Effect of improved home ventilation on asthma control and house dust mite allergen levels

Gillian R.Wright,[1] Stirling Howieson,[2] Charles McSharry,[3] Alex D. McMahon,[4] Rekha Chaudhuri,[1] Joyce Thompson,[6] Iona Donnelly,[3] Richard G. Brooks,[7] Lisa Jolly,[3] Lawrence McAlpine,[5] Eva M. King,[8] Martin D. Chapman,[8] Stuart Wood,[6] Neil C. Thomson.[1]

Departments of Respiratory Medicine[1] and Immunology,[3] Division of Immunology, Infection and Inflammation, University of Glasgow, Glasgow, UK. Department of Architecture and Building Science,[2] University of Strathclyde, Glasgow, UK. Robertson Centre for Biostatistics,[4] University of Glasgow, Glasgow, UK. Department of Respiratory Medicine, Monklands Hospital,[5] Airdrie, UK. Section of General Practice, Division of Community-Based Sciences,[6] University of Glasgow, Glasgow, UK. Department of Economics, University of Strathclyde, Glasgow, UK.[7] Indoor Biotechnologies, Inc, Charlottesville, US. [8]

Address for correspondence and guarantor:

Professor Neil C. Thomson, Department of Respiratory Medicine, Division of Immunology, Infection and Inflammation, University of Glasgow & Gartnavel General Hospital, Glasgow, G12 OYN. UK.

Telephone: 44-141-211 3241 Fax: 44-141-211 3464

E-mail: n.c.thomson@clinmed.gla.ac.uk

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Dedication

This paper is dedicated to the memory of Dr Stuart Wood, Senior Lecturer in General Practice at the University of Glasgow, who died in March 2006. His kindness, encouragement and enthusiasm for the project are greatly missed.

ABSTRACT

Objective

To determine the effects of improved home ventilation on house dust mite levels and the control of asthma.

Design

A randomized double-blind placebo-controlled parallel group trial.

Setting

Participants were recruited from General Practice and Hospital Respiratory Clinics in the West of Scotland.

Participants

120 adults with asthma who were allergic to house dust mite *Dermatophagoides pteronyssinus*.

Interventions

Mechanical heat recovery ventilation (MHRV) units were installed in all homes. Half of the units were activated at randomisation. All homes had carpets steam cleaned and new bedding and mattress covers at baseline.

Main outcome measures

The primary outcome was morning peak expiratory flow at 12 months.

Results

At 12 months, the change in mean morning peak expiratory flow, as compared with baseline, did not differ between the mechanical ventilation group and the control group [mean difference 13.5 liters per minute, 95% CI. -2.6 to 29.8, p=0.100]. However, evening mean peak expiratory flow was significantly improved in the mechanical ventilation group [mean difference 24.5 liters per minute, 95% CI. 8.9 to 40.1, p=0.002] and there were fewer hospitalizations for asthma (0 vs. 4, p=0.029). Indoor relative humidity was reduced in mechanically ventilated homes, but there was no difference between the groups in Der p 1 levels, compared with baseline, to account for the clinical changes.

Conclusions

The addition of mechanical heat recovery ventilation to conventional house dust mite eradication strategies did not achieve a reduction in house dust mite levels, but did improve some indices of asthma control.

Trial registration

ClinicalTrials.gov number NCT00148096

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INTRODUCTION

The prevalence of asthma in the western world has increased over the last generation,[1] in parallel with a warmer indoor microclimate.[2] Increased insulation, double glazing and modern building construction have improved standards of heating and energy efficiency in homes, but with reduced ventilation.[3] A warm, humid indoor environment favours the growth of the house dust mite population.[4] Sensitivity to the house dust mite is the most common allergy associated with asthma in the UK.[5]

Studies of occupational asthma[6] and altitude[7] infer that the environment may directly affect symptoms of asthma. Accordingly, allergen avoidance has been advocated as an important aspect of asthma management, yet the evidence for its efficacy is limited.[8] Large studies of conventional measures to eradicate dust mites, such as mite-impermeable mattress covers, have not shown a benefit for asthma symptoms.[9,10] However, Morgan et al[11] found significant improvement in asthma when a number of allergens were targeted in combination with an educational intervention and smoking cessation advice.

As house dust mites thrive in moist conditions, an additional eradication strategy would be to reduce indoor air humidity by improving ventilation. Mechanical heat recovery ventilation is a method of active ventilation using both an extract and a supply fan. Outdoor air is supplied at ambient humidity into the living room and bedroom, and extracted from the kitchen and bathroom. There is evidence that mechanical ventilation reduces indoor air humidity and the house dust mite allergen burden, but the clinical effects on asthma have not been proven.[12,13] The hypothesis is

that domestic mechanical heat recovery ventilation, in addition to allergen avoidance measures, can improve asthma control of those sensitive to house dust mite allergen, by attenuating re-colonisation rates.

METHODS

Participants

Participants 16 to 60 years of age were eligible if they had asthma for more than one year, were on regular inhaled corticosteroids and had daily symptoms. Participants were recruited from general practice and hospital clinics in Lanarkshire, Scotland, UK. Variable airflow obstruction of ≥12% on spirometry[14] or ≥15% on peak expiratory flow (PEF) readings[15] or a symptom score of ≥0.86 on the Asthma Control Questionnaire (ACQ)[16,17] was required for inclusion. Participants had a minimum forced expiratory volume in 1 second (FEV_1) of >50% predicted at baseline and had not had an exacerbation in the previous month. Spirometric measurements were recorded using an electronic spirometer (Vitalograph, Buckingham, UK), before and after inhaled salbutamol (400 μg).[18] PEF measurements were taken at home using a mini-Wright peak flow meter (Clement Clarke, Harlow, UK). Allergy to *D. pteronyssinus* was determined by positive skin prick test, defined as a wheal diameter of ≥3mm greater than negative control at 15 minutes; solutions supplied by ALK Abello, Hungerford, UK.[19] Participants were excluded if they were likely to move house or had a pet that provoked their symptoms. Participants were enrolled in the study by the clinical team between April 2003 and November 2005.The Lanarkshire

Research Ethics Committee approved the study. All participants gave written informed consent.

Study design

This was a randomised, double-blind, placebo-controlled, parallel group study to evaluate the effect of home installation of mechanical heat recovery ventilation (MHRV), in addition to conventional eradication strategies, in adults with asthma who were sensitive to *Dermatophagoides pteronyssinus*.

MHRV system

Homes of eligible participants were surveyed to assess suitability for installation. Homes were excluded if installation was technically difficult or if there was asbestos in ceiling materials. MHRV units (HR250 or HR800) were fitted in the roof space or hallway cupboard in 120 suitable homes by 'Vent-Axia™' (Crawley, UK). These energy efficient units extract air continuously from the kitchen and bathroom and deliver pre-warmed air via insulated ducts into the bedroom and living room (Figure 1). The system provided an additional 0.5 air exchanges per hour to the living room and bedroom.

Clinical assessments

Participants attended a baseline visit where spirometry was recorded and the ACQ[16] and St. George's Respiratory Questionnaire[20] were completed. The EQ-5D questionnaire'[21] was used as a standardised generic instrument for valuing health-related quality of life. Each score is categorised and 'quality of life years' (QALYs)

can be calculated from the difference in health states due to an intervention. Participants compiled a 2-week PEF diary prior to the visit. Nasal symptoms were recorded on a visual analogue score.[22] Serum total IgE and *D. pteronyssinus* and pollen-specific IgE were measured by commercial enzyme-immunoassay[23] (Sweden Diagnostics Ltd, Milton Keynes, UK).

House dust allergen, humidity and other environmental measurements

The architect team attended the home for a baseline visit. The bedroom, living room floor and bed surface were vacuumed at a rate of $1m^2$ per minute to obtain complete dust samples using a Dyson model - DC14 (Dyson, London, UK). The dust samples were filtered and weighed and a standardised soluble extract prepared. The extract concentration of allergens from house dust mite (Der p 1, Der p 2), cat dander (Fel d1) and dog dander (Can f1) were measured using fluorescent multiplex array technology (Indoor Biotechnologies, Charlottesville, VA).[24] The microbial content of dust was estimated by measuring soluble extract concentrations of bacterial endotoxin and fungal β(1-3) glucan (Associates of Cape Cod Inc., East Falmouth, MA, USA). Plasma cotinine was measured using a microplate competitive enzyme immunoassay (Cozart Bioscience Ltd, Abingdon, Oxford, U.K.),

Temperature and humidity were recorded at 90 minute intervals for 12 months in the living room and bedroom using thermohygrographs, 'Gemini Tiny Tag Ultra two channel' dataloggers (Gemini, Chichester, UK). The critical equilibrium humidity, at which no water is gained or lost by the house dust mite, is 73% relative humidity at 25ºC.[4] As maintaining relative humidity below 50% is a common recommendation

for reducing dust mites in the home,[25] the proportion of time that relative humidity fell below 50% was calculated.

Allergen avoidance measures

Once baseline measurements were complete, allergen eradication took place in all homes. Carpets were cleaned with a "Medivac" steam cleaner at the rate of $1m^2$ per minute (Medivac Healthcare Ltd., Cambridge, UK). New pillows, duvets and mattress covers were supplied to all participants ("Naturelle" range, Medivac Healthcare Ltd., Cambridge, UK).

Randomisation

Randomisation was performed in sequential blocks of four using an automated telephone answering system at the Robertson Centre for Biostatistics, University of Glasgow, UK, by the architect team. Accordingly, a fused electrical spur was switched in the roof space by the architect to activate half of the units. The unit activation device was concealed from the patient and the clinical research team.

Follow-up

Participants were followed up at 3, 6, 9 and 12 months after randomisation, until April 2007. Participants measured morning and evening PEF for 2 weeks before each visit. At each visit, spirometry was performed, ACQ score was recorded and requirements for oral corticosteroids, hospitalisations, General Practice or Emergency Department visits were noted. The St. George's Respiratory questionnaire, the EuroQol questionnaire and nasal visual analogue scores and questionnaires were repeated at 6

and 12 months after randomisation. At 12 months, blood samples for IgE serology, dust samples and humidity measurements were taken and placebo units activated.

Statistical analysis

The sample size was based upon a parallel group design, using a standard deviation of 40 liters/min for mean morning PEF. The study was intended to have 64 evaluable participants per group (n=128), in order to have 80% power (at the 5% significance level) to calculate a difference of 20 liters/min.

The primary analysis was a comparison between groups of the change over baseline in morning PEF. Secondary endpoints were evening PEF, ACQ scores, exacerbation and hospitalisation rates, spirometry, quality-of-life, *Der p 1* levels and humidity readings in the homes, IgE levels and economic evaluations. If 12 month data were not available, 9 month data would be used instead. The main analyses were carried out with ANCOVA models adjusted for baseline severity. The analyses were firstly carried out on an intention to treat basis. A list of 'major protocol violators' consisting of those with premature activation by the electrician and randomisation errors was created and the remaining population were denoted the 'per protocol' set. The primary and secondary endpoints were repeated for the 'per protocol' set. Binary endpoints such as hospitalizations were compared by odds-ratios, the attendant 95% confidence interval and tested by Mantel-Haenszel chi-squared test.

RESULTS

Baseline characteristics of participants

A total of 4986 participants were invited to participate, 482 attended clinical screening and 216 fulfilled the clinical entry criteria (Figure 2). Fifty-three subjects did not fulfill all housing criteria and 43 did not wish to have the MHRV unit installed. Units were installed in 120 homes, 119 underwent randomisation. Baseline demographic characteristics of those randomized were similar (Table 1).

Outcome measures

Clinical outcomes

100 participants attended follow-up at 12 months. The clinical outcome measures are listed in Table 2. The change in mean morning PEF did not differ between the MHRV group and the control group [mean difference 13.5 litres per minute, 95% CI -2.6 to 29.8, P=0.100]. However, there was a significant improvement in the MHRV group compared to the control group in mean evening PEF [mean difference 24.5 litres per minute, 95% Cl 8.9 to 40.1, P= 0.002] (Figure 3).

The ACQ score significantly improved in the MHRV group at 3 months [mean difference, -0.44, 95% Cl -0.76 to -0.12, p=0.008], but not thereafter. There were statistically fewer hospitalisations for asthma over the 12 month period in the MHRV group than in the control group (0 vs. 4, p=0.029). Values for spirometry, use of rescue medication, St. George's Respiratory Questionnaire score, requirements for oral corticosteroids, General Practitioner or Emergency department visits with asthma

did not differ between the two groups. Rhinitis visual analogue scores for sneezing, nasal discharge and nasal blockage significantly improved in the MHRV group compared to the control group at 6 months [sneezing, mean difference, -1.07, C.L. – 2.05 to -0.10, p=0.032; nasal discharge, mean difference, -1.36, 95% Cl -2.30 to -0.42, p=0.005; nasal blockage, mean difference, -1.65, 95% Cl -2.74 to -0.56, p=0.004], but not at 12 months. In the economic analysis there was a gain of 0.02 QALYs per MHRV patient. Eighteen major protocol violators were excluded from the 'per protocol' analysis. Fifteen were due to premature activation of the unit by the site electrician and three were randomisation errors. The 'per protocol' analysis confirmed that of the intention-to-treat analysis. Exacerbations of asthma are reported in Table 2 on page 27. No adverse events were reported relating to the installation of the MHRV unit.

Indoor relative humidity and temperature

MHRV significantly reduced mean relative humidity in the bedrooms for a sustained period from October until February and in the living room from December to February (Figure 4). The median (range) percent of time homes achieved a reduction in the indoor relative humidity below 50% was greater in the MHRV group than in the control group in the bedroom [44.1% (range 6.6% to 95.5%) vs. 28.9% (range 0.2% to 81.7%), p=0.001] but not in the living room [47.0% (range 9.9% to 93.3%) and 39.5% (0.5% to 83.2%), p=0.256].

Concentration of allergens and microbial products in house dust, and serum IgE levels

At 12 months, the changes in mean Der p 1 and Der p 2 concentrations in the bed, bedroom and living room carpets, as compared with baseline concentrations, did not differ between the MHRV group and the control group, nor were there differences in total or house-dust mite specific IgE. There were also no significant differences in secondary analyses of cat dander allergen (Fel d1), dog dander allergen (Can f1), β (1-3) glucan or endotoxin. (Table 2)

DISCUSSION

This randomised, double-blind placebo-controlled study examined the effect of the installation of domestic mechanical heat recovery ventilation (MHRV) on asthma control in adults sensitive to house dust mite allergen. It was based on the hypothesis that a warm, humid environment favours growth of the house dust mite population and that decreasing indoor air humidity with mechanical ventilation would reduce the dust mite allergen burden and improve asthma control.

Statement of principal findings

We found that there were improvements in some indices of asthma control at 12 months: increased evening PEF and fewer hospital admissions with asthma. Indoor relative humidity was reduced in the autumn and winter months in ventilated homes, but there was no difference between Der p 1 levels between the groups to account for the clinical changes. There were improvements in ACQ and Rhinitis visual analogue scores in the MHRV group after 6 months, which were short lasting, and may imply

that the MHRV intervention was most effective when combined with recent mite eradication strategies.

Strengths and weaknesses of the study

The strengths of the study are that it was a large community-based randomised trial utilising expertise from different disciplines. Participants reflected the general population with asthma with a GP diagnosis of asthma, daily symptoms and house dust mite sensitivity were sufficient for inclusion. Randomisation was effectively concealed from the participants and the clinical team. As 100 of a projected optimum number of 128 participants completed follow-up, the power of the study may not have been sufficient to detect a significant change in morning PEF.

Relation to previous research

Two previous small studies have examined the efficacy of MHRV for asthma. Warner and colleagues[12] showed a non-significant improvement in histamine PC_{20} ($p=0.085$), but no change in lung function or symptom scores with MHRV and high energy vacuum cleaning. Htut[26] found a decrease in bronchial hyperreactivity at 12 months after MHRV and steam cleaning. Our study provides weight to the evidence that improved ventilation might have a beneficial effect on asthma control.

Although the Der p 1 and Der p 2 levels fell in both groups, there was no difference between the MHRV group and the control group, adjusted for baseline. There was no difference between the groups in change in serum house-dust mite specific IgE antibody. This suggests that the MHRV system reduced indoor relative humidity to levels that were insufficient to impact on mite levels. Maintaining relative humidity

below 50% is a common recommendation for reducing dust mites in the home.[25] The MHRV unit achieved a relative humidity less than 50% in the winter months in the bedrooms more frequently than in the control group. However, although it may be statistically significant, it may not be environmentally significant as the fluctuation of humidity levels may permit mite survival. For example, a New Zealand study[27] showed that, although active ventilation did reduce relative humidity to less than 50% for 7 months of the year, there were no effects on mite levels because values were below the critical equilibrium humidity for only 39% of the total of 24-hour periods for which measurements were made. In another UK study, Fletcher[30] also found no impact of MHRV on Der p 1. It is possible that 12 months was too short a period to measure a difference in seasonally affected mite re-colonisation rates, after steam cleaning and barrier bedding were implemented across both cohorts.

One reason for this lack of efficacy in mite control may be related to climate.[29] For ventilation to reduce indoor humidity, the outdoor air humidity must be sufficiently lower than that inside. A Danish study observed 11 subjects with allergic asthma who were moved to 'healthy' homes with MHRV and found that a reduction of indoor absolute humidity was associated with a fall in dust mites and an improvement in indices of asthma control. However, there is an important difference between the cold winters of Scandinavia where the ambient air relative humidity was very low, compared with the high humidity ambient wet air during the milder winters of temperate regions of western Europe and New Zealand. Based on these observations, a future development in the intervention would be a humidistat controller (set at 50%) linked to a variable flow fan unit to ensure humidity suppression during the colder months.

Unanswered questions and future research

As the beneficial clinical effect of MHRV is not explained by a reduction in exposure to house dust mites, which other alternative explanations can be considered? No difference in cat or dog allergens, or in bacterial endotoxin levels in dust samples was demonstrated between the groups. Maintaining relative humidity below 50% has been recommended for controlling mould.[31] Burr and co-workers recently conducted an unblinded mold eradication trial that included improved home ventilation and found symptomatic improvement in wheeze, medication use and rhinitis.[32] In our study no difference between fungal glucan exposure was observed between the groups. Other possible explanations are a reduction in environmental tobacco smoke, respiratory viruses[33] or another component of indoor air quality such as particulate matter or volatile organic compounds. Increased relative humidity by itself is reported to be sufficient for increasing respiratory and other general symptoms.[34,35] There appears to be a dose-response relationship between asthma and living in damp housing, with respiratory symptoms more common in subjects living in damp homes. Action to improve damp housing conditions may therefore favourably influence asthma morbidity.

Finally, in the MHRV group there was gain of 0.02 QALY per subject. If the cost of installation is approximately £2000, the small QALY gain comes at a high price, albeit offset by a small reduction in hospitalisations. However, if the clinical results are sustained for the lifetime of the MHRV unit (10-20 years), the intervention may be more cost-effective.

In conclusion, this randomised controlled trial has shown clinical benefits of improved home ventilation in asthma control not explained by reduced levels of house dust mites. Future research should determine the mechanism of this effect.

'What this paper adds' box

What is already known on this subject House dust mite allergy is commonly associated with asthma. The warm, humid environment in modern homes favours the house dust mite population. The effect of improved ventilation on asthma control is not known.
What this paper adds This randomised controlled trial has shown clinical benefits of improved home ventilation in asthma control. However, this was not explained by reduced levels of house dust mites. Future research should determine the mechanism of this effect.

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CONFLICT OF INTEREST STATEMENT

Dr S. Howieson declares that 'Vent-axia ™' provided funding for salaries for technical members of his research team at the University of Strathclyde. All other authors declare that the answers to the questions on the competing interest from are all 'No' and therefore have nothing to declare.

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The research team was independent from these funding bodies.

STUDY SPONSOR

The Study sponsor was Glasgow Biomedicine.

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Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	MHRV Group	Control Group
No. of participants	60	59
Age (years)	41.6 (±9.6)	42.3 (±10.7)
Gender Female - no. (%)	41 (68.3)	32 (54.2)
Race or ethnic group -no. (%)		
Caucasian	58 (96.7)	58 (98.3)
Asian	2 (3.3)	1 (1.7)
Smoking –no. (%)		
Smoker	12 (20.0)	17 (28.8)
Ex-smoker	7 (11.7)	13 (22.0)
Never smoker	41 (68.3)	29 (49.1)
Plasma cotinine [all subjects] ng/ml, median (IQR)	3.4 (2.0-63.0)	3.2 (2.0-68.0)
Duration of asthma (years)	22.1 (±14.1)	20.1 (±13.9)
BMI (kg/m²)	28.4 (±5.5)	29.6 (±6.3)
Morning PEF (litres/min)	414.5 (±116.9)	409.1 (±91.6)
Evening PEF (litres/min)	428.2 (±112.4)	426.9 (±94.9)
Spirometry (% predicted)		
FEV_1 Prebronchodilator	83.7 (±18.0)	82.7 (±17.7)
Postbronchodilator	86.6 (±18.1)	89.5 (±15.6)
FVC Prebronchodilator	93.5 (±13.6)	95.0 (±15.4)
No. of puffs of a short-acting β-agonist (daily)	3.5 (±2.5)	4.0 (±3.7)
Asthma Control Questionnaire Score (0 to 6)	2.0 (±1.1)	2.0 (±1.0)
St. George's Questionnaire Score (0 to 100%)	35.3 (±23.9)	34.6 (±20.4)
Co-morbidity no. (%)		
Hypertension	5 (8.3)	8 (13.6)
Previous Myocardial infarction	0 (0.0)	1 (1.7)
Previous Stroke	1 (1.7)	2 (3.4)
Angina	2 (3.3)	3 (5.1)
Diabetes	3 (5.0)	2 (3.4)
Hayfever or other nasal allergy	44 (73.3)	47 (79.7)
Eczema	15 (25.0)	14 (23.7)
Other respiratory	0 (0.0)	1 (1.7)

Characteristic	MHRV Group	Control Group
Inhaled corticosteroid- beclomethasone equivalent µg, median (IQR)	1000 (800-2000)	800 (400-1200)
Current other asthma medication No. (%)		
β_2-agonist (short-acting inhaled)	60 (100.0)	58 (98.3)
β_2-agonist (short-acting oral)	1 (1.7)	1 (1.7)
β_2-agonist (long-acting)	41 (68.3)	34 (57.6)
Theophylline	4 (6.7)	4 (6.8)
Anti-cholinergic	5 (8.3)	6 (10.2)
Leukotriene receptor antagonist	15 (25.0)	9 (15.3)
Oral steroid	4 (6.7)	3 (5.1)
Rhinitis visual analogue scale (1 to 10)		
Sneeze	4.3 (±3.1)	4.2 (±2.7)
Nasal discharge	3.7 (±3.1)	4.3 (±3.1)
Nasal blockage	4.7 (±3.0)	4.8 (±3.1)
Serum IgE antibody		
HDM (kU_A/L)	15.8 (±25.8)	20.4 (±31.6)
Der p 1 (µg per gram of dust)		
Bed	4.9 (±14.4)	2.2 (±5.1)
Bedroom carpet	3.0 (±7.5)	1.7 (±3.6)
Living room carpet	2.7 (±7.4)	3.1 (±6.2)

Definition of abbreviations: No., number; Plus-minus values are means ± Standard Deviation; HDM, house dust mite.

Table 2. Comparison of clinical outcomes at baseline and 12 months.

Outcome	MHRV (mean ± SD)	Placebo (mean ± SD)	Adjusted difference ANCOVA (95% Cl)	p value
PEF am (litres/min)				
Baseline	414.5±116.9	409.1±91.6		
12 months	419.2±127.9	395.8±96.0		
Change	6.4±38.8	-7.1±38.5	13.59 (-2.66 to 29.85)	0.100
PEF pm (litres/min)				
Baseline	428.2±112.4	426.9±94.9		
12 months	436.1±124.7	405.9±93.4		
Change	12.0±36.4	-12.4±37.9	24.56 (8.97 to 40.15)	**0.002**
ACQ (0-6)				
Baseline	2.0±1.1	2.0±1.0		
12months	1.5±1.1	1.8±1.1		
Change	-0.4±0.7	-0.1±1.0	-0.25 (-0.57 to 0.08)	0.141
Rescue meds (no. of puffs)				
Baseline	3.5±2.5	4.0±3.7		
12 month	3.5±2.8	3.5±3.4		
Change	0.0± 1.9	0.1±2.3	-0.04 (-1.00 to 0.92)	0.936
St George's (0-100)				
Baseline	35.3±23.0	34.6±20.4		
12 months	29.7±24.4	31.2±19.9		
Change	-5.2±13.7	-2.1±12.4	-2.83 (-7.82 to 2.16)	0.262
FEV_1 pre (% predicted)				
Baseline	83.7±18.0	82.7±17.7		
12 month	86.6±18.1	82.5±16.9		
Change	1.8±8.3	1.0±11.3	1.32 (-2.56 to 5.19)	0.502
Exacerbations number				
Oral steroids	12	17	0.51 (0.21-1.22)	0.124
ED visits	4	2	1.78 (0.31-10.16)	0.512
GP visits	0	1		0.282
GP out of hours	24	22	0.90 (0.42-1.93)	0.795
Hospitalisations	0	4		**0.029**
Sneezing VAS				
Baseline	4.3 (±3.1)	4.2 (±2.7)		
6 months	2.9 (±2.4)	4.1 (±2.9)		
Change	-1.1 (±2.8)	0.0 (±2.8)	-1.07 (-2.05 to -0.10)	**0.032**
12 months	2.6 (±2.6)	3.1 (±2.3)		
Change	-1.7 (±3.0)	-0.8 (±2.3)	-0.76 (-1.70 to 0.18)	0.111

Nasal discharge				
VAS				
Baseline	3.7 (±3.1)	4.3 (±3.1)		
6 months	2.7 (±2.7)	4.3 (±2.8)		
Change	-0.8 (±2.5)	0.4 (±2.8)	-1.36 (-2.30 to -0.42)	**0.005**
12 months	2.7 (±2.9)	3.4 (±2.4|)		
Change	-0.9 (±3.1)	-0.5 (±2.7)	-0.46 (-0.47 to 0.55)	0.371
Nasal blockage				
VAS				
Baseline	4.7 (±3.0)	4.8 (±3.1)		
6 months	3.1 (±2.8)	4.3 (±2.8)		
Change	-1.3 (±2.8)	0.3 (±3.2)	-1.65 (-2.74 to -0.56)	**0.004**
12 months	3.7 (±3.0)	4.0 (±3.0)		
Change	-0.9 (±3.1)	-0.5 (±3.2)	-0.51 (-1.68 to 0.66)	0.392
Der p 1 (µg/g)				
Bed				
Baseline	4.9 (±14.4)	2.2 (±5.1)		
12 months	0.7 (±1.5)	2.6 (±9.6)		
Change	-3.2 (-6.7 to 0.4)	-1.3(-2.3 to -0.2)	-0.32 (-0.84 to 0.21)	0.232
Der p 1(µg/g)				
Living Room				
Baseline	2.7 (± 7.4)	3.1(± 6.2)		
12 months	0.9 (± 2.0)	1.0(± 2.1)		
Change	-1.9 (-4.0 to 0.2)	-2.8(-4.7 to -0.9)	0.1 (-0.8 to 0.9)	0.850
Der p 1 (µg/g)				
Bedroom carpet				
Baseline	3.0 (±7.5)	1.7 (±3.6)		
12 months	2.3 (±11.1)	1.5 (±1.8)		
Change	-0.4 (-4.7 to 3.8)	-0.5 (-1.6 to 0.6)	1.46 (-2.65 to 5.57)	0.482
Der p 2 (µg/g)				
Bed				
Baseline	1.1 (±2.2)	0.9±2.1		
12 months	0.3 (±0.7)	1.0±4.0		
Change	-0.6(-1.0 to -0.3)	-0.6 (-1.0 to -0.1)	-0.04 (-0.16 to 0.08)	0.496
Der p 2(µg/g)				
Living room				
Baseline	1.2±3.1	1.4±3.1		
12 months	0.9±3.3	0.5±1.3		
Change	-0.2 (-1.5 to 1.1)	-1.3 (-2.4 to -0.2)	0.56(-0.65 to 1.77)	0.359
Der p 2 (µg/g)				
Bedroom carpet				
Baseline	1.7±3.6	1.0±2.0		
12 months	1.6±7.3	0.9±1.3		
Change	0.1(-2.4 to 2.7)	-0.3 (-0.7 to 0.2)	1.07(-1.63 to 3.76)	0.433
Cat allergen				
Bed				
Baseline	2.9±5.5	3.3±0.6		
12 months	3.3±5.6	3.4±0.2		
Difference	0.0(-1.3 to 1.4)	0.4(-1.7 to 2.5)	-0.29(-2.63 to 2.06)	0.809

Cat allergen				
Living Room				
Baseline	2.1±3.8	2.7±5.0		
12 months	3.5±5.9	4.6±7.9		
Difference	1.1(-0.5 to 2.7)	2.9(0.8 to 5.0)	-1.81(-4.35 to 0.73)	0.161
Cat allergen				
Bedroom carpet				
Baseline	3.1±5.4	4.0±7.8		
12 months	3.6±5.1	3.3±5.6		
Difference	0.3(-1.1 to 1.8)	-1.1(-3.9 to 1.7)	0.61(-1.59 to 2.81)	0.582
Dog allergen				
Bed				
Baseline	22.2±41.8	21.5±3.8		
12 months	25.4±56.1	11.0±31.7		
Difference	-1.7(-12.1 to 8.7)	-8.4(-23.5 to 6.7)	7.22(-8.64 to 23.07)	0.368
Dog allergen				
Living Room				
Baseline	97.7±461.4	29.8±50.8		
12 months	41.9±71.9	34.8±53.1	-3.17(-29.36 to 23.03)	
Difference	-67.1(-207.1 to 73.0)	5.8(-11.9 to 23.4)		0.811
Dog allergen				
Bedroom Carpet				
Baseline	29.8±57.9	26.2±54.1		
12 months	34.4±59.1	26.2±4.1		
Difference	-1.4(-13.9 to 11.2)	7.2(-6.6 to 21.1)	-5.20(-22.49 to 12.09)	0.551
IgE to HDM				
Baseline	15.8 (± 25.8)	20.4(± 31.6)		
12 months	15.5 (± 24.2)	16.5 (± 26.1)	2.09 (-5.67 to 9.85)	
Change	-0.3 (±21.7)	-3.8 (±13.9)		0.592
Mold				
β(1-3) glucan				
Living Room				
(µg/g dust)				
Baseline	322.0(±453.2)	390.8(±582.2)		
12 months	108.9(±111.7)	113.4(±37.2)		
Change	-241.6(±486.9)	-360.7(±657.0)	-7.8 (-26.0 to 10.2)	0.389
Mold				
β(1-3) glucan				
Bed (µg/g dust)				
Baseline	347.1(±483.3)	255.5(±304.1)		
12 months	99.3(±50.8)	77.8(±35.4)		
Change	-273.9(±544.5)	-214.3(±366.4)	22.7 (-0.4 to 45.9)	0.055
Mold				
β(1-3) glucan				
Bedroom carpet				
(µg/g dust)				
Baseline	351.5(±966.6)	226.9(±216.9)		
12 months	107.5(±39.4)	114.2(±64.9)		
Change	-270.5(±1063.7)	-142.6(±233.8)	-15.4 (-40.4 to 9.5)	0.222

Endotoxin (EU) **Bed**				
Baseline	3539(±3213.8)	4479 (±3475.9)		
12 months	4583 (±3450.3)	5952 (±3617.5)		
Change	1109 (±3934.9)	1253 (±4969.5)	-1187.5 (-2935.7 to 560.7)	0.180
Endotoxin (EU) **Living Room**				
Baseline	5136.2(±2990.8)	6318.4(±2891.1)		
12 months	7776.9(±2548.9)	6986.0(±2589.9)		
Change	2666.1(±4488.0)	555.6(±4418.9)	497.2 (-679.6 to 1674.1)	0.403
Endotoxin (EU) **Bedroom carpet**				
Baseline	5725 (±3202.5)	5005 (±3438.0)		
12 months	6996 (±3047.0)	6916 (±2754.5)		
Change	1148 (±4541.9)	1902 (±3823.0)	-64.6 (-1465.6 to 1336.28)	0.927

Definition of abbreviations: Data represented as mean (+/- Standard Deviation), CI confidence interval. Values represent mean difference (CI) compared with baseline. Peak expiratory flow rate (PEF), Forced expiratory volume in 1 second (FEV_1), Asthma Control Questionnaire (ACQ) score (range, 0 to 6, with higher scores indicating worse asthma control). St. George's Respiratory Questionnaire (range, 0 to 100, with higher scores indicating worse quality of life). ED, Emergency Department, GP, General Practitioner. Rhinitis VAS, visual analogue scale (range, 1 to 10, with higher scores indicating worse symptoms). Immunoglobulin E (IgE), Dermatophagoides pteronyssinus allergen 1 and 2 (Der p 1 and Der p 2), Endotoxin units (EU)

FIGURE LEGENDS

Figure 1. Mechanical heat recovery ventilation system.

The mechanical heat recovery unit extracts air from the kitchen and bathroom (orange ducts) and delivers outdoor air warmed by exchanging heat in baffles with outgoing air via ducts into the bedroom and living room (red ducts). As designed and installed by 'Vent-Axia'™

Figure 2 Study Profile

Figure 3 Morning and evening peak expiratory flow measurements at baseline and during follow-up.

(a) At 6 and 12 months, the change in mean morning peak expiratory flow (PEF), as compared with baseline, did not differ between the MHRV group and the control group
(b) At 6 and 12 months, the change in mean evening PEF, as compared with baseline, was significantly greater in the MHRV (mechanical heat recovery ventilation) group compared to the control group [6 months, P=0.015 and at 12 months, P=0.002].

Figure 4 Relative humidity values and temperature over 12 months

The fortnightly mean (standard deviation on one-side) relative humidity and temperature in the bedroom and living room show an annual periodicity with the lowest levels in March. MHRV reduced humidity in the bedrooms during April (* $p<0.05$) and then for a sustained period from October until February († $p<0.001$). The humidity in the living room was significantly reduced (* $p<0.05$) from December to February. There was no effect of MHRV on temperature.

Figure 1. Mechanical heat recovery ventilation system.

Figure 2 Study profile

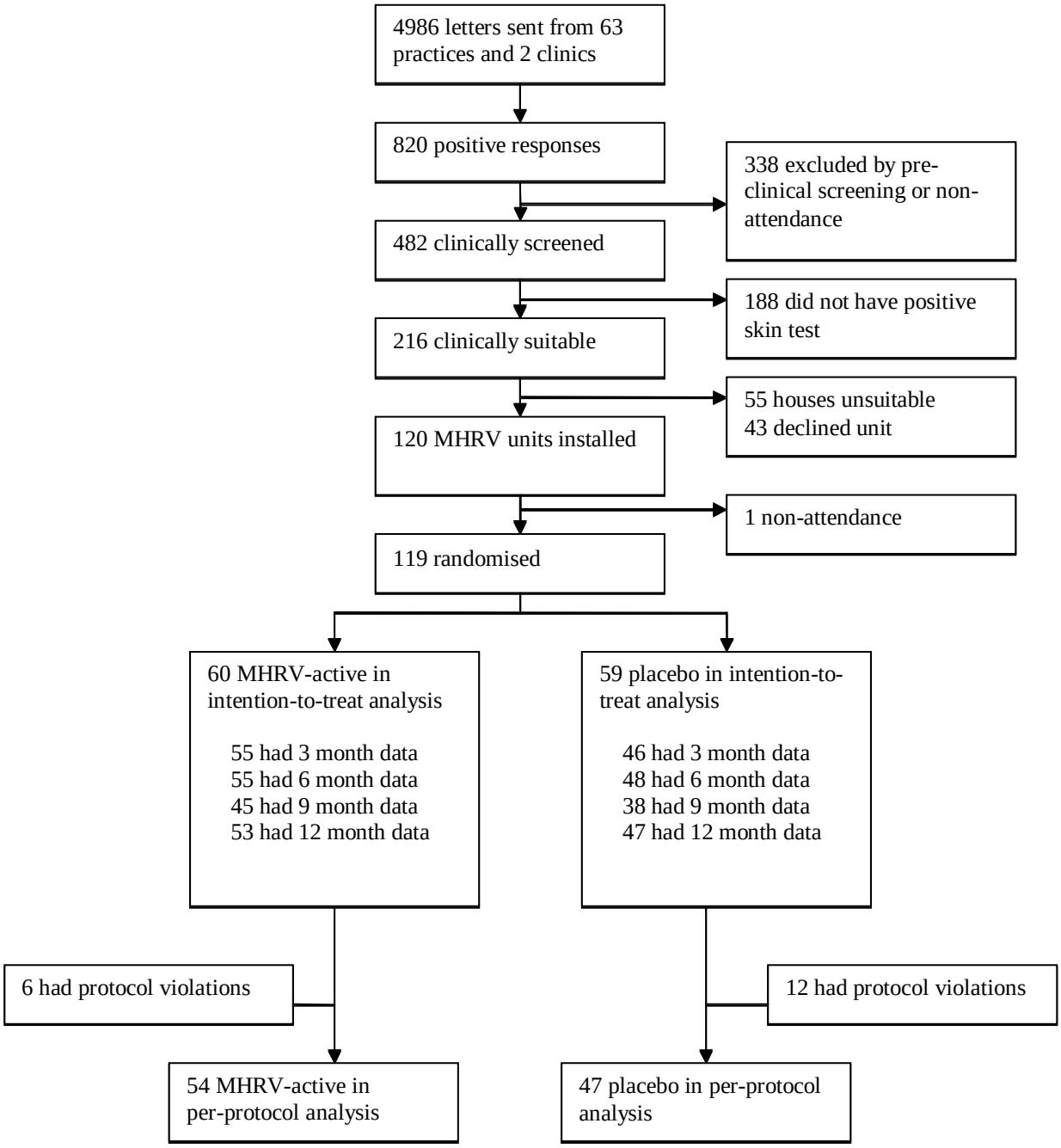
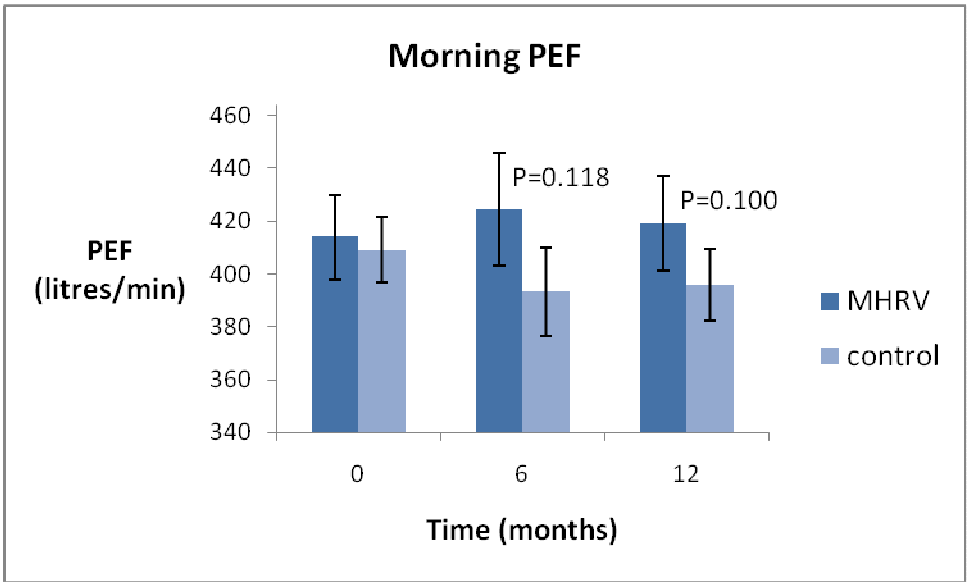


Figure 3 Morning and evening peak expiratory flow at baseline and during follow-up.



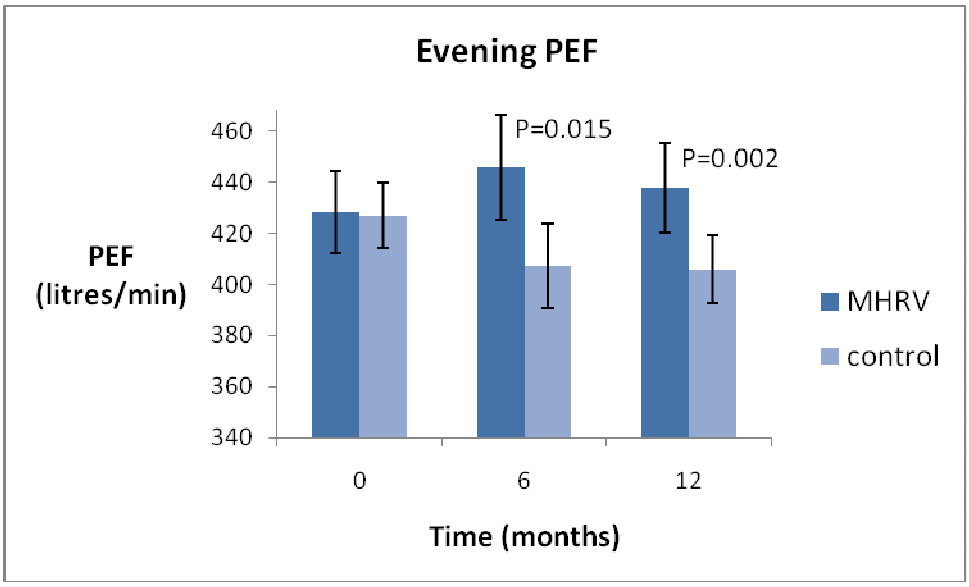


Figure 4 Relative humidity and temperature values over 12 months in MHRV and control groups