ASTHMA AND THE ENVIRONMENT

Effects of volatile organic compounds, damp, and other environmental exposures in the home on wheezing illness in children

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Background: The effects of indoor exposure to volatile organic compounds (VOCs), including formaldehyde, on respiratory health are not clearly understood. The aim of this study was to determine the independent effects of VOCs and other common environmental exposures in the home on the risk and severity of persistent wheezing illness in children.
Methods: Total volatile organic compounds, formaldehyde, nitrogen dioxide, damp (on a four category scale of % wood moisture equivalent), and environmental tobacco smoke (from salivary cotinine) were measured objectively in the homes of 193 children with persistent wheezing illness and 223 controls aged 9–11 years in Nottingham, UK.
Results: The risk of wheezing illness was significantly increased only in relation to damp (odds ratio (OR) per increasing category = 1.32 (95% confidence interval (CI), 1.00 to 1.75)), and was unrelated to the other exposures measured. Among cases, formaldehyde and damp were associated with more frequent nocturnal symptoms (OR per increasing quartile and category, respectively, 1.45 (1.06 to 1.98) and 1.97 (1.10 to 3.53)), significantly more so in atopic cases, but there was no effect of total volatile organic compounds, nitrogen dioxide, or cotinine.
Conclusions: Domestic volatile organic compounds are not a major determinant of risk or severity of childhood wheezing illness, though formaldehyde may increase symptom severity. Indoor damp increases both the risk and severity of childhood wheezing illness.

Studies of the respiratory health effects of air pollution to date have focused primarily on outdoor sources, and the effects of indoor pollutants are less clearly understood. In particular the effects of volatile organic compounds (VOCs), a diverse group of organic chemicals that arise from synthetic materials and furnishings, have received relatively little attention. In adults, adverse effects of VOCs on the risk of asthma or related symptoms have been suggested,[1 2] although a study looking at formaldehyde—also a VOC—found no association.[3] In children, only the effects of formaldehyde have been investigated, and findings in relation to asthma risk have been conflicting.[3–5] The effects of this group of pollutants in the aetiology of asthma therefore remain unclear.

Other indoor exposures have been more widely studied and implicated in causing respiratory morbidity in children, including damp and moulds,[6] environmental tobacco smoke,[7 8] and nitrogen dioxide (NO_2),[9] but the independent effects of these and VOC exposures have not been clearly established. Some uncertainty also arises from the use of self reported rather than objective measures of home dampness,[10] and of proxy markers of NO_2 exposure,[11 12] and it is not clear whether the reported association between damp and respiratory symptoms is attributable to increased sensitisation to indoor allergens.[13] We have therefore used objective measures of domestic exposure to VOCs, including formaldehyde, and damp, environmental tobacco smoke, and NO_2 to estimate the independent effects of these pollutants on the risk and severity of persistent wheezing illness in a case–control study of 9–11 year old children, and to explore the modifying effect of allergen sensitisation on any effects seen.

METHODS

Selection of subjects

Cases and controls for the study were selected from children in primary school years 1 and 2 (aged six to eight years) who participated in a study of traffic pollution exposure and childhood wheezing illness among Nottingham school children in 1995/96.[14] As the source of our cases, we identified all 835 children who had parent reported wheeze in the past year in this previous study. A random sample of 860 children (including 140 who had reported wheeze) was taken from participants of the 1995/96 study to provide the source of our controls, and also to act as a group in which to investigate other outcomes cross sectionally (analyses not presented here). To determine eligibility for the current study, we sent a letter to the parents of each child in late 1998, explaining the study, asking about the child's current wheezing using the same question as previously,[14] and asking if they were willing for their child to take part in the present study. Reminder letters were sent to non-responders through the schools. Of those who replied and expressed an interest in participating, we defined all children with wheeze in the past year in both 1995/96[14] and 1998 as cases, and all those with no reported wheeze in the past year on both occasions as controls. Ethical approval for the study was granted by the Nottingham City hospital ethics committee.

Data collection

Study subjects were visited at home between October 1998 and May 1999 by a researcher, who explained the study procedures to both the child and parent and obtained written parental consent. A saliva sample was taken for cotinine assessment, and skin prick tests to cat, *Dermatophagoides*

pteronyssinus, mixed grasses, *Aspergillus fumigatus*, *Alternaria tenuis*, *Penicillium notatum*, saline, and histamine (Diagenics, Newark, UK) were carried out. Surface wall moisture (damp) was measured in the main living room, the kitchen, and the child's bedroom using a surveyor's moisture meter (Protimeter Surveymaster SM, Protimeter, Marlow, UK), and recorded as per cent wood moisture equivalent (WME) on a four category scale (high >20, medium 15.1 to 20, low 10.1 to 15, and very low 0 to 10). Where possible measurements were taken approximately 30 cm above the skirting board on an outside wall. Mould growth was assessed visually on the walls in the same rooms and recorded as none, slight ($\leqslant$5% coverage), or extensive (>5% coverage). NO_2 was monitored in the kitchen using a passive diffusion sampling tube (AEA Technology, Harlow, UK) and VOCs were monitored in the child's bedroom using a Perkin-Elmer type sampling tube packed with Tenax TA (Building Research Establishment, Watford, UK), both over a four week period. Formaldehyde was measured using a diffusive sampling badge (GMD 570 Series dosimeter), left in the child's bedroom for three days. A computerised questionnaire was administered to the parent which asked about household factors, including smoking in the home and ownership of pets, as well as factors relating to the child, including drug treatments for asthma and early life factors. Information on parental occupation was available from the 1995/96 questionnaire responses. Cases were provided with a mini-Wright peak flow meter (Clement Clarke, Essex, UK) and asked to record morning and evening peak flow (best of three blows) and night-time and daytime symptom score (symptoms included any of wheezing, chest tightness, breathlessness, or cough) on a scale of 0 to 5 in a peak flow diary over a four week period. Persistent wheezing illness status was validated using the general practitioners' (primary care) records in those providing additional written consent.

Chemical analyses

Saliva samples were frozen until ready for cotinine analysis, carried out by radioimmunoassay. NO_2 concentrations were assessed using spectrophotometry analysis techniques according to AEA Technology protocols. VOC samplers were analysed by thermal desorption and gas chromatography with flame ionisation detection to provide concentrations of total volatile organic compounds, representing the sum of all VOCs with boiling points between 70℃ and 285℃, and the individual VOCs benzene, toluene, ethylbenzene, xylene, limonene, and undecane. Formaldehyde badges were analysed by solvent desorption and liquid chromatography. Concentrations of NO_2, VOCs, and formaldehyde are reported in $\mu g/m^3$ and represent mean concentrations for the exposure period.

Statistical analyses

Concentrations of NO_2, VOC (total and individual), and formaldehyde were categorised in quartiles, based on the distributions in the random cross sectional group. A binary variable representing any visible mould in the home was computed. Cotinine was treated as a binary variable representing detectable (2 ng/ml or more) and undetectable (<2 ng/ml) concentrations, and where numbers were sufficient, those with detectable levels were further categorised as above and below the median.

The independent effects of exposures on case–control status were assessed using multiple logistic regression. Among the cases only, relations between each exposure variable and measures of disease severity—namely peak flow variability, frequent symptomatic days, and frequent symptomatic nights (symptoms recorded in a diary on 10% or more of days/nights)—were explored using multiple linear or logistic regression as appropriate. Peak flow variability was computed as the ''two lowest per cent mean peak expiratory flow'' with the first two days' readings excluded, as described elsewhere,[15] for all children with at least 30 valid peak flow readings of a possible total of 52. This variable was negatively skewed and was therefore transformed by cubing to achieve normality.

In the regression models, categorical exposure variables were fitted as both unordered and ordered factors, and if comparison of the two models provided no evidence of departure from linearity, results were presented for the trend in risk per increasing category of exposure. Analyses were initially controlled for age, sex, and socioeconomic status. Two markers of socioeconomic status were available: the Carstairs deprivation index based on area of residence,[16] and social class based on parental occupation. The effect of including important exposures in the model together and of controlling for other potential confounding variables—including preterm birth, low birthweight, mode of infant feeding, maternal smoking during pregnancy, birth order, pet ownership, road traffic exposure (distance of home to nearest main road and local traffic activity), and season during which visit was made—were explored.

All analyses were then stratified by atopic status, where atopy was defined as a positive skin test (an average of largest wheal diameter and its perpendicular at 15 minutes of at least 2 mm greater than the saline control response) to at least one of the allergens tested, to determine any confounding or modifying effect of atopy on the relations seen.

The case–control analysis was repeated in the restricted subset of validated cases of persistent wheezing illness and validated controls. This comprised cases with a recording in their general practitioner's notes of prescribed asthma drug treatment at the time (including the preceding year) of the current study, and controls with no record of prescribed asthma treatment at the time (including the preceding year) of both the original and the current study.

Before the study we calculated that 250 cases and 250 controls would provide in excess of 80% power to detect as significant a trend across the quartiles of pollutant exposure such that the odds ratio for the highest quartile relative to lowest was 2.

RESULTS

Participation rates

Of the 1555 children approached, replies with current wheezing information were obtained for 841 children (54%) and of these, 243 were identified as eligible for inclusion as a case and 383 as a control. The remaining 215 children had changed wheeze status between 1995 and 1998. Home visits were carried out for all the 193 cases (79% of those eligible) and 223 controls (59%) who consented to participate.

Participants tended to be of higher social class than non-participants, and this was most evident among controls (table 1).

Subject characteristics

Study subjects comprised just over 50% boys, with a roughly equal distribution of 9, 10, and 11 year olds and over 80% of subjects having lived in their current home for at least three years (table 2). There was little difference between cases and controls with respect to sex, age, or length of time in their current home. A significantly greater proportion of cases than controls were atopic (68% *v* 26%, p<0.001; table 2). We used the Carstairs deprivation index (computed from current post code) to adjust for socioeconomic status in all analyses, because this was more strongly related to case status (table 2), but the results were similar with adjustment for parental occupation.

Table 1 Comparison of participating and non-participating cases and controls

	Eligible cases			Eligible controls		
	Participants (n = 193)	Non-participants (n = 50)	p Value	Participants (n = 223)	Non-participants (n = 160)	p Value
Sex						
Boys	107 (55%)	24 (48%)		113 (51%)	83 (52%)	
Girls	86 (45%)	26 (52%)	0.35	110 (49%)	77 (48%)	0.82
Year of birth						
1987	36 (19%)	6 (12%)		44 (20%)	25 (16%)	
1988	93 (48%)	23 (46%)		98 (44%)	82 (51%)	
1989	64 (33%)	21 (42%)	0.33	81 (36%)	53 (33%)	0.38
Carstairs index in 1995/6* (mean (SD))	0.95 (3.96)	1.60 (4.20)	0.33	0.39 (3.45)	0.84 (3.71)	0.24
Social class in 1995/6						
I: Professional	37 (19%)	8 (16%)		38 (17%)	10 (6%)	
II: Managerial/technical	69 (36%)	10 (20%)		96 (43%)	62 (39%)	
III: skilled non-manual	29 (15%)	10 (20%)		33 (15%)	26 (16%)	
III: skilled manual	34 (18%)	15 (30%)		35 (16%)	29 (18%)	
IV-V: partly/un-skilled	8 (4%)	2 (4%)		9 (4%)	14 (9%)	
Economically inactive/ missing	16 (8%)	5 (10%)	0.22	12 (5%)	19 (12%)	0.003

*Higher Carstairs index denotes greater social deprivation.

Associations with case–control status

There was no evidence of an association between persistent wheezing illness and total VOCs, individual VOCs, or formaldehyde (table 3). A positive dose related association between damp in the living room and case status was identified (age, sex, and Carstairs adjusted odds ratio (OR) per increasing category = 1.32 (95% confidence interval (CI), 1.00 to 1.75)) (table 3), but not with damp measured in the kitchen or the child's bedroom. Visible mould was only identified in 11 homes (nine cases and two controls), but was significantly associated with an increased risk of wheezing illness (adjusted OR = 5.10 (1.07 to 24.17)) (table 3). Cases were non-significantly more likely to have cotinine in their saliva than controls (table 3), but the same proportion of cases and controls had levels above the median (10% each). There was no difference between cases and controls in the reported level of smoking in the home. Mean levels of NO_2 were higher in subjects from homes where gas was used for cooking (50.4 μg/m^3) than where gas was not used (21.2 μg/m^3, $p<0.001$ for *t* test), but neither marker of exposure was related to case status.

Table 2 Characteristics of cases and controls

	Cases	Controls	p Value
Sex			
Boys	107 (55%)	113 (51%)	
Girls	86 (45%)	110 (49%)	0.33
Age (years)			
9	68 (35%)	83 (37%)	
10	73 (38%)	72 (32%)	
11	52 (27%)	68 (31%)	0.48
Years lived in home			
<3 years	30 (16%)	38 (17%)	
⩾3 years	162 (84%)	183 (82%)	
Missing	1 (0.5%)	2 (1%)	0.82
Atopic*			
Yes	132 (68%)	57 (26%)	
No	60 (31%)	161 (72%)	
Missing	1 (0.5%)	5 (2%)	<0.001
Carstairs index based on current residence† (mean (SD))	0.87 (3.90)	0.17 (3.40)	0.055

*Atopy defined by at least one positive (2 mm or greater than saline response) skin test to allergens tested.
†Higher Carstairs index denotes greater social deprivation.

Stratification by atopic status suggested that the effect of living room damp was greater among atopic children (adjusted OR per increasing category of damp = 1.51 (0.95 to 2.40)) than among non-atopic children (OR = 1.02 (0.65 to 1.61)) for whom no effect was evident, although the interaction was not statistically significant. This observed effect was not attributable to any one specific allergen sensitisation. There were too few participants sensitised to moulds or exposed to moulds to assess interactions involving these variables.

Details of asthma drug treatment prescriptions were obtained from general practitioners' records of 115 cases, of whom 85 (74%) were confirmed as cases, and those of 164 controls, of whom 147 (90%) were confirmed as controls. In an analysis restricted to these validated cases and controls, the magnitude of the effect of living room damp was not appreciably changed (adjusted OR per increasing category = 1.41 (0.98 to 2.03)).

Associations with respiratory morbidity among cases

Of the 193 cases studied, most were reported to have used a reliever inhaler in the past year (170; 88%), and about half of these (84) were also reported to be taking other drugs for asthma. Diary cards with sufficient measures of peak flow to estimate variability were returned by 127 cases (66%). No significant associations between peak flow variability and indoor exposures were identified.

Of the 146 cases (76%) for whom complete data on night-time symptoms were available, 77 (53%) were defined as frequently symptomatic. The reporting of frequent night-time symptoms was significantly related to formaldehyde level (age, sex, and Carstairs adjusted odds ratio per increasing quartile = 1.45 (1.06 to 1.98)) and damp in the bedroom (adjusted OR per increasing category = 2.51 (1.36 to 4.64)), kitchen (1.90 (1.03 to 3.51)), and living room (1.97, (1.10 to 3.53)) (table 4). For daytime symptoms, 143 had complete data, of whom 93 (65%) were frequently symptomatic. Increased odds ratios for formaldehyde (adjusted OR per increasing quartile = 1.40 (1.00 to 1.94)) and damp were seen, although for damp, only levels in the living room reached significance (adjusted OR per increasing category = 1.86 (1.02 to 3.42)) (table 4). For both night-time and daytime symptoms, mutual adjustment for formaldehyde and damp and further control for other potential confounding variables collected made little difference to the associations seen. None of the other exposures measured was

Table 3 Distribution of indoor exposures in cases and controls and associated odds ratios

Exposure	Level	Cases (No (%) exposed)	Controls (No (%) exposed)	Crude OR	95% CI	Adjusted OR*	95% CI
Total VOCs	0 to 176	49 (25.9%)	58 (26.4%)	1		1	
($\mu g/m^3$) (n = 409)	176.1 to 293	65 (34.4%)	56 (25.5%)	1.37	0.82 to 2.32	1.30	0.76 to 2.21
	293.1 to 506	36 (19.0%)	53 (24.1%)	0.80	0.46 to 1.42	0.72	0.40 to 1.30
	>506	39 (20.6%)	53 (24.1%)	0.87	0.50 to 1.53	0.85	0.48 to 1.52
p Value				0.22		0.20	
p Trend				0.29		0.25	
Formaldehyde	0 to 16	49 (25.8%)	58 (27.1%)	1		1	
($\mu g/m^3$) (n = 404)	16.1 to 22	46 (24.2%)	48 (22.4%)	1.13	0.65 to 1.98	1.14	0.65 to 2.00
	22.1 to 32	51 (26.8%)	57 (26.6%)	1.06	0.62 to 1.81	1.08	0.62 to 1.86
	>32	44 (23.2%)	51 (23.8%)	1.02	0.59 to 1.78	1.04	0.59 to 1.82
p Value				0.97		0.97	
p Trend				0.99		0.93	
Living room damp (n = 357)	Very low	46 (27.5%)	65 (34.2%)	1		1	
	Low	90 (53.9%)	100 (52.6%)	1.27	0.79 to 2.04	1.37	0.84 to 2.25
	Moderate	19 (11.4%)	17 (8.9%)	1.58	0.74 to 3.36	1.60	0.73 to 3.49
	High	12 (7.2%)	8 (4.2%)	2.12	0.80 to 5.60	2.48	0.90 to 6.82
p Value				0.36		0.27	
p Trend				0.07		0.05	
Kitchen damp (n = 301)	Very low	31 (22.1%)	39 (24.2%)	1		1	
	Low	77 (55.0%)	92 (57.1%)	1.05	0.60 to 1.84	1.14	0.64 to 2.02
	Moderate	25 (17.9%)	21 (13.0%)	1.50	0.71 to 3.16	1.65	0.77 to 3.55
	High	7 (5.0%)	9 (5.6%)	0.98	0.33 to 2.92	1.03	0.33 to 3.16
p Value				0.71		0.61	
p Trend				0.52		0.41	
Bedroom damp n = 355	Very low	57 (34.5%)	81 (42.6%)	1		1	
	Low	90 (54.5%)	88 (46.3%)	1.45	0.93 to 2.28	1.49	0.94 to 2.36
	Moderate	16 (9.7%)	15 (7.9%)	1.22 †	0.60 to 2.49	1.26 †	0.60 to 2.64
	High	2 (1.2%)	6 (3.2%)				
p Value				0.26		0.24	
p Trend				0.25		0.23	
Visible mould (n = 415)	None	183 (95%)	221 (99%)	1		1	
	Yes	9 (5%)	2 (1%)	5.43	1.16 to 25.46	5.10	1.07 to 24.17
p Value				0.03		0.04	
Cotinine (n = 411)	Absent	147 (76.6%)	183 (83.6%)	1		1	
	Present	45 (23.4%)	36 (16.4%)	1.56	0.95 to 2.54	1.41	0.84 to 2.37
p Value				0.08		0.20	
NO_2 ($\mu g/m^3$) (n = 414)	0 to 22	57 (29.8%)	59 (26.5%)	1		1	
	22.1 to 34	43 (22.5%)	57 (25.6%)	0.78	0.46 to 1.34	0.66	0.38 to 1.16
	34.1 to 58	48 (25.1%)	52 (23.3%)	0.96	0.56 to 1.63	0.87	0.50 to 1.50
	>58	43 (22.5%)	55 (24.7%)	0.81	0.47 to 1.39	0.67	0.38 to 1.18
p Value				0.76		0.40	
p Trend				0.67		0.30	

*Adjusted for age, sex, and Carstairs deprivation index.
†For two highest categories combined in relation to the lowest.
CI, confidence interval; OR, odds ratio; VOCs, volatile organic compounds.

associated with symptom status (table 4), including visible mould, which was only present in the homes of nine cases.

Restriction of the analysis to atopic cases only increased the size of the formaldehyde and living room damp effects on frequent night-time symptoms (adjusted OR per increasing exposure category = 2.06 (1.37 to 3.09) and 2.70 (1.29 to 5.68), respectively), whereas no effects were seen among non-atopic cases. The interaction with atopy was significant for both formaldehyde (p = 0.004) and damp (p = 0.048). Similar effects were seen for frequent daytime symptoms (atopic cases only: adjusted OR = 1.68 (1.10 to 2.57) and 2.05 (0.96 to 4.38) for formaldehyde and damp, respectively), although when assessed formally, interactions were not significant.

DISCUSSION

In this study we identified a significant effect of formaldehyde concentrations in the home on symptom exacerbation among children with wheezing illness, with evidence of an exposure–response relation and of increased susceptibility in atopic subjects. Our findings also show strong exposure–response associations between objectively measured damp in the home and both the risk of persistent childhood wheezing illness and symptom frequency among those with wheezing illness, again with associations particularly evident among atopic subjects. We found no evidence to support an adverse effect of VOCs other than formaldehyde, or the previously implicated NO_2, on children's respiratory health, and no obvious effect of environmental tobacco smoke.

To ensure reliable case–control ascertainment, we defined our cases and controls in terms of consistent parental reporting of wheeze status on two occasions three years apart. We also validated case and control status using data on prescribed asthma drug treatment obtained from the child's family doctor records, and found similar results in the validated group. While it is possible that parents' prior knowledge of damp in the home may have led them to

Table 4 Proportion of cases reporting frequent night-time and daytime symptoms by level of indoor exposures and associated odds ratios

		Frequent night-time symptoms				Frequent daytime symptoms			
Exposure	Level of exposure	n	No (%) positive	Adjusted OR*	95% CI	n	No (%) positive	Adjusted OR*	95% CI
Total VOCs (μg/m^3)	0 to 176	34	15 (44.1)	1		34	21 (61.8)	1	
	176.1 to 293	50	26 (52.0)	1.46	0.58 to 3.63	48	32 (66.7)	1.29	0.50 to 3.32
	293.1 to 506	25	15 (60.0)	2.29	0.76 to 6.86	24	15 (62.5)	1.18	0.39 to 3.62
	>506	34	19 (55.9)	1.65	0.61 to 4.43	34	22 (64.7)	1.19	0.43 to 3.26
p Value			0.64	0.51			0.97	0.96	
p Trend			0.28	0.26			0.91	0.82	
Formaldehyde (μg/m^3)	0 to 16	39	16 (41.0)	1		37	23 (62.2)	1	
	16.1 to 22	35	17 (48.6)	1.40	0.54 to 3.62	34	16 (47.1)	0.47	0.17 to 1.25
	22.1 to 32	36	19 (52.8)	1.61	0.62 to 4.19	37	27 (73.0)	2.00	0.71 to 5.65
	>32	33	22 (66.7)	3.33	1.23 to 9.01	32	24 (75.0)	2.08	0.71 to 6.11
p Value			0.18	0.12			0.06	0.02	
p Trend			0.03	0.02			0.09	0.05	
Living room damp	Very low	32	13 (40.6)	1		33	17 (51.5)	1	
	Low	70	37 (52.9)	2.02	0.81 to 5.04	68	47 (69.1)	2.33	0.93 to 5.83
	Mod/high	24	16 (66.7)	3.86	1.20 to 12.45	23	17 (73.9)	3.23	0.97 to 10.78
p Value			0.15	0.08			0.15	0.10	
p Trend			0.05	0.02			0.07	0.04	
Kitchen damp	Very low	25	9 (36.0)	1		24	14 (58.3)	1	
	Low	55	31 (56.4)	2.49	0.90 to 6.89	55	38 (69.1)	1.71	0.59 to 4.96
	Mod/high	23	15 (65.2)	3.56	1.05 to 12.08	20	13 (65.0)	1.37	0.38 to 5.00
p Value			0.10	0.10			0.65	0.62	
p Trend			0.04	0.04			0.61	0.60	
Bedroom damp	Very low	45	16 (35.6)	1		44	28 (63.6)	1	
	Low	65	36 (55.4)	2.32	1.04 to 5.16	64	40 (62.5)	0.95	0.42 to 2.14
	Mod/high	14	11 (78.6)	7.03	1.66 to 29.79	13	10 (76.9)	1.72	0.41 to 7.32
p Value			0.01	0.01			0.62	0.71	
p Trend			0.003	0.003			0.56	0.64	
Cotinine	Absent	113	57 (50.4)	1		112	73 (65.2)	1	
	Present	32	19 (59.4)	1.22	0.52 to 2.87	30	19 (63.3)	0.86	0.35 to 2.13
p Value			0.37	0.65			0.85	0.74	
NO_2 (μg/m^3)	0 to 22	46	25 (54.3)	1		45	31 (68.9)	1	
	22.1 to 34	32	18 (56.3)	0.95	0.37 to 2.48	32	22 (68.8)	1.02	0.37 to 2.82
	34.1 to 58	34	17 (50.0)	0.76	0.30 to 1.92	34	21 (61.8)	0.67	0.25 to 1.78
	>58	34	17 (50.0)	0.77	0.30 to 1.96	32	19 (59.4)	0.67	0.25 to 1.79
p Value			0.94	0.91			0.78	0.74	
p Trend			0.61	0.50			0.32	0.32	

*Adjusted for age, sex, and Carstairs deprivation index.
CI, confidence interval; Mod, moderate; OR, odds ratio; VOCs, volatile organic compounds.

overreport wheeze, they were unaware of our hypothesis relating to damp, and the majority of homes with high surface wall moisture had no visible mould. Disease severity data were recorded in diaries by the children themselves, who are unlikely to be influenced by any knowledge of exposures.

We used objective measures of indoor exposures to improve validity and to eliminate self reporting bias, and these exposure data were collected by standardised techniques and analysed by laboratories blind to health status to minimise observer bias. Although the use of one-off measurements as markers of more long term exposure is likely to introduce some misclassification, particularly with respect to the pollutant gases which are subject to greater day to day variability than damp, this misclassification is unlikely to be systematic. Exclusion of those 31 cases and 40 controls who had moved home during the three year period on which case status was based had little effect on the results (data not presented). We restricted the study population to two school years to reduce confounding by age, and we were also able to adjust our analyses for numerous potential confounding variables, although confounding by other unmeasured factors cannot be ruled out.

A substantial proportion of the original study population declined to participate in the present study, but in the event our participants were similar to the target population with respect to age and sex, though they tended to be of higher social class, particularly among controls. It is unlikely, however, that this would explain the observed effect of living room damp on risk of wheezing illness, as living room surface wall moisture was not associated with social class in the random cross sectional sample. Formaldehyde was also unrelated to social class and therefore the observed effects on symptom severity among cases are also unlikely to reflect any social class related selection bias. As parents were unaware of specific exposures under study at the time of recruitment, it is unlikely that any known exposures would have influenced their willingness to volunteer for the study.

Our finding of an adverse effect of domestic formaldehyde exposure on respiratory symptoms among children with wheezing illness, but no effect on risk of underlying disease, has only been reported once previously.[5] That study, by Garrett *et al*,[5] looked at 7 to 14 year olds with a similar range of exposure, and also measured nitrogen dioxide and fungal spores but not to our knowledge other VOCs or

environmental tobacco smoke. We saw no effect of formaldehyde on asthma risk, unlike Krzyzanowski *et al* [3] and Rumchev *et al*,[4] although in those studies an increased risk was evident above 74 and 60 μg/m^3, respectively, and only 10 of our study homes reached such levels. Other studies reporting an association between respiratory symptoms and measured formaldehyde[1] or indoor painting—a source of formaldehyde[2]—have been in adults only. In the light of two previous studies reporting a positive association between indoor formaldehyde and risk of sensitisation in children,[5 17] the question arises as to whether our results could be explained by the frequently symptomatic children tending to have greater sensitisation. However, we found this not to be the case as the relation between formaldehyde and respiratory morbidity remained when restricted to atopic cases only.

While numerous previous studies have reported associations between respiratory health and damp, few have used objective measures of damp. Those that have, however, have tended to report findings in accordance with ours, with exposure–response relations with asthma risk and severity reported in 5 to 44 year olds[18] and in children.[19] A smaller study by Martin *et al* reported increased occurrence of respiratory symptoms in children living in homes classified by environmental health officers as damp, compared with those living in non-damp homes, but statistical significance was only reached for the outcome ''any respiratory symptom'' and not for wheeze.[20] The role of sensitisation in these relations has been investigated previously in a case–control study by Verhoeff *et al*,[13] who found odds ratios for asthma in relation to objectively measured damp and mould to be generally greater than 1 and stronger among atopic than non-atopic individuals, but none was statistically significant. However, exposure was based on visible damp/mould and dichotomised into present or absent only, which may explain why the reported effects were weaker than ours. While Verhoeff concluded that sensitisation plays an important role in explaining the relation between damp and symptoms, our findings suggest a true adverse effect of damp on asthma risk and morbidity exists, but primarily among sensitised children. It has been suggested that the effect of damp on respiratory health is partly explained by house dust mite antigen exposure.[21] We had no measure of this.

Conclusions

The indoor home environment may have an important effect on wheezing illness in children, with dampness increasing both risk and severity and formaldehyde increasing symptom severity only. Our study also suggests that children sensitised to domestic allergens are more susceptible to these influences. We further conclude, however, that exposure to VOCs as a whole—and exposure to the individual VOCs benzene, toluene, ethylbenzene, xylene, limonene and undecane—does not appear to be a determinant of the risk or severity of childhood wheezing illness.

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