer months, and similar seasonal variations were seen in 84 participants in this study who had repeat measures taken in different seasons (data not shown). Exacerbations of chronic obstructive airways disease occur in the winter months and to reduce confounding by season all our health outcome analyses have been controlled for season.

HONO (and indoor NO_2) is a primary product of gas combustion and is also formed by the reaction of NO_2 with surface water. The two measures are correlated and these correlations reduce the power and hamper interpretation of analyses to observe health effects. To date, studies examining the association of indoor NO_2 with respiratory outcomes have provided conflicting results. Our results suggest that this may be because of failure to measure and account for HONO. HONO remained significantly associated with low FEV_1 and with airway obstruction after controlling for relevant confounders, whereas NO_2 failed to reach statistical significance. When both pollutants were considered simultaneously, the negative association of HONO with lung function was still observed, although the widening of the confidence intervals produced statistically non-significant results. However, the direction of the association between NO_2 and lung function was altered. In small studies, mutual adjustment of these two pollutants may mask associations of either with health outcomes, and larger studies are required. The dearth of studies in which both have been measured has been identified as a gap in our understanding of the health effects of gas appliances.[6] In a study of infants in which both HONO and NO_2 were measured, however, the authors concluded that NO_2, but not HONO, was associated with reduced lung function.[21]

HONO interferes with measures of NO_2 made by passive sampling.[4] In the ranges measured in this study, it is likely that "one for one" interference occurs and the "true" NO_2 readings are inflated by about 10% (for example, from 30 ppb to 33 ppb).[4] We have re-analysed our data on the assumption that the "true" NO_2 value (in ppb) is the reading from our passive sampler minus the HONO value (in ppb). This reduces the correlation of HONO with NO_2 ($r = 0.71$) but does not alter our conclusions.

There is growing awareness of the potential for HONO to contribute to the health effects of ambient pollution. It is a source of hydroxyl radicals, particularly in the morning in the outdoor environment, and research is underway to assess HONO production from motor vehicles. In homes where indoor HONO levels are high, photodissociation of only a small proportion to produce free radicals in indoor air could represent an important contribution to daily individual exposure.

The decrements in lung function that we have observed are relatively small and are not associated with a statistically significant ($p>0.05$) increase in symptoms. While the magnitude of the effect at the individual level may be small, the public health significance of small shifts in mean lung function within a population may be considerable.[22 23]

Previous work in this population has suggested that women—and particularly atopic women—are at an increased risk of symptoms on exposure to gas cooking appliances.[9] Clinical studies[24] and epidemiological studies[25] examining the health effects of NO_2 also suggest that they may be enhanced in atopic subjects. In this study there is no evidence that atopic subjects or women are susceptible subgroups of the population, but the power of this study to detect effect modification by sex or atopy is limited.

In summary, our study in young adults living in England suggests that high indoor levels of HONO generated during combustion of gas inside the home are associated with small but measurable decrements in lung function. Further work is required to determine the extent to which indoor HONO is converted to free radicals and whether HONO is of greater importance than NO_2 in the indoor and outdoor environment. In the meantime, the advice to all users of unvented gas appliances remains the same—these appliances should be well maintained and used in well ventilated areas.

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