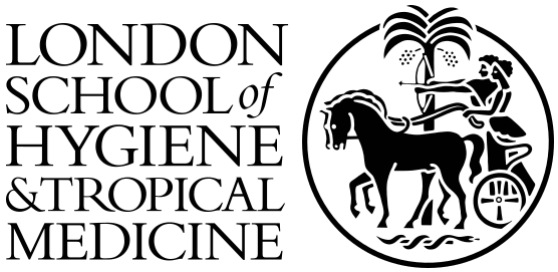

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ORIGINAL ARTICLE

Control of Exposure to Mite Allergen and Allergen-Impermeable Bed Covers for Adults with Asthma

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ABSTRACT

BACKGROUND

The effectiveness of avoidance of house-dust-mite allergen (*Dermatophagoides pteronyssinus* 1 [Der p1]) in the management of asthma is uncertain.

METHODS

We conducted a double-blind, randomized, placebo-controlled study of allergen-impermeable bed covers involving 1122 adults with asthma. The primary outcomes were the mean morning peak expiratory flow rate over a four-week period during the run-in phase and at six months and the proportion of patients who discontinued inhaled corticosteroid therapy as part of a phased-reduction program during months 7 through 12. Der p1 was measured in mattress dust in a 10 percent random subsample of homes at entry and at 6 and 12 months.

RESULTS

The prevalence of sensitivity to dust-mite allergen was 65.4 percent in the group supplied with allergen-impermeable bed covers (active-intervention group) and 65.1 percent in the control group supplied with non-impermeable bed covers. The concentration of Der p1 in mattress dust was significantly lower in the active-intervention group at 6 months (geometric mean, 0.58 μg per gram vs. 1.71 μg per gram in the control group; P=0.01) but not at 12 months (1.05 μg per gram vs. 1.64 μg per gram; P=0.74). The mean morning peak expiratory flow rate improved significantly in both groups (from 410.7 to 419.1 liters per minute in the active-intervention group, P<0.001 for the change; and from 417.8 to 427.4 liters per minute in the control group, P<0.001 for the change). After adjustment for base-line differences (by analysis of covariance), there was no significant difference between the groups in the peak expiratory flow rate at six months (difference in means, active-intervention group vs. control group, −1.6 liters per minute [95 percent confidence interval, −5.9 to 2.7] among all patients [P=0.46] and −1.5 liters per minute [95 percent confidence interval, −6.9 to 3.9] among mite-sensitive patients [P=0.59]). There was no significant difference between the groups in the proportion in whom complete cessation of inhaled corticosteroid therapy was achieved (17.4 percent in the active-intervention group and 17.1 percent in the control group) or in the mean reduction in steroid dose, either among all patients or among mite-sensitive patients.

CONCLUSIONS

Allergen-impermeable covers, as a single intervention for the avoidance of exposure to dust-mite allergen, seem clinically ineffective in adults with asthma.

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Exposure to high levels of dust-mite allergen among patients with asthma who are allergic to dust mites is associated with greater severity of disease and increased use of health care,[1,2] but the clinical effectiveness of avoidance of mite allergen by patients with asthma remains controversial. Removal of mite-sensitive children with asthma from their homes to the low-allergen environment of high-altitude sanitariums improves airway reactivity and reduces airway inflammation,[3,4] but other factors besides the avoidance of mites may be responsible for these improvements.

There are conflicting data on the effectiveness of domestic mite-allergen control in patients with asthma.[5-11] It also remains unclear whether a major reduction in personal exposure, similar to that achieved at high altitudes, can be achieved in homes. Since mite allergens become airborne only after the disturbance of dust, it seems likely that most exposure occurs in bed. In recent years, comfortable water-vapor–permeable, mite-allergen–impermeable bed covers have been marketed that substantially reduce the level of exposure to allergen in bed.[12] In a pragmatic, randomized trial involving typical adult patients with asthma in primary care, we tested the hypothesis that allergen-impermeable bed covers improve asthma control.

METHODS

STUDY DESIGN

We conducted a randomized, parallel-group, double-blind, placebo-controlled trial of mite-allergen avoidance (with the use of allergen-impermeable covers for mattresses, pillows, and quilts or identical-appearing covers that were not impermeable to mite allergen) among adult patients with asthma who were registered with 154 general practices in the Medical Research Council's General Practice Research Framework. The multicenter research ethics committee and all the local research ethics committees approved the study. All patients gave written informed consent.

STUDY PARTICIPANTS

Letters of invitation were sent to all patients 18 to 50 years of age with physician-diagnosed asthma who were regularly taking inhaled corticosteroids and were enrolled in participating practices. Patients already using allergen-impermeable bed covers or using less than 100 μg of albuterol per day or the equivalent were excluded. At entry (before randomization), serum *Dermatophagoides pteronyssinus*–specific IgE was measured in a central laboratory by immunoassay (UniCAP, Pharmacia–Upjohn), and sensitization was defined by a concentration of more than 0.35 kU per liter.[13] Patients and assessors were unaware of the patients' mite-sensitivity status. Randomization was performed at the coordination center, and the minimization technique was used to generate the randomization schedule. The minimization procedure ensured balance between the randomized groups within each practice and according to pet ownership or nonownership, smoking status, and mite-specific IgE levels.

STUDY PROCEDURES

Consenting, eligible patients were randomly assigned to receive either mattress, pillow, and quilt covers impermeable to *D. pteronyssinus* 1 (Der p1) (vapor-permeable Allergy Control barrier [Allergy Control Products]) or non-impermeable polyester–cotton (control) covers. The covers were fitted by a research nurse and left on the bedding for one year. No specific washing instructions for bed covers or any other information on the avoidance of mites was given to patients in either group.

The homes of all patients were visited at the start of the study, and the homes of a 10 percent random sample of the patients were also visited at 6 and 12 months. Dust samples were collected by the vacuuming of a 1-m² area of the mattress for two minutes through a filter device (ALK). The samples were assayed for Der p1 with the use of a two-site immunometric enzyme-linked immunosorbent assay.[14]

STUDY SCHEDULE AND OUTCOMES

Patients who responded to the invitation completed a screening questionnaire. Those who met the criteria for inclusion were seen by study nurses and completed a detailed questionnaire capturing data on medication use, pet ownership, smoking history, time spent away from home, and use of allergen-impermeable covers. A blood sample was collected for measurement of serum mite-allergen–specific IgE.

Patients then commenced a four-week run-in phase, during which they completed a diary card documenting morning and evening peak expiratory flow rate (recording the best of three efforts [Mini-Wright flowmeter, Clement Clarke International]), scores for daytime and nighttime symptoms, and beta-agonist use. Those who satisfactorily complet-

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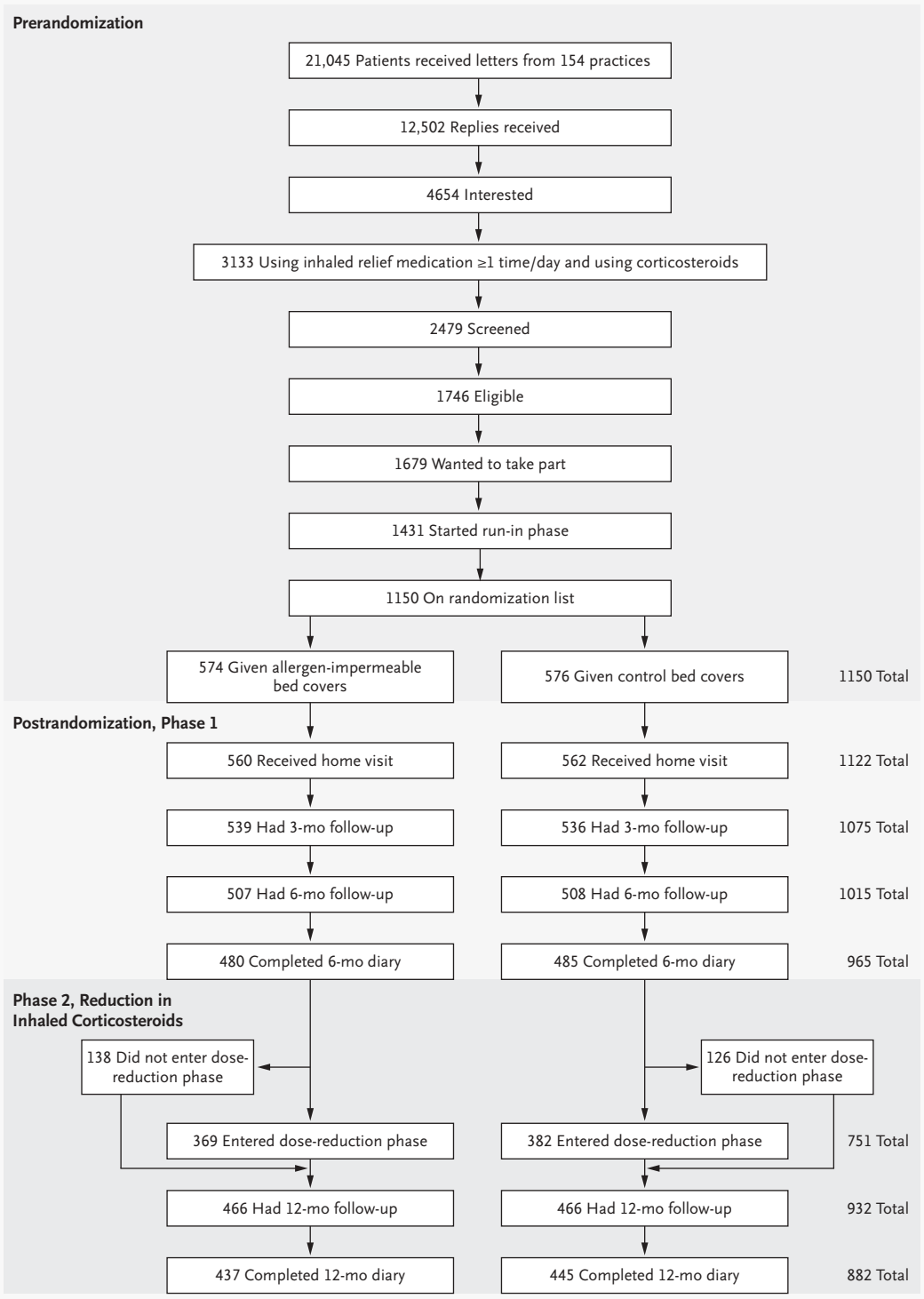

Figure 1. Profile of the Trial.

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Table 1. Base-Line Characteristics of the Study Population.*

Characteristic	All Patients		Mite-Sensitive Patients	
	Active-Intervention Group (N=560)	Control Group (N=562)	Active-Intervention Group (N=366)	Control Group (N=366)
Age — yr	36.4±8.4	36.9±8.2	35.4±8.0	35.9±8.0
Sex — no. (%)				
Male	192 (34.3)	214 (38.1)	148 (40.4)	159 (43.4)
Female	368 (65.7)	348 (61.9)	218 (59.6)	207 (56.6)
Race — no. (%)†				
White	548 (97.9)	552 (98.2)	359 (98.1)	359 (98.1)
Other	12 (2.1)	10 (1.8)	7 (1.9)	7 (1.9)
Smoking history — no. (%)				
Ever smoked	254 (45.4)	281 (50.0)	149 (40.7)	177 (48.4)
Current smoker	131 (23.4)	134 (23.8)	70 (19.1)	80 (21.9)
Cat or dog owner — no. (%)	306 (54.6)	307 (54.6)	192 (52.5)	192 (52.5)
Mite-specific IgE level — no. (%)				
<0.35 kU/liter	194 (34.6)	196 (34.9)		
0.35–0.69 kU/liter	18 (3.2)	29 (5.2)		
0.70–3.49 kU/liter	51 (9.1)	53 (9.4)		
3.50–17.49 kU/liter	87 (15.5)	82 (14.6)		
17.50–49.99 kU/liter	69 (12.3)	83 (14.8)		
50.00–99.99 kU/liter	63 (11.2)	35 (6.2)		
≥100.00 kU/liter	78 (13.9)	84 (14.9)		
Concentration of Der p1 in mattress dust — no. (%)‡				
<2 μg/g of dust	290 (51.8)	273 (48.6)	189 (51.6)	176 (48.2)
2–10 μg/g of dust	124 (22.1)	140 (25.0)	82 (22.4)	93 (25.5)
>10 μg/g of dust	146 (26.1)	148 (26.4)	95 (26.0)	96 (26.3)
Symptoms occurring at least once/day — no. (%)				
Wheezing	205 (36.6)	225 (40.0)	129 (35.2)	144 (39.3)
Cough	231 (41.2)	227 (40.4)	124 (33.9)	129 (35.2)
Breathlessness	209 (37.3)	206 (36.7)	122 (33.3)	128 (35.0)
Chest tightness	139 (24.8)	155 (27.6)	98 (26.8)	96 (26.2)
Waking at night	81 (14.5)	91 (16.2)	51 (13.9)	46 (12.6)
Inability to participate in activities	30 (5.4)	30 (5.3)	16 (4.4)	17 (4.6)

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Table 1. (Continued.)

Characteristic	All Patients		Mite-Sensitive Patients	
	Active-Intervention Group (N=560)	Control Group (N=562)	Active-Intervention Group (N=366)	Control Group (N=366)
Diary data				
Evening peak expiratory flow — liters/min§	424.0±93.1	429.6±93.9	435.9±91.0	441.1±90.0
Diurnal variation in peak expiratory flow — %§	4.1±7.5	4.5±8.4	4.5±7.8	4.8±8.0
Percentage of symptom-free days	24.8±28.0	24.6±29.5	25.1±27.3	23.4±29.0
Percentage of symptom-free nights	39.1±33.5	38.4±34.3	37.8±32.6	37.9±34.1
Corticosteroid used — no. (%)				
Beclomethasone	458 (81.8)	438 (77.9)	309 (84.4)	291 (79.5)
Budesonide	41 (7.3)	56 (10.0)	20 (5.5)	35 (9.6)
Fluticasone	61 (10.9)	68 (12.1)	37 (10.1)	40 (10.9)
Daily dose of inhaled corticosteroids — μg				
Beclomethasone				
Median	400	400	400	400
Range	100–3200	50–200	100–2000	100–2000
Budesonide¶				
Median	1000	1000	1000	1000
Range	200–4000	200–8000	200–4000	200–4000

* Plus–minus values are means ±SD. Der p1 denotes *Dermatophagoides pteronyssinus 1*.
† Race was self-reported.
‡ Data were missing for one patient in the control group.
§ Data are means of within-person means.
¶ Doses of fluticasone were doubled and subsumed under budesonide.

ed diary cards for at least 14 days were then randomly assigned to receive allergen-impermeable or placebo bedding. At randomization, the patients completed the St. George's Respiratory Questionnaire regarding quality of life, which was administered again after 6 and 12 months.

During phase 1 (months 1 through 6), patients were asked to maintain their usual inhaled corticosteroid therapy. They were seen at their physicians' offices after three months and after six months; diary cards and monitoring of the peak expiratory flow rate were completed for the four-week period preceding the six-month visit. During phase 2 (months 7 through 12), patients were invited to participate in a program of controlled reduction of inhaled corticosteroid therapy, during which they visited the study nurse monthly. The corticosteroid-reduction protocol was based on the protocol used in a previous study and was individually tailored, with the dose being reduced by 25 to 50 percent each month and the final decrement occurring in two stages if the dose in question could be delivered in two separate inhaled doses.[15] Asthma control was monitored on the basis of the peak expiratory flow rate and the level of use of the beta-agonist inhaler.

The reduction of inhaled corticosteroid therapy continued until either all inhaled corticosteroid use had been discontinued or asthma control deteriorated according to predefined criteria (a mean peak expiratory flow rate for the previous seven days that was less than 85 percent of the mean value during the run-in phase; an increase of more than six inhalations in the daily dose of a beta-agonist for the previous three days, as compared with the run-in phase; or a determination by the patient, the primary care physician, or the nurse that asthma control had deteriorated sufficiently that the reduction

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of inhaled corticosteroid therapy should be halted or reversed). Patients in whom asthma control deteriorated reverted to the preceding dose of inhaled corticosteroids and continued to receive this dose until the end of the study.

OUTCOME MEASURES

The primary outcome measure for phase 1 was the morning peak expiratory flow rate, calculated as the mean of all measurements recorded during the four weeks preceding the six-month visit, with control (by analysis of covariance) for the mean of all measurements recorded during the four-week run-in period. The primary outcome measure for phase 2 was the proportion of patients who discontinued inhaled corticosteroid therapy.

The secondary outcome measures for phase 1 were the evening peak expiratory flow rate, the use of beta-agonists, the scores for daytime and nighttime symptoms, the rate of exacerbation, the number of days of work missed, and the score on the St. George's Respiratory Questionnaire regarding quality of life (range of scores, 0 to 100, with higher scores indicating worse quality of life). The secondary outcome measure for phase 2 was the proportionate reduction in the dose of inhaled corticosteroids by the end of the study.

STATISTICAL ANALYSIS

Differences in continuous variables measured at base line were adjusted for the base-line level with the use of analysis of covariance, except for the quality-of-life score, which was analyzed in terms of the proportion of patients with improvement from base line; this and other proportions were compared with the use of the Pearson chi-square test. Because of the highly skewed distribution of the number of asthma-related days of work missed, the confidence interval for the difference in this variable was estimated with the use of a bias-corrected bootstrap method with 1000 replicates. Proportionate reductions in the dose of inhaled corticosteroids were compared with the use of the Mann–Whitney U test. All analyses were performed with the use of Stata software, version 7.0 (Stata). All primary analyses were restricted to the mite-sensitive population, with secondary analyses including all subjects.

On the basis of preliminary data, the standard deviation for the 28-day mean peak expiratory flow rate was estimated to be 112 liters per minute, and the correlation coefficient for the 28-day means measured six months apart was estimated to be 0.69. On the basis of these data, a study with 750 mite-sensitive patients who completed phase 1 would have a statistical power of more than 90 percent (at a 5 percent level of significance) to detect a difference of 20 liters per minute in the peak expiratory flow rate between the groups. Furthermore, such a study would have a statistical power of more than 90 percent to detect a 50 percent increase (from 25.0 percent to 37.5 percent) in the proportion of patients in whom inhaled corticosteroid therapy could be discontinued.

RESULTS

STUDY PATIENTS

Figure 1 shows the numbers of patients screened and included in the trial. Of 4654 interested patients, 2479 were screened, and 1431 were deemed to be eligible and entered the run-in phase. At the end of the run-in phase, 1150 patients were considered to be suitable for the study, of whom 1122 were randomly assigned to receive either allergen-impermeable bed covers (560 patients [the active-intervention group]) or control bed covers (562 patients [the control group]) and received a home visit. At randomization, 65 percent of patients (732) were mite-sensitive, 55 percent had pets, and 24 percent were current smokers (Table 1). Of those who underwent randomization, 1015 (90 percent) completed follow-up at 6 months, and 932 (83 percent) completed follow-up at 12 months. Diary data were received from 965 of the 1015 patients at 6 months and 882 of the 932 at 12 months.

ADHERENCE AND ADVERSE EVENTS

At 12 months, 31 patients in the active-intervention group had removed their bed covers, as compared with 12 patients in the control group ($P=0.003$). A total of 173 patients withdrew from the study (90 in the active-intervention group and 83 in the control group), mainly for reasons unrelated to the bedding. The frequency of adverse events was low (a total of 24 asthma-related events, 14 in the active-intervention group and 10 in the control group). There was one death due to asthma in the placebo group during phase 1.

LEVELS OF EXPOSURE

The base-line mite-allergen levels were typical of those seen in the United Kingdom, with approximately one quarter of beds having levels higher than 10 μg per gram of dust, one quarter having 2 to 10 μg per gram of dust, and one half having less than 2 μg per gram of dust (Table 1). There was no significant

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difference in levels of mite-allergen exposure between groups at base line (geometric mean, 1.34 μg per gram in the active-intervention group vs. 1.36 μg per gram in the control group). In the 10 percent subsample, there was a significant difference between the two groups in the level of exposure to mite allergen at 6 months (geometric mean, 0.58 μg per gram vs. 1.71 μg per gram; P=0.01 for the difference with adjustment for the base-line level), but not at 12 months (1.05 μg per gram vs. 1.64 μg per gram; P=0.74 for the difference with adjustment for the base-line level).

Table 2. Measurements at Base Line.*

Outcome	All Patients		Mite-Sensitive Patients	
	Active-Intervention Group (N=560)	Control Group (N=562)	Active-Intervention Group (N=366)	Control Group (N=366)
Morning peak expiratory flow (liters/min)	411.0±93.2	415.5±93.4	421.3±91.7	424.6±88.8
Puffs of a beta-agonist				
Daytime	2.93±2.04	2.74±1.85	2.89±2.03	2.74±1.81
Nighttime	1.42±1.13	1.50±1.35	1.42±1.11	1.41±1.04
Symptom score				
Daytime	1.35±0.76	1.35±0.77	1.28±0.70	1.34±0.73
Nighttime	0.94±0.69	0.96±0.70	0.93±0.65	0.94±0.68
Quality-of-life score	33.1±16.3	32.6±16.9	30.5±15.2	30.4±15.6

* Plus–minus values are means ±SD. Data for morning peak expiratory flow and number of puffs of relief medication are the means of within-person means. Data for the symptom scores are the means of within-person medians. The quality-of-life score is the total score on the St. George's Respiratory Questionnaire (range, 0 to 100, with higher scores indicating worse quality of life).

OUTCOMES

The study groups were closely matched at base line (Tables 1 and 2). At the end of phase 1, there were no significant differences between the groups in the primary outcome measure (morning peak expiratory flow rate) or the secondary outcome measures (the use of beta-agonists, the symptom scores, the rates of exacerbations, and the quality-of-life scores) between the active-intervention and control groups, either overall or among mite-sensitive patients (Table 3 and Fig. 2). There was a difference of borderline statistical significance with regard to the number of days of work missed, which should be interpreted cautiously in view of the number of comparisons performed.

A total of 480 patients in the active-intervention group and 485 patients in the control group had data for the morning peak expiratory flow rate at both base line and six months. The peak expiratory flow rate improved significantly in both groups (from 410.7 to 419.1 liters per minute in the active-intervention group [P<0.001] and from 417.8 to 427.4 liters per minute in the control group [P<0.001]). After adjustment for base-line differences with the use of analysis of covariance, there was no significant difference between the two groups (difference in means, active-intervention group vs. control group, −1.6 liters per minute [95 percent confidence interval, −5.9 to 2.7] among all patients [P=0.46] and −1.5 liters per minute [95 percent confidence interval, −6.9 to 3.9] among mite-sensitive patients [P=0.59]).

During phase 2, 14 percent of the randomized patients discontinued inhaled corticosteroid therapy completely, with a mean reduction in the dose of corticosteroids of almost 50 percent among the patients who began the dose-reduction phase. This rate of discontinuation and dose reduction was achieved with no overall reduction in the quality-of-life score or deterioration in the morning peak expiratory flow rate (Table 4). There was no significant difference between the groups, either overall or among mite-sensitive patients, in either the primary outcome (percentage of all randomized patients no longer receiving inhaled corticosteroids; relative risk of discontinuation, 1.02) or the secondary outcomes (mean proportionate reduction in the dose of inhaled corticosteroids among all patients entering the dose-reduction phase, 47 percent in the active-intervention group vs. 48 percent in the control group) (Table 4). Further analysis of a subsample of patients with high sensitivity to mite allergen (specific IgE level, >10 kU per liter) and a high base-line level of mite allergen in their mattress (>10 μg per gram of dust) revealed no significant difference between the groups in the mean morning peak expiratory flow rate during month 6 of phase 1 (mean, 416.5 liters per minute among 56 patients in the active-intervention group vs. 424.4 liters per minute among 74 patients in the control group; difference, with adjustment for base-line levels, 3.12 liters per minute [95 percent confidence interval, −10.1 to 16.3]; P=0.64).

DISCUSSION

Dust-mite-allergen–impermeable covers are widely available, recommended, and prescribed for patients with asthma. However, our study has demonstrated that, in the absence of other mite-control

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Table 3. Outcomes at Six Months (Phase 1).*

Outcome	All Patients					Mite-Sensitive Patients				
	Active-Intervention Group	Control Group	Unadjusted Difference (95% CI)	Adjusted Difference (95% CI)	P Value	Active-Intervention Group	Control Group	Unadjusted Difference (95% CI)	Adjusted Difference (95% CI)	P Value
Morning peak expiratory flow										
No. with data	480	485				313	315			
Base line — liters/min	410.7	417.8				421.0	426.7			
6 Mo — liters/min	419.1	427.4	–8.3 (–20.4 to 3.7)	–1.6 (–5.9 to 2.7)	0.46	429.3	436.2	–6.9 (–21.4 to 7.5)	–1.5 (–6.9 to 3.9)	0.59
Use of a beta-agonist, daytime										
No. with data	476	479				312	311			
Base line — no. of puffs	2.91	2.73				2.84	2.71			
6 Mo — no. of puffs	2.24	2.26	–0.02 (–0.27 to 0.23)	–0.15 (–0.32 to 0.02)	0.08	2.23	2.24	–0.01 (–0.31 to 0.30)	–0.10 (–0.30 to 0.11)	0.36
Use of a beta-agonist, nighttime										
No. with data	472	468				306	309			
Base line — no. of puffs	1.36	1.47				1.33	1.39			
6 Mo — no. of puffs	1.17	1.27	–0.10 (–0.26 to 0.06)	–0.02 (–0.13 to 0.10)	0.78	1.13	1.19	–0.05 (–0.21 to 0.12)	–0.01 (–0.14 to 0.12)	0.89
Symptom score, daytime										
No. with data	480	480				315	310			
Base line	1.32	1.33				1.25	1.32			
6 Mo	1.07	1.09	–0.02 (–0.12 to 0.08)	–0.02 (–0.10 to 0.06)	0.65	1.03	1.03	0.00 (–0.12 to 0.12)	0.05 (–0.05 to 0.14)	0.34
Symptom score, nighttime										
No. with data	479	479				315	308			
Base line	0.92	0.94				0.90	0.92			
6 Mo	0.76	0.76	0.00 (–0.08 to 0.09)	0.01 (–0.06 to 0.08)	0.77	0.76	0.69	0.07 (–0.04 to 0.17)	0.07 (–0.01 to 0.15)	0.07
Days of work missed										
No. with data	390	405				260	269			
No. of days	0.11	0.25	–0.15 (–0.29 to –0.02)	—		0.10	0.23	–0.13 (–0.28 to 0.009)	—	
	No./Total No. (%)		Relative Risk (95% CI)			No./Total No. (%)		Relative Risk (95% CI)		
Exacerbations	52/507 (10.3)	61/508 (12.0)	0.85 (0.60 to 1.21)		0.38	38/329 (11.6)	27/327 (8.3)	1.40 (0.88 to 2.24)		0.16
Improved quality of life	351/492 (71.3)	357/498 (71.7)	1.00 (0.92 to 1.08)		0.90	236/321 (73.5)	234/320 (73.1)	1.01 (0.92 to 1.10)		0.91

* Data for morning peak expiratory flow and number of puffs of relief medication (during the daytime or during the nighttime) are the means of within-person means. Data for the symptom scores (daytime or nighttime) are the means of within-person medians. Data for the number of days of work missed are the means for the month preceding the visit; for these analyses, the bootstrap method was used to calculate the confidence interval (CI) for the difference between the means. Data for exacerbations are the proportions of patients with at least one hospital visit or one course of oral corticosteroids during the previous six months. Data for the quality-of-life score are the proportions of patients with a total score on the St. George's Respiratory Questionnaire that was lower at six months than at base line (i.e., the proportions of patients with improved quality of life). Differences between groups represent the value in the active-intervention group minus the value in the control group. Adjusted differences were adjusted for the base-line value.

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measures, they are clinically ineffective for routine management of adult asthma in primary care. No effect was seen even in the subgroup of patients with high levels of mite-specific IgE and high levels of exposure to mite allergens.

As in most studies of allergen avoidance, we observed a significant improvement in most of the outcomes in both the active-intervention group and the control group. Although mattress covers did not themselves affect asthma, participation in the study appeared to have some effect (without any difference in the pattern of improvement between mite-sensitive patients and those who were not sensitized to mites). The morning peak expiratory flow rate increased in both groups, the level of use of short-acting beta-agonists was reduced, the rates of asthma-free days and nights increased, and the quality of life improved. Concurrently, a substantial proportion of patients in both groups were able to discontinue inhaled corticosteroid therapy or reduce their dose of corticosteroids. The reasons for this reduction in use are not known. It may represent a regression to the mean, although it is possible that the use of an additional polyester–cotton bed cover has a small clinical effect.

The reductions in exposure seem limited in terms of micrograms per gram of dust, and at one year, it appeared that the intervention had failed. However, expression of the data in terms of the allergen concentration underestimates the reduction in exposure in studies of bed covers. The total amount of allergen recovered (in micrograms per square meter of the mattress) would more adequately reflect the effect of the intervention, but the use of this measure requires accurate weighing of dust samples, which was not performed in this multicenter study. The polyurethane-coated covers we used are the most widely used type available. An experimental study demonstrated no detectable mite-allergen passage with the use of the same covers, in contrast to a substantial amount of leakage of allergen through the polyester–cotton control cover.[16] Furthermore, a recent clinical study involving children in Denmark in which identical bed covers were used demonstrated a significant reduction in allergen levels over a 12-month period when the data were expressed in terms of the total amount of allergen recovered.[17]

A Cochrane meta-analysis has attempted to determine whether mite-sensitive patients with asthma benefit from measures that aim to reduce their exposure to mite allergen in their homes.[18] Although individual studies have been small and inconclusive, the meta-analysis concluded that current chemical and physical methods seem ineffective and cannot be recommended for the treatment of asthma. However, this meta-analysis has been criticized on the grounds that insufficiency of the evidence does not imply that an intervention is ineffective.[19,20] The results of our study are in agreement with the conclusions of the meta-analysis. Similarly, a recent study reported a lack of clinical effectiveness of impermeable covers for bedding in patients with allergic rhinitis.[21]

It is difficult to conduct double-blind, placebo-controlled trials of allergen avoidance: the combination of allergy testing and home visits may be a potent stimulus for a change in behavior, with a resulting increase in cleaning and a reduction in aller-

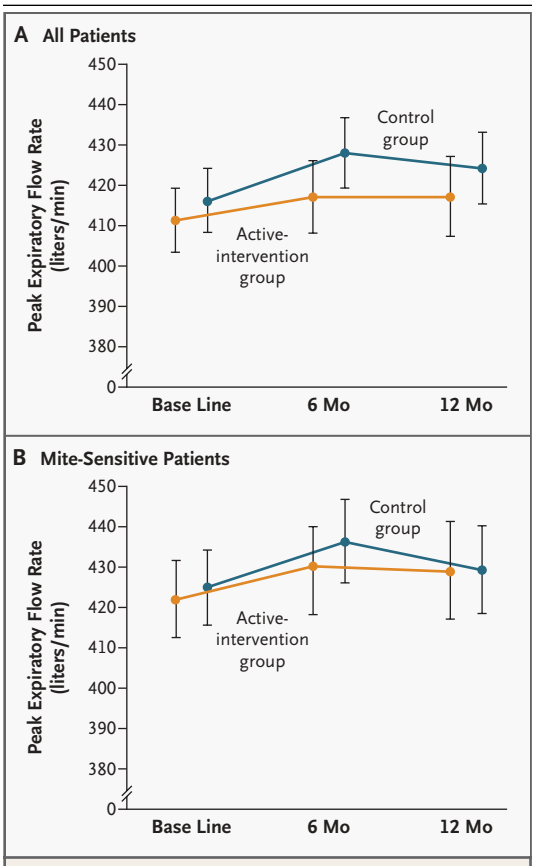

Figure 2. Mean Morning Peak Expiratory Flow Rate in the Active-Intervention and Control Groups at Base Line, 6 Months, and 12 Months among All Patients (Panel A) and among Mite-Sensitive Patients (Panel B).

Data points represent the geometric means, and I bars the 95 percent confidence intervals.

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Table 4. Outcomes at 12 Months (Phase 2).*

Outcome	All Patients					Mite-Sensitive Patients				
	Active-Intervention Group	Control Group	P Value	Relative Risk (95% CI)	P Value	Active-Intervention Group	Control Group	P Value	Relative Risk (95% CI)	P Value
Discontinuation of corticosteroid therapy — no./total no. (%)										
Among patients with 12-mo follow-up	80/459 (17.4)	79/463 (17.1)		1.02 (0.77 to 1.36)	0.88	49/296 (16.6)	54/294 (18.4)		0.90 (0.63 to 1.28)	0.56
Among all randomized patients†	80/560 (14.3)	79/562 (14.1)		1.02 (0.76 to 1.36)	0.91	49/366 (13.4)	54/366 (14.8)		0.91 (0.63 to 1.30)	0.59
Mean reduction in the dose of corticosteroids‡										
Among patients beginning dose-reduction protocol§										
No. of patients	366	380				245	247			
Percent reduction	47	48	0.84			47	48	0.74		
Among patients with 6-mo follow-up¶										
No. of patients	504	506				327	325			
Percent reduction	36	37	0.65			36	37	0.71		
Reduced quality-of-life score — no./total no. (%)‖	339/450 (75.3)	334/451 (74.1)		1.01 (0.94 to 1.10)	0.66	210/288 (72.9)	219/285 (76.8)		0.95 (0.86 to 1.04)	0.28
			Unadjusted Difference (95% CI)	Adjusted Difference (95% CI)				Unadjusted Difference (95% CI)	Adjusted Difference (95% CI)	
Mean morning peak expiratory flow			–5.9	3.4	0.19			0.1	5.2	0.11
No. of patients	445	437	(–18.4 to 6.5)	(–1.7 to 8.4)		283	282	(–15.1 to 15.4)	(–1.1 to 11.5)	
12 Mo — liters/min**	418.6	424.5				431.4	431.3			

* CI denotes confidence interval.
† Patients with missing data were assumed not to have discontinued corticosteroid therapy.
‡ The percent reduction was calculated as 100 × (the six-month dose – the final dose) ÷ the six-month dose. P values were derived by the Mann–Whitney U test.
§ The final dose of corticosteroids was calculated from the number of successfully completed steps in the reduction protocol.
¶ Patients with six-month follow-up who did not begin the reduction protocol were considered to have had a reduction of 0 percent if they were still using corticosteroids and to have had a reduction of 100 percent if they were no longer using corticosteroids.
‖ Data are the proportions of patients with a total score on the St. George's Respiratory Questionnaire that was lower at 12 months than at base line.
**Data are the means of within-person means. Differences represent the mean in the active-intervention group minus the mean in the control group. The adjusted differences were adjusted for the base-line value.

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gen levels in the control group. In a recent study examining the effect of combined mite and cockroach control, children were randomly assigned to an active group, a placebo group, and an additional control group in which no home visits occurred until the end of the study.[22,23] The outcomes in the two intervention groups were significantly better than those among the children whose homes were not visited. In our study, patients were unaware of their mite-sensitization status, which minimized the risk that patients in the control group might undertake allergen-avoidance measures. Furthermore, 90 percent of the participants had only one home visit, which reduced the likelihood of a change in behavior. The inclusion of a "no-treatment" control group would not have affected the interpretation of the data on the effect of the intervention.

Allergen levels in the United Kingdom are similar to those seen in other areas of the world with temperate climates but are substantially lower than those in Australia and New Zealand, for example. Nevertheless, the lack of any benefit even in patients with high levels of exposure to allergen suggests that these results are likely to be widely applicable.

The high proportion of pet owners in our study could have affected the potential benefit of a reduction in the level of exposure to mite allergen. However, it is unlikely that the results of a study of this size would be confounded by sensitivity and exposure to other allergens. Furthermore, this was a pragmatic clinical trial investigating the effect of a simple, practical intervention, which mimicked real-life clinical practice as much as possible. We deliberately decided not to conduct a study in a carefully selected minority of patients, with strict criteria for inclusion and exclusion and extensive intervention, since the results of such a study might not be widely applicable. It remains possible that a much more stringent intervention in a carefully selected group of patients could have some effect, but that possibility was not addressed in the current study. We have previously demonstrated that a complex environmental intervention (including the use of allergen-impermeable covers, weekly washing of bedding in hot water, the use of high-efficiency vacuum cleaners, and the replacement of carpets with hard floors) is effective in creating a low-allergen environment for the primary prevention of asthma,[12] but this type of intervention is neither practical nor acceptable for the majority of patients with asthma within the context of primary care.

In the current study, the bed covers were well tolerated, and compliance was good. Slightly more patients in the active-intervention group than in the control group had removed the covers by the end of the study, but the absolute difference in numbers was small. The slightly higher rate of noncompliance is most likely attributable to the sweating that is associated with the use of an impermeable cover.

How can we explain the discrepancy between studies of mite avoidance in children that suggest some benefit[6,8,17] and the data from our study and other studies involving adults that show no improvement in asthma control?[5,10,21] Occupational asthma may be a useful model: although early diagnosis and removal from the workplace where the exposure has occurred are associated with recovery,[24] a long duration of exposure in sensitized subjects leads to persistent and sometimes progressive deterioration of asthma control, even if the exposure has ceased.[25] Thus, early detection and immediate cessation of exposure may be important factors for a favorable prognosis.

In conclusion, the use of allergen-impermeable bed covers as a single intervention for the avoidance of mite allergen seems clinically ineffective for the routine management of asthma in adults in primary care. If mite avoidance is to be used in the treatment of asthma, we need to understand better how and where to measure the level of personal exposure to mite allergens, how to reduce it effectively, who is likely to benefit most, and when the intervention should be started.

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