

A review of the effects of impermeable bedding encasements on dust-mite allergen exposure and bronchial hyper-responsiveness in dust-mite-sensitized patients

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Summary

Background Sensitization and exposure to dust-mite antigens are causative factors in the development and exacerbation of asthma. Impermeable bedding encasements are considered a first-line treatment to reduce dust-mite antigen exposure in clinical asthma-management guidelines. Public-health recommendations for environmental asthma treatments should be based on the weight of evidence supporting the reliability of environmental interventions so that uncertainties regarding their effectiveness can be accurately communicated to patients, and so that limited public-health resources can be most effectively utilized.

Objective To evaluate the strength of a clinical-trial evidence supporting the efficacy of bedding encasements as an asthma treatment.

Methods A narrative review was conducted of all clinical trials involving bedding encasement for the treatment of asthma. Collective statistical analyses were also performed to characterize the quantitative effect of bedding encasement on dust-mite allergen exposure and bronchial hyper-responsiveness (BHR) when used by asthma patients.

Results Over 30 clinical trials were reviewed. Of those studies reporting adequate exposure and BHR results, four reported significant reduction in dust-mite allergen exposure and concomitant BHR reduction in active-treatment groups using bedding encasements. In 10 studies, mite-allergen exposure was reportedly decreased during the study, but BHR was not changed in the active-treatment group or was reduced to a similar degree in the active-treatment and control groups. Five other studies reported a lack of significant effect of the intervention on exposure and BHR. Collective paired analyses found that the effect of bedding encasement on allergen exposure and BHR tended toward only a modest, non-significant improvement. Collectively, effects of bedding encasement on BHR and dust-mite allergen exposure were modestly correlated only when the baseline exposure was above 2 µg Type 1 antigen per gram settled dust.

Conclusion Although bedding encasement might be an effective asthma treatment under some conditions, when implemented in clinical trials by asthma patients, its effectiveness is inconsistent and appears to be, at best, modest. Therefore, its significance as a reliable asthma management modality for any individual asthma patient is uncertain. Where resource constraints are significant, targeting the use of variably effective interventions such as bedding encasements toward those patient sub-populations most likely to derive substantial benefit may gain the largest net public-health benefit.

Keywords allergen avoidance, asthma, bedding, bronchial hyper-responsiveness, clinical trial, dust mite, encasement, environmental intervention, mattress

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Introduction

Sensitization and exposure to house dust mite (HDM) (*Dermatophagoides* spp.) allergens are causally related to both development and exacerbation of asthma [1–4]. In geographic

regions where dust mites are prevalent, residential dust-mite allergen exposure is associated with sensitization, airway inflammation and increased risk of exacerbations [5, 6]. Conversely, dust-mite-sensitized asthma patients who are moved to high-altitude or hospital environments where dust mites are absent have reduced symptoms, reduced airway inflammation markers and improved lung function [7–12]. Based on these observations, and because of the prominence of dust-mite sensitization and exposure in allergic asthma, many techniques have been suggested to reduce dust-mite allergen

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exposure in patients' homes, with the goal of achieving clinical improvement similar to that seen when patients are completely removed from the source of exposure [13, 14].

Numerous clinical trials to assess the effectiveness of dust-mite allergen-avoidance methods have been conducted, and the results have been reviewed previously [13–20]. The general conclusion from this body of literature has been that, while some types of allergen-avoidance methods are not particularly effective (e.g., chemical treatments [14], air filtration [21]), the concept of residential dust-mite allergen avoidance is supported as an effective approach to asthma treatment in clinical trials [4]. However, the weight of evidence supporting this conclusion has been questioned based on the results of a formal meta-analysis of randomized, controlled trials combining all forms of dust-mite allergen avoidance [15].

The use of impermeable bedding encasements is one specific dust-mite allergen-avoidance treatment that has become a nearly universal component of clinical asthma-management guidance for health-care providers and allergic patients [14, 19, 20]. Their use is considered a first-line dust-mite control measure, usually in combination with regular hot-water laundering of bed linens. Recommendations for the use of bedding encasements appear to be based on evidence from a small number of clinical trials where mite-allergen exposure was reduced and lung function improved when encasements were used by asthma patients in their home [22, 23]. However, other well-designed clinical trials have failed to observe reduced asthma morbidity, even when dust-mite allergen exposure appeared to be significantly reduced [24–27].

Clinical asthma management recommendations for the universal use of bedding encasements as an allergen-avoidance treatment for dust-mite-sensitized asthma patients have potential economic implications for patients and for public-health agencies. For instance, if encasements are considered necessary and effective asthma treatments, their costs could be reimbursable under the US Medicaid program. Similarly, a substantial investment in resources would be committed by community-based asthma intervention programmes that choose to include universal provision of bedding encasements as a component of their protocols. The reliability of obtaining reduced dust-mite allergen exposure and concomitant health benefits from the use of bedding encasements needs to be assessed to be able to make effective, evidence-based public-health recommendations for interventions or health-care expenditures in the face of limited resources and competing priorities.

A thorough review evaluating the weight of evidence for the effectiveness of bedding encasements when used by asthma patients has not been published. The literature on dust-mite allergen avoidance was reviewed and clinical trials incorporating some form of bedding encasement were analysed to determine whether sufficient evidence exists to support bedding encasement as a practical and clinically effective method of dust-mite allergen avoidance when used by sensitized asthma patients.

Materials and methods

Literature review

English-language articles in the open literature were sought that included tests of any form of impermeable bedding

encasement as a component of asthma disease management in a clinical trial. Studies were divided into two categories for qualitative review – clinical trials where bedding encasement was the only active treatment tested and clinical trials where encasement was combined with one or more other allergen-avoidance treatments. Clinical trials were only included in the review if all study subjects were sensitized to HDM allergens (in one case, about 65% of control and treatment patients were sensitized [27]). All clinical studies of bedding encasement were considered in the review – regardless of study design features such as randomization, blinding or use of placebo controls – in order to provide a complete picture of the literature evaluating this allergen-avoidance technique. In cases where a conference abstract and a subsequent full article did not appear to represent precisely the same data set, both were included.

Quantitative analyses

Quantitative exposure and clinical data were obtained from each study to develop a statistical model relating changes in exposure to changes in objective lung function measures in asthma patients. The analyses focused on bronchial hyper-responsiveness (BHR) as a sensitive marker for how well a patient's asthma is being controlled and as a standardized outcome measure less subject to bias than self-reported endpoints such as symptoms or peak flow. Studies were included in the quantitative analysis when they reported pre-intervention and post-intervention histamine provocation concentration (PC₂₀) or dose (PD₂₀) associated with a 20% decrease in forced expiratory volume in 1 s (FEV₁).

Exposure estimates were based on total Type 1 dust-mite allergen content or whole mite counts in mattress-settled dust. An approximate equivalency of 50 whole mites/g dust to 1 µg Type 1 dust mite antigen/g dust was used when results were reported as whole mite concentration [4, 28].

Exposure and outcome indices were calculated for each study based on reported measures at baseline and at the final time point reported for the intervention phase of each study. Both indices were calculated as ratios of mean baseline and ending exposure or outcome measures such that values > 1 indicated improvement over the course of the intervention. For each study, baseline and ending exposure and outcome were estimated by the mean or median value reported for each treatment group in the study design (hereafter referred to as the mean value). In cases where central values were not reported, an arithmetic mean of the individual data points extracted from the study was calculated. If two groups both included encasement among their treatments, a weighted mean for the two groups was computed, using the groups' sample sizes as the weights.

A few studies used encasement as a control against which to compare some additional avoidance treatment (i.e., no non-encasement control group was included). The encasement control in those studies was considered to be the 'active' treatment group for purposes of the paired and dose-response analyses, with no corresponding control data.

Statistical analysis

Parametric statistical analyses were performed on log₁₀-transformed means or indices. Comparisons between baseline

and ending mean values for BHR and mite exposure were tested with paired *t*-tests. Wilcoxin signed-rank tests were used to examine the direction of change in paired, untransformed exposure and BHR metrics. Linear regression was used to relate BHR index (BHR_{In}) to exposure index (EXP_{In}). Analyses were performed on data weighted by the study sample size. All statistical analyses were performed in SYSTAT v. 9 (SPSS Inc.).

Results

Qualitative review

Thirty-three articles and conference abstracts were found that contained original data from clinical trials of allergen avoidance in asthma patients and that included some form of bedding encasement as a component of treatment (Table 1). Study designs were diverse and ranged from small, uncontrolled studies to randomized, double-blind, placebo-controlled designs. Studies also varied in their presentation of quantitative exposure and clinical-endpoint data.

Twelve studies (13 intervention periods) reported the results of clinical trials involving only bedding encasement as the active treatment [26, 27, 29–38]. Type 1 dust-mite antigen concentration in mattress dust was significantly reduced in the active group in eight of the 10 intervention periods for which exposure results were reported, with roughly 2–10-fold decreases compared with baseline concentrations after study periods ranging from 2 to 12 months. Control-group dust-mite antigen concentrations in mattress dust were unchanged or decreased to a lesser degree than for the active treatment groups.

BHR as assessed by histamine or methacholine provocation testing [26, 31, 32, 35, 36], dust mite provocation testing [34, 36], exercise provocation [37] or by an unspecified provocation agent [33] was not significantly improved compared with baseline in six of the nine BHR data sets for the active treatment group. In five of those cases, a significant decrease in allergen exposure was reported. Other clinical measures, including baseline FEV_1 , symptom scores, self-reported peak expiratory flow (PEF), total serum IgE, dust-mite skin reactivity, inhaled steroid dose and blood eosinophil markers were unchanged or changed to the same degree for active and control groups in most cases. There was a decrease in one serum eosinophil protein marker in the active group in one study [32] and improvements in baseline FEV_1 , symptom score and PEF variability in the active group in another [37]. Nasal symptoms improved in the active-treatment group compared with baseline, but not compared with controls, in one study [26] and steroid dose decreased to a greater degree in the active group than in the control group in one study, although BHR improvement did not differ [34].

The remaining 21 clinical trials were all combined-treatment studies that included bedding encasement as one of the treatment components [22–25, 28, 29, 39–53]. A statistically significant reduction in mattress dust-mite exposure was reported in the active-treatment group in 12 of 17 studies where dust sampling was conducted (Table 1). In two of these studies, there was also a significant decrease in dust-mite allergen exposure in the control group [24, 25]. Of the seven studies where dust-mite allergen concentration was the reported exposure metric, four had significant exposure

reductions in the active treatment group, but only two of those [23, 44] had a baseline value above the level associated with an increased risk of sensitization ($2\mu\text{g/g}$) [4–6] and achieved a final level at or below that level.

A significant reduction in BHR (assessed by histamine challenge in all studies) in the active treatment group, not accompanied by a similar reduction in the control group, was achieved in three of 11 combined-treatment studies [22, 23, 42]. In one study that included an encasement-only group and an encasement+HEPA air filtration group, a significant BHR reduction was achieved only in the encasement+HEPA filtration group [40]. Of the seven other studies without a significant BHR reduction in the active encasement treatment group, five reported significant reductions in dust-mite exposure in that group [24, 25, 39, 44, 50].

No consistent pattern of changes in other measures of asthma morbidity was found among the 19 combined-treatment studies reporting any other clinical results. Seven studies reported no significant changes in any measured clinical parameters in control or active treatment groups [29, 44, 46–48, 50, 52]. Among the remaining studies, improvements in subjective symptoms scores, non-challenge lung function (FEV_1 or PEF) or total IgE were each reported in about one-half of the studies (not all the same studies).

Quantitative analyses

The direction of change in allergen levels (all metrics combined) was towards decreased exposure at study end in the active-treatment groups (18/19 decreased, Wilcoxin $Z = 3.3$, $P < 0.001$; Table 2) and also in the control groups (13/16 decreased, Wilcoxin $Z = 2.0$, $P = 0.049$). However, the mean difference in active-treatment group exposure levels between baseline and study end did not attain statistical significance among all studies reporting Type 1 dust-mite allergen concentration as the exposure metric ($t = 1.35$, $P = 0.20$, $N = 15$). The result for control-group baseline vs. study-end exposure levels was also not significant ($t = 0.53$, $P = 0.61$, $N = 13$).

BHR decreased to some degree (i.e., histamine PC_{20} or PD_{20} increased) in almost all studies in the active-treatment group (11/12 increased PC/PD_{20} , Wilcoxin $Z = -3.0$, $P = 0.0029$; Table 2). The direction of change was also towards decreased BHR in a majority of control groups, but was not significant (6/9 increased PC/PD_{20} , Wilcoxin $Z = -1.2$, $P = 0.21$). However, the mean decrease in BHR, as measured by histamine PC_{20} , was not significant for either the active-treatment ($t = -0.76$, $P = 0.47$, $N = 9$) or control ($t = -0.41$, $P = 0.70$, $N = 7$) groups in collective analyses.

BHR and exposure indices were unrelated based on a weighted linear regression model of the $\log_{10}$ -transformed indices for all studies reporting appropriate data (Table 3). Limiting the regression analysis to those studies where the baseline exposure level was at least $2\mu\text{g/g}$ did not result in a significant linear relationship, although the per cent variation in BHR_{In} explained by a variation in EXP_{In} increased from about 1% to about 17%. One study [44] in this subset had regression diagnostics suggestive of a relatively large influence on the regression. Exposure in the encasement group was decreased in this study by about 60-fold, but BHR was unchanged. A sensitivity analysis removing the data point from the regression confirmed its strong influence and resulted in a

Table 1. Qualitative summary of clinical trials evaluating bedding encasement as an asthma treatment

Design†	Duration (months)	Total N	Other treatments‡	Effect on HDM exposure*		Effect on BHR*		Other clinical parameters improved*		Reference	Included in statistical analyses?§
				Control	Active	Control	Active	Control	Active		
nr pr sb pc	0.5	<9	None	ND	ND	ND	ND	ND	–	29	No
nr ub uc	3	5	None	ND	ND	ND	ND	ND	Symptom score, PEF, drug use	30	No
r usb pc	6	31	None	ND	+	ND	–	ND	IgE	31	No
r sb pc	3	31	None	–	+	ND	–	–	Eosinophil marker	32	Yes
r db pc	12	52	None	–	+	–	+	–	PEF, drug use	33	Yes
r db pc	12	38	None	+	+	–	+	–	–	35	Yes
r db pc	12	27	None	–	+	–¶	–¶	–	–	36	No
r ub uc	4	12	None	–	–	–	–	–	Symptom scores, PEF var, baseline FEV ₁	37	Yes
r db pc	6	47	None	ND	ND	ND	ND	ND	–	38	No
r db pc	12	30	None	–	+	–	–	Quality-of- life	Quality-of-life, nasal symptoms	26	Yes
r db pc	12	47	None	–	+	+**	+**	–	Decreased steroid use	34	Yes
r db pc	6	965	None	–	+	ND	ND	PEF††	PEF††	27	No
r db pc	12	882	None	–	–	ND	ND	Decreased steroid use††	Decreased steroid use††	27	No
nr ub uc	3–12	14	cg	ND	+	ND	ND	ND	Symptom scores, IgE	41	Yes
r ub c	1.5	32	cg	ND	ND	ND	ND	–	–	48	No
nr ub c	1	20	cg	ND	ND	–	+	–	Wheeze, drug use, PEF	42	No
nr pr sb c	1	<9	f	ND	ND	ND	ND	–	–	29	No
r ub c	12	42	cg cr	–	+	–	+	–	Symptom scores, spirometry, PEF, drug use, IgE	22	Yes
ur ub xc	3	25	cg	+	+	–	–	–	IgE	24	Yes
r sb? c	12	16	d	–	+	–	+	ND	ND	23	Yes
r sb c	6	35	a d	–	–	–	–	–	–	52	Yes
r ub c	6	40	d	–	–	–	–	ND	ND	49	Yes
ur ub pc	7	23	cg cr d	ND	–	ND	ND	–	PEF	43	No
r db pc	6	49	a	–	+	–	–	–	Symptoms, drug use, baseline FEV ₁	39	Yes
r ub uc	3	26	cg a	ND	+	–	–	–	–	50	Yes
r db pc	12	71	a	–	+	ND	ND	–	Symptom scores	28	Yes
r db c	6	45	f	–	+‡‡	–	+‡‡	ND	Eosinophils, IgE	40	Yes
r ub pc	6	21	cg cr d	–	–	ND	ND	–	PEF	51	Yes
ur ub uc	12	18	h	ND	+	ND	–	ND	–	44	Yes
r db pc	5	157	a	+	+	–	–	Baseline FEV ₁	Baseline FEV ₁	25	Yes
r db c	3	10 or 15	cg f a	ND	+?	ND	ND	ND	–	46, 47§§	No
r sb pc c	12	85	cg p	–¶¶	–¶¶	ND	ND	Acute visits	Acute visits	53	No
ur db c	12	208	cg f d	ND	ND	ND	ND	?	Symptom scores, drug use, PEF	45	No

Study subjects all sensitized to house dust mite (HDM) antigen. BHR, bronchial hyper-responsiveness; PEF, peak expiratory flow; FEV₁, forced expiratory volume in 1 s; PC₂₀, provocation concentration; PD₂₀, provocation dose.

*+, significant improvement; –, no significant change; ND, not done; includes qualitative results reported relative to controls and results for all exposure and BHR metrics. †Study design parameters: r, randomized; nr, not randomized; pr, paired; sb, single blinded; db, double blinded; ub, unblinded; usb, blinding unspecified; pc, placebo control; c, control without placebo or placebo unspecified; xc, cross-over control; uc, uncontrolled. ‡Other treatments: cg, cleaning or laundry guidance; f, air filtration; cr, carpet removal; a, acaricide; d, denaturant; h, hyposensitization; p, pesticide application. §Only studies with appropriate exposure data (dust mite allergen loading or concentration) and/or appropriate bronchial hyper-responsiveness data (histamine PC₂₀ or PD₂₀) were included in quantitative statistical analyses (Tables 2 and 3). ¶Dust-mite antigen provocation BHR and histamine provocation BHR both negative. || Interim values were significantly reduced compared to controls. **Dust-mite antigen provocation BHR rather than histamine. ††Several other secondary outcomes were also not significant comparing control and active groups. ‡‡Significant effect only in combined treatment group (encasements+HEPA filtration). §§Unclear whether these two references represent one study or two. ¶¶About one-third of homes in placebo and active groups had > 70% reduction from baseline; no formal statistics, but results in two groups were similar. || || Effects only seen in the placebo control group, not in untreated control; results in placebo and active groups did not differ.

significant linear relationship between BHR and dust-mite allergen exposure for the remaining groups ($R^2 = 0.43$, $P = 0.04$, $N = 10$). The slope of this model suggests that an average 2-fold increase in PC₂₀ would require a 10-fold average decrease in Type 1 allergen concentration in mattress

dust from a baseline concentration $> 2 \mu\text{g/g}$. For all linear models, the modelled $\log(\text{BHR}_{1n})$ intercept was in the direction of slightly improved BHR at no change in exposure from baseline to study end (0.038–0.18). However, none of the intercept coefficients was significantly different from zero.

Table 2. Paired comparisons of collective results for baseline and study end from clinical trials evaluating bedding encasement as an asthma treatment

			Weighted* arithmetic (geometric) mean					
Active treatment or control group	Metric	Units	Baseline	End	Log-scale difference	N (pairs)	t	P
Paired t-test results								
Active	Type 1 dust mite allergen concentration	µg/g	12.8 (5.5)	3.1 (0.88)	0.80	15	1.35	0.20
Control	Type 1 dust mite allergen concentration	µg/g	8.3 (4.8)	7.7 (3.5)	0.14	13	0.53	0.61
Active	BHR (histamine PC ₂₀)	mg/L	2.1 (1.1)	3.2 (1.6)	− 0.19	9	− 0.76	0.47
Control	BHR (histamine PC ₂₀)	mg/L	1.7 (1.0)	2.0 (1.3)	− 0.11	7	− 0.41	0.70
Active treatment or control group	Metric	Units	# Baseline mean > end mean	# Baseline mean ≤ end mean	N (pairs)	Wilcoxin Z	P	
Wilcoxin signed-rank test results								
Active	All dust mite exposure metrics	Mixed	18	1	19	3.3	<0.001	
Control	All dust mite exposure metrics	Mixed	13	3	16	2.0	0.049	
Active	BHR (histamine PC ₂₀ or PD ₂₀)	Mixed	1	11	12	− 3.0	0.0029	
Control	BHR (histamine PC ₂₀ or PD ₂₀)	Mixed	3	6	9	− 1.2	0.21	

BHR, bronchial hyper-responsiveness; PC₂₀, provocation concentration; PD₂₀, provocation dose.

*Weighted by study sample size.

Table 3. Linear regression analysis of BHR_{in} and EXP_{in} from clinical trials evaluating bedding encasement as an asthma treatment

Results included in model	Regression model*†	R ²	N	t‡	P
All studies	Log(BHR _{in}) = 0.03log(EXP _{in}) + 0.18	0.012	21	0.49	0.63
Baseline exposure ≥ 2 µg/g	Log(BHR _{in}) = 0.19log(EXP _{in}) + 0.092	0.17	11	1.4	0.20
Baseline exposure ≥ 2 µg/g and reference [44] censored	Log(BHR _{in}) = 0.33log(EXP _{in}) + 0.038	0.43	10	2.4	0.04

BHR_{in} were derived for those studies reporting histamine PC₂₀ or PD₂₀. EXP_{in} were derived for those studies reporting Type 1 dust mite allergen concentration or loading. BHR_{in}, bronchial hyper-responsiveness index; EXP_{in}, exposure index; PC₂₀, provocation concentration; PD₂₀, provocation dose.

*Weighted by study sample size. †BHR_{in} = (mean bronchial hyper-responsiveness at study end)/(mean bronchial hyper-responsiveness at baseline); EXP_{in} = (mean exposure at baseline)/(mean exposure at study end). ‡For test of slope estimate vs. zero.

Discussion

Based on the collective evidence from the studies reviewed, there does not appear to be strong support from clinical trials for the reliable effectiveness of bedding encasement as a practical allergen-avoidance treatment that can be readily implemented by asthma patients in their homes. Among those studies with adequate exposure and BHR data, four studies reported improvement in BHR in dust-mite-sensitive asthmatics concomitant with dust-mite antigen exposure reduction following bedding encasement [22, 23, 33, 35]. However, 14 studies of bedding encasement in patients' homes either failed to show an improvement in BHR, even though dust-mite antigen exposure was reduced [24–26, 32, 36, 37, 39, 44, 50] or were unable to demonstrate a significant reduction in dust-mite exposure compared with baseline or with controls [43, 49, 51–53]. One study found a similar improvement in BHR in active-treatment and control groups despite a much larger exposure decrease in the active group compared with the controls [34].

It is conceivable that intervention trials might demonstrate improvements in clinical outcomes such as reduced symptoms without observing reductions in BHR. However, the use of bedding encasement in published clinical trials was not consistently associated with improvement in other endpoints,

including self-reported symptoms, medication use, baseline lung function or acute medical visits. In several cases, improvements in these endpoints in the intervention group were accompanied by similar improvements in the placebo group.

Quantitatively, the average dust-mite antigen exposure in the studies reviewed here was decreased approximately 4-fold, but was not reduced below 2 µg Type 1 antigen/g dust and was not quite statistically significant. Similarly, BHR showed a modest, non-significant average decrease in the active-treatment groups. The qualitative and quantitative results do indicate that bedding encasement has the potential to reduce dust-mite antigen exposure in mattress dust and improve lung function in asthma patients. However, as a practical measure, the effectiveness achieved when implementing bedding encasement is inconsistent and it appears to be, at best, modest. Therefore, its significance as a reliable asthma management modality for any individual asthma patient is uncertain.

Since mid-2002, five randomized, double-blind, placebo-controlled clinical trials of bedding encasements as the sole or primary allergen-avoidance treatment for dust-mite-sensitized asthma or rhinitis patients have been published [26, 27, 34, 38, 54]. The only clinical improvement demonstrated in these five studies was a decrease in inhaled steroid use in one

active-treatment group compared with baseline and controls [34]. Other clinical outcome measures in that study and all outcome measures in the other four studies (including BHR, peak flow, allergen-specific nasal provocation testing, pulmonary and nasal symptom scores and quality-of-life) were either unchanged in both groups, or were improved to the same degree in the treatment and control groups. This despite significant decreases in dust-mite antigen levels in mattress dust in all active-treatment groups compared with baseline and to controls in the four studies where dust sampling was conducted. The current analysis is consistent with conclusions from these studies that most dust-mite-sensitized patients are unlikely to derive substantial clinical benefit from the use of bedding encasements as their sole allergen-avoidance treatment.

In an editorial accompanying the two most recent studies, Platts-Mills suggested that placebo effects and unrecognized confounders (e.g., other allergens, endotoxin, changes in physical activity) could be obscuring the correct interpretation of allergen-avoidance interventions [55]. Interpretation of bedding-encasement trials (and, by extension, other dust-mite avoidance trials) may also be affected by exposure misclassification with respect to the primary allergen of concern (i.e., dust mites). By focusing almost exclusively on antigen in mattress dust as the exposure indicator in these studies, clinically meaningful exposure reduction may have been frequently over-estimated. For instance, De Blay et al. [56] reported that airborne dust-mite allergen was not reduced in rooms where dust-mite allergen levels were effectively reduced on mattress surfaces by encasement. They suggested that the mattress base was a continuing source of airborne allergen. Carpeting and upholstered furniture are other potential dust-mite allergen sources in the home that may contribute significantly to overall exposure, despite adequate control of bedding exposure [57].

Reservoir sampling *per se* may also be a contributing factor to the inconsistent relationship between presumed exposure reduction and clinical improvement. Antigen concentration in settled dust is only a surrogate for what would presumably be more relevant measures of exposure such as inhaled dose or allergen dose delivered to the lung [4]. It is well known that the relatively rapid settling of the large particles carrying dust-mite antigens in undisturbed air makes assessing inhaled exposure difficult under quiescent conditions [58–60]. However, some dust-mite allergens are carried on smaller particles and can be detected in air after reservoir disturbance [61]. The assumption that a reduction in proxy allergen exposure due to an allergen-avoidance protocol implies a reduction in inhaled dose may be faulty if the amount of inhaled allergen from exposure to transient airborne-allergen peaks is not well correlated with total reservoir allergen load. Personal air sampling for inhaled allergens using an intranasal sampler has the potential to improve the precision of estimating relevant changes in allergen exposure due to avoidance protocols by integrating inhaled dose over all domestic activities and allergen sources during a given time period [62–68]. This approach is more likely to reflect accurately exposure from transient spikes in airborne antigen levels due to disturbance of sources than simple grab samples of room air and could be a significant improvement to the design of allergen-avoidance intervention trials.

If bedding encasements alone do not adequately control dust-mite allergen exposure because of other sources in the home, more comprehensive avoidance protocols attempting to control many sources simultaneously might be expected to have better success [55]. However, in the studies reviewed here, combined treatment protocols were not noticeably more effective than were protocols employing only encasements. The complex requirements of implementing comprehensive allergen-avoidance protocols in patients' homes may reduce compliance and thereby compromise the protocol's potential effectiveness [19]. Factors including cost, patient or parental stress, lack of time, feelings by parents of neglecting their child in order to comply with protocols, disagreements between partners about housework or other aspects of allergen avoidance, lack of confidence that changes would help and complacency have all been cited by patients or their parents as reasons for failing to comply fully with allergen avoidance recommendations or protocols [69–72]. Even when patients had increased knowledge regarding all dust-mite allergen-avoidance recommendations, they were not significantly more likely to implement those recommendations than less knowledgeable patients [73], although they did implement bedding encasement more frequently. There is emerging evidence that compliance with allergen-avoidance protocols can be improved through direct in-home educational efforts, as opposed to simple written or oral instructions from providers, and by providing allergen-avoidance materials free of charge [74–78].

Certain patients may be more likely to benefit from the use of bedding encasements than others. In a multi-centre study of patient counselling and home-environment interventions in inner-city children with asthma, most of the benefits observed in reduced symptom days accrued among patients with severe asthma [75]. An economic follow-up of patients in that study also found that net cost savings in terms of reduced medical costs relative to the cost of the intervention were only observed in the severe-asthma subset [79]. Where resource constraints are significant, targeting the use of variably effective interventions such as bedding encasements toward those patient sub-populations most likely to derive substantial benefit (in terms of disease status and/or reduction in medical costs) may gain the largest net public-health benefit. If universal recommendation of bedding encasements or other interventions of similarly variable effectiveness is deemed prudent, patients should be fully informed that the degree of benefit to be gained by an individual patient is uncertain, that it may be small and that achieving a clinically meaningful benefit may require continued compliance with several allergen-avoidance techniques.

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