

REVIEW

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A reintroduction of environmental mite allergen control strategies for asthma treatment and the debate on their effectiveness

Frank E. van Boven¹  | Lidia R. Arends^{2,3} | Gert-Jan Braunstahl^{4,5} | Roy Gerth van Wijk¹

¹Department of Internal Medicine, Section of Allergology, Erasmus Medical Center, Rotterdam, The Netherlands

²Department of Biostatistics, Erasmus Medical Center, Rotterdam, The Netherlands

³Department of Psychology, Education & Child Studies, Erasmus University Rotterdam, Rotterdam, The Netherlands

⁴Department of Pulmonology, Sint Franciscus Vlietland Groep, Rotterdam, The Netherlands

⁵Department of Pulmonology, Erasmus Medical Center, Rotterdam, The Netherlands

Correspondence

Frank E. van Boven, Department of Internal Medicine, Section of Allergology, Erasmus Medical Center, Rotterdam, The Netherlands.

Email: f.vanboven5@gmail.com

Summary

Asthma affects three hundred million people worldwide. The effectiveness of house dust mite allergen control for asthma treatment is debatable. One aspect that has been little discussed in existing meta-analyses is the possible role of environmental strategies. Here, we reintroduce the previously defined strategies for mite allergen control and discuss their importance to the debate on clinical effectiveness. The strategy of concurrent bedroom interventions is related to the combined use of a priori defined interventions, while the strategy of exposure-based control relates to the treatment of relevant textiles after assessing exposure. The air purification strategy aims to purify the human breathing zone of airborne allergens. In Western European patient practice, the use of these strategies differs. A post hoc study of the dominant Cochrane review by Gøtzsche and Johansen (*Cochrane Database of Systematic Reviews*, 2008, Art. No: CD001187) appears to indicate that a majority of the underlying trials reported on the strategy of concurrent bedroom interventions, which were mainly executed in a minimal manner. Some trials have reported on the air purification strategy and may potentially alter the debate on effectiveness. No trial has reported on the strategy of exposure-based control. We therefore hypothesize that the absence of evidence for the effectiveness of mite allergen control for asthma treatment applies to the strategy of concurrent bedroom interventions. The evidence-based effectiveness of the exposure-based control strategy appears to be undetermined. The results of our post hoc reanalysis urge that future meta-analyses of mite allergen control should a priori define the environmental strategy under study. Future trials of mite allergen control are warranted to test the exposure-based strategy as well as the sparsely tested strategy of air purification.

KEYWORDS

allergens, asthma, environment, house dust mite allergen control, strategy of avoidance

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1 | INTRODUCTION

Asthma affects hundreds of millions of people worldwide, and its prevalence is still rising.^{1,2} The role of house dust mite allergy in asthma is evident; however, it is not exclusive.³ Therapies have been developed for the treatment of allergic asthma, including avoidance of mite allergen exposure, immunotherapy and pharmacological treatment.⁴ However, the effectiveness of mite allergen control has become debatable,⁵ and existing guidelines show a lack of consensus on mite allergen control.⁶⁻⁸ Therefore, gaining knowledge of the clinical effectiveness of avoiding allergen exposure should still be considered a research priority compared to controlling other types of exposure.^{9,10}

The debate on the effectiveness of mite allergen control for the treatment of asthma has not been characterized by progress. For instance, repeated comments have been made on the meta-analysis by Gøtzsche et al,^{5,11,12} pointing to the benefits of multiple trigger therapy in a large trial.¹³ However, these types of comments have previously been rejected by Gøtzsche et al,¹⁴ who said: "none of the correspondents have provided data (at the same level of evidence) to the contrary. Nevertheless, investigators¹⁵ continue to mention the benefits of trials excluded previously by Gøtzsche and Johansen¹⁶ One novelty seems to be the introduction of a hypothesis by Tovey and Ferro that the debate on effectiveness calls for personalized avoidance by a better understanding of the nature of allergen exposure.¹⁷

A little-discussed aspect of the question of clinical effectiveness is the role of mite allergen control strategies. Strategies have been defined to avoid house dust mite allergen exposure (see the section "Strategies for mite allergen control"), including total avoidance,¹⁸ exposure-based control,¹⁹ concurrent bedroom interventions,²⁰ purification of the breathing air,²¹ and a sojourn in a mite-free (alpine) environment.²² Environmentally, the reduction in exposure by different strategies is not necessarily equivalent. It remains unclear whether the absence of evidence of the clinical effectiveness of mite allergen control relates to any particular strategy. In this review, we reintroduce previously defined strategies for mite allergen control and discuss their importance to the debate on clinical effectiveness, including future investigations.

2 | STRATEGIES FOR MITE ALLERGEN CONTROL

2.1 | Initial strategies

Among mono- and multi-trigger approaches,²³ strategies can be considered to control exposure to house dust mites and their allergens. Prior strategies have related to the removal of the patient to a mite-free environment. A sojourn in a Swiss alpine mite-free environment has been used more than a hundred years and shown to benefit asthmatic patients temporarily.²² Platts-Mills et al²⁴ removed patients for 2 months or more to a dust-free hospital environment, resulting in significantly reduced bronchial hyperreactivity. These prior strategies were continued by the strategy of total avoidance of the home environment of the asthmatic patients. This strategy of

total avoidance has defined a combination of measures aiming for an indoor environment completely free of living and dead house dust mites as well as their faecal products.^{18,25} The measures developed have included mainly acaricidal products and mite-impermeable covers. However, it became clear that the strategy of total avoidance is rarely achievable by patients in the long term.²⁶

2.2 | Textile-based strategies

Meanwhile, strategies were defined to gain the benefits of rigorous and intensive total avoidance using a more efficient approach. Colloff²⁰ defined a set of a priori defined barriers, called integrated avoidance. We redefine this approach as the strategy of concurrent bedroom interventions: a combined approach aimed at controlling house dust mite exposure by primarily treating the bedroom environment with a priori defined barriers. The original strategy comprises a total of seven barriers. In a more recent publication, Colloff updated the strategy to nine barriers.²⁷ The five primary barriers consist of (a) fitting of mite-impermeable covers to all bedding; (b) monthly hot laundering of the bedding; (c) removal of the bedroom carpet; (d) weekly vacuuming of other textiles with a high-efficiency particulate air (HEPA) filter vacuum cleaner; (e) removal of upholstered furniture, rugs, mattresses, and bedding to the outside environment for 12 hours to dry, heat and/or freeze, followed by vacuuming. An alternative is presented if a primary barrier cannot be executed (four alternatives). The strategy of concurrent bedroom interventions as positioned by Colloff²⁰ garnered less attention (three citations, Google Scholar, retrieved October 21, 2018). This strategy was introduced at the conference Mites, Asthma and Domestic Design II in Sydney.

Around the same period, van Bronswijk¹⁹ introduced the strategy of selective avoidance. We redefine this strategy as exposure-based control: a combined approach based on the assessment of the actual exposure in the home environment, followed by the extermination of mites and removal of all relevant sources of allergenic dust. This strategy assumes the existence of a hygienic threshold for allergen exposure above which symptoms will develop (2 µg/g dust).²⁵ A simple colorimetric test was introduced in patient practice that related the actual exposure in the home environment to the hygienic threshold.²⁸ In the worst case, the exposure-based strategy results in total avoidance of the home environment. The strategy of exposure-based control gathered only two citations (Google Scholar, retrieved October 22, 2018). We hypothesize that the low number of citations is due to the publication of this strategy at a conference (International Conference on Insect Pest in the Urban Environment, Cambridge) rather than a peer-reviewed journal.

The measures that constitute the textile-based strategies can be differentiated into short-term and long-term measures. Short-term measures aim to directly reduce allergen exposure, such as the use of chemical products or washing textiles at 60°C.¹⁸ These types of measures must be repeated throughout the year. Long-term measures aim to control allergen exposure only after one or more climatic seasons by lowering the relative humidity in niches during the heating season (cold climates) or by airing textiles outside during the

summer (hot climates).^{27,29} Humidity control is an environmental intervention aiming to eradicate living mites but not directly the allergenic mite faeces.¹⁹ The mite faeces remain allergenic for a very long time,³⁰ thus urging humidity control for use in conjunction with co-acting environmental methods.²⁷ We judge the sole intervention of humidity control as a general improvement of indoor air quality (fresh air) by reducing indoor humidity levels³¹ but not aiming at the primary control of mite allergen exposure. In addition to improving the general quality of the indoor air, long-term measures are useful for reducing the need to repeat short-term measures with high frequency. The reduced need for repeated intensive cleaning of the home makes mite allergen control more achievable by patients in the long term.

2.3 | Breathing-zone-related strategies

While both the concurrent bedroom interventions strategy and the exposure-based strategy focus on the elimination of allergen emissions from textiles, the air purification strategy aims to purify the human breathing zone of airborne allergens by use of a HEPA filter capturing at least 85% of particles with a diameter of 0.3 μm .³² Particles of larger size, such as mite faeces (diameter approximately 10–40 μm ³³), are captured at a higher percentage. HEPA filters can be used at varying environmental settings, from a laminar airflow in the breathing zone during sleep³⁴ to the use of portable devices in the bedroom³⁵ or an air filtration unit in the living room.³⁶

2.4 | Mixed strategies

Finally, we introduce mixed strategies, referring to a combination of strategies that differ in aim or therapy, such as combining the effectiveness of steroids, immunotherapy, and impermeable covers from different trials in one meta-analysis without subgrouping. We consider the mixed strategies somewhat unwieldy. Even if they are clinically effective, the results of mixed strategies are less usable or less efficient for patient practice, particularly when a strategy is not completely executed. For instance, patient practice does not combine a partial impermeable cover with a partial HEPA filter. An exception is the case when all data from a study result from concurrent and completely executed strategies. Therefore, insight into the effectiveness of a single strategy is relevant for evidence-based clinical decision-making.

3 | EVIDENCE SUPPORTING THE STRATEGIES

3.1 | List of meta-analyses

In the section above, we reintroduced the environmental strategies for mite allergen control. After the introduction of textile-based strategies in the early 1990s, the first meta-analysis was performed to assess the effectiveness of mite allergen control at the highest level of evidence.⁵ This meta-analysis was later continued in a Cochrane review.³⁷ In this meta-analysis, Gøtzsche and Johansen

included trials on mite-impermeable covers as well as air purification; thus, they investigated a mixture of strategies. The next meta-analysis studied the effectiveness of purifying the air using air filtration for the treatment of allergic asthma.³⁸ All treatment groups investigated included the use of a HEPA filter, sometimes combined with mite-impermeable covers. The HEPA filters were studied in varying environmental settings. Macdonald et al³⁹ studied the effectiveness of textile-based strategies for the primary and tertiary prevention of asthma. They reported on the number of days ill due to asthma and a lung function parameter combining the FEV₁ with the peak flow.³⁹ Campbell and Gibson⁴⁰ attempted to study the effects of feather bedding, but the selected trials did not meet the inclusion criteria. In another Cochrane review, Singh and Jaiswal⁴¹ studied the effectiveness of humidity control for the treatment of asthma. We believe that the environmental strategy studied by Singh and Jaiswal yields a general improvement of indoor air quality (fresh air) but not mite control. Crocker et al²³ investigated the effectiveness of home-based multi-trigger interventions. The meta-analysis by Crocker et al²³ included a small number of patients with house dust mite allergic asthma (34%). Three meta-analyses on the effectiveness of concurrent bedroom interventions using mite-impermeable covers were introduced in 2014. Arroyave et al⁴² included seven trials on the treatment of asthma. In the same year, van Boven⁴³ generated a hypothesis regarding the effectiveness of mite-impermeable covers using a meta-analysis. Van Boven⁴³ limited the intervention to trials that covered all bedding elements (mattress, duvet, and pillow), fitting it to the definition of the strategy of concurrent bedroom interventions.²⁷ Huiyan et al⁴⁴ investigated six trials on mite-impermeable covers combined with one trial on humidity control. Three of the trials investigated by Huiyan et al^{38–44} were also included in the analysis by Gøtzsche and Johansen.³⁷ To some extent, many meta-analyses can be considered to represent subsets of the large meta-analysis by Gøtzsche and Johansen.³⁷

3.2 | Clinical effectiveness

Clinical benefits in patients with house dust mite allergy-related asthma were reported by small meta-analyses. McDonald et al³⁸ reported a significant standardized mean difference in the asthma symptom score (95% CI: –0.69 to –0.25; 88 patients) and the sleep disturbance (95% CI: –1.44 to –0.42; 47 patients). Macdonald et al³⁹ found a positive reduction in the number of days ill (95% CI: –0.59 to –0.13 by two trials). Van Boven⁴³ observed that the more bedroom interventions were combined, the higher the reduction in the mite load from the mattress when the load was high at baseline ($P = 0.02$; nine trials). Among the listed meta-analyses, the meta-analysis by Gøtzsche and Johansen³⁷ dominates the debate. While Gøtzsche and Johansen were unable to demonstrate any clinical benefit based on 55 trials, Bousquet et al⁴⁵ concluded from this meta-analysis that the use of a single intervention measure is not effective. Pingitore and Pinter⁴⁶ mentioned that Gøtzsche and Johansen included trials reporting no reduction in mite allergen exposure. As the meta-analysis by Gøtzsche and Johansen³⁷ reports

on a mix of strategies without subgrouping, the role of the specific strategies remains unclear.

4 | THE POSSIBLE ROLES OF STRATEGIES IN EFFECTIVENESS: AN EXAMPLE

4.1 | Methods

The debate on effectiveness is dominated by the large and rigorous meta-analysis by Gøtzsche and Johansen.³⁷ This meta-analysis on a mix of strategies did not subgroup for possible differences between mite allergen control strategies. We post hoc subgrouped the results by Gøtzsche and Johansen³⁷ into categories based on the environmental strategy used for mite allergen control. The extractions as published by Gøtzsche and Johansen³⁷ were the basis of this reanalysis. Outcomes were limited to the number of patients improved, the medication usage, the asthma symptom score, the forced expiratory volume in one-second (FEV₁), and the histamine or methacholine concentration that caused a 20% reduction in FEV₁ (PC₂₀).

The assessment of the type of strategy as studied in the underlying trials yielded three judgements:

- Assessing the strategy used to control mite allergen exposure. The strategy was defined as “concurrent bedroom interventions” for any a priori defined intervention aimed at reducing the mite allergen load while not assessing the relevant sites of exposure in the home environment.
- If the intervention was judged to follow the strategy of concurrent bedroom interventions, we assessed the number of barriers used.
- If the strategy of concurrent bedroom interventions was not followed consequently, the number of barriers was set at one. For instance, the single treatment of a carpet in the living room was judged as one barrier (Barrier 4: Vacuuming of other textiles²⁷).

Effect sizes were calculated by a random-effects model with the Metafor package 2.0.0⁴⁷ in R (version 3.4.1).⁴⁸ Subgroup analysis yielded a calculation of the effect size related to the environmental control strategy. We continued subgrouping the strategy of concurrent bedroom interventions to the use of one barrier or two or more barriers. For other statistical aspects, we referred to the original study by Gøtzsche and Johansen.³⁷ The level of significance was set to $\alpha = 0.05$. The magnitude of the standardized mean difference (SMD) was judged to be small for an SMD of 0.2, medium for an SMD of 0.5, and large for an SMD of 0.8.⁴⁹

4.2 | Results of the subgrouping analysis

Gøtzsche and Johansen³⁷ investigated mixed strategies in 55 randomized trials (concurrent bedroom interventions, air purification, and combinations). Thirty-six of these trials reported on one or more outcomes of interest (Table 1; Refs. 34-36,50-82). Thirty trials tested an intervention based on the strategy of concurrent bedroom interventions, of which twenty-three interventions were classified as one

barrier (77%). Seven trials were classified as investigating two or three barriers (23%). Six trials investigated the air purification strategy. No trial reported on an investigation of the strategy of exposure-based control. The remaining subgroups that reported on one barrier (concurrent bedroom interventions) included a total of 3031 patients (74%), the subgroups that reported on two or more barriers included 817 patients (20%), and the subgroups that reported on air purification included 258 patients (6%).

The SMD in asthma symptom scores ranged from SMD = -0.03 to -0.53 , with all *P*-values ranging from 0.19 to 0.87 (Table 2). Heterogeneity ranged from $I^2 = 54\%$ -91%. For FEV₁, the SMD ranged from $+0.07$ to $+0.17$, with *P*-values ranging from 0.08 to 0.81 and negligible heterogeneity ($I^2 = 0\%$ -28%; Table 3). Three subgroups reported on PC₂₀ outcome, with the SMD ranging from -0.12 to $+0.05$ ($P = 0.45$ -0.80; Table 4). The subgroups showed no heterogeneity ($I^2 = 0\%$). For medication usage, two subgroups reported an SMD = -0.04 to -0.17 ($P = 0.46$ -0.49; $I^2 = 0\%$; Table 5). The risk ratio for the number improved in the subgroups of concurrent bedroom interventions was 0.85-1.07 ($P = 0.77$ -0.87), with an absence of heterogeneity (Table 6). In the subgroup of air purification, we found a non-significant risk ratio of 0.67 ($P = 0.61$), with an absence of heterogeneity.

4.3 | Discussion of the subgrouping analysis

Overall, post hoc subgrouping shows that the environmental intervention studied in the meta-analysis by Gøtzsche and Johansen³⁷ relates predominantly to the concurrent bedroom interventions strategy and little to the air purification strategy. A majority of the underlying trials reported on the strategy of concurrent bedroom interventions with one barrier or when performed in an inconsistent manner that was also classified as one barrier. When grouping the outcomes of the strategy of concurrent bedroom interventions as one barrier or two or more barriers, as well as the strategy of air purification, all effect sizes were not significant. The outcome of the asthma symptom score showed a non-significant increase in the SMD, from zero in the subgroup with one barrier to a small effect in the subgroup with two barriers, to a larger effect in the group with air purification. The opposite of this non-significant increase in the magnitude of the effect size was a decrease in the number of patients, which was low in the subgroup with two barriers ($n = 246$) and very low in the subgroup with air purification ($n = 70$). A similar and smaller tendency was observed in the outcome of medication usage. The subgroup with one barrier showed zero effect, compared to a small effect in the subgroup with air purification. However, the number of patients decreased from 1043 in the subgroup with one barrier to 72 in the subgroup with air purification. The absence of significance in air purification may be explained by the small number of patients studied. However, we cannot exclude the possibility that the variation in outcomes played a role. These results suggest that the reintroduction of strategies has the potential to alter the debate on effectiveness. As our analysis was post hoc, it indicates a need to include the strategy of mite allergen control as a factor when defining meta-analysis protocols.⁸³

TABLE 1 Environmental strategy categories of the trials studied by Gøtzsche and Johansen³⁷

Trial	Author	Year	Strategy	Barriers	Remark
1	Antoniceili	1991	Air purification	NA	
2	Bahir	1997	Concurrent bedroom	1	
3	Burr	1980A	Concurrent bedroom	1	
4	Burr	1980B	Concurrent bedroom	1	
5	Carswell	1996	Concurrent bedroom	3	
6	Chang	1996	Concurrent bedroom	1	
7	Chen	1996	Concurrent bedroom	1	
8	Cinti	1996	Concurrent bedroom	1	Strategy extracted from description by Gøtzsche and Johansen
9	Cloosterman	1999	Concurrent bedroom	2	
10	De_Vries	2007	Concurrent bedroom	1	
11	Dharmage	2006	Concurrent bedroom	1	
12	Dieteman	1993	Concurrent bedroom	1	
13	Dorward	1988	Concurrent bedroom	1	
14	Ehnert	1992	Concurrent bedroom	2	
15	Fang	2001	Concurrent bedroom	1	
16	Geller-Bernst	1995	Concurrent bedroom	1	
17	Halken	2003	Concurrent bedroom	1	
18	Htut	2001	Concurrent bedroom	1	
19	Huss	1992	Concurrent bedroom	1	
20	Kroidl	1998	Concurrent bedroom	1	
21	Maesen	1977	Air purification	NA	
22	Marks	1994	Concurrent bedroom	2	
23	Reiser	1990	Concurrent bedroom	1	
24	Rijssenbeek	2002	Concurrent bedroom	3	
25	Sette	1994	Concurrent bedroom	1	
26	Shapiro	1999	Concurrent bedroom	2	
27	Sheikh	2002	Concurrent bedroom	1	
28	Thiam	1999	Concurrent bedroom	2	
29	Van_der_Heide	1997A	Concurrent bedroom	1	
30	Verrall	1988	Air purification	NA	
31	Walshaw	1986	Concurrent bedroom	1	
32	Warburton	1994	Air purification	NA	
33	Warner	1993	Air purification	NA	
34	Woodcock	2003	Concurrent bedroom	1	
35	Wright	2009	Concurrent bedroom	1	
36	Zwemer	1973	Air purification	NA	

5 | GENERAL DISCUSSION

5.1 | A reintroduction of strategies

This review reintroduces previously defined strategies for mite allergen control. Both the concurrent bedroom interventions strategy and the exposure-based strategy were introduced in the early 1990s. These strategies did not attract much attention by researchers, possibly because these strategies were not published in peer-reviewed journals. Both textile-based strategies built on the first-

line reduction or prevention of allergen emissions from textiles are of primary importance in patient practice. Other defined strategies include air purification and a sojourn to an (alpine) mite-free environment. The latter two strategies are sparsely studied and not commonly advised in patient practice, possibly due to their costs. Only the strategy of removing patients from an environment with high mite allergen exposure is clearly accepted as effective.^{14,24} Most of the recent meta-analyses of textile-based mite allergen control for the treatment of asthma do not relate their findings to a strategy.^{37,39,40,42,44}

TABLE 2 Standardized mean differences in asthma symptom scores related to environmental strategy in the meta-analysis by Gøtzsche and Johansen³⁷

Strategy	SMD	95% CI	Patients (n)	P-value	I ²
Sojourn high altitude	NA	NA	NA	NA	NA
Total avoidance	NA	NA	NA	NA	NA
Exposure-based	NA	NA	NA	NA	NA
Concurrent bedroom	-0.07	-0.35 to 0.21	1415	0.62	68%
1 barrier	-0.03	-0.37 to 0.32	1169	0.87	54%
2-3 barriers	-0.25	-0.89 to 0.40	246	0.43	91%
Air purification	-0.53	-1.35 to 0.30	70	0.19	68%
Mixed strategies	-0.13	-0.40 to 0.15	1485	0.35	72%
Gøtzsche & Johansen ^a	-0.06	-0.16 to 0.05	1485	0.29	68%

^aStandardized mean differences as calculated by Gøtzsche and Johansen³⁷ with a fixed-effect model.

TABLE 3 Standardized mean differences in FEV₁ related to environmental strategy in the meta-analysis by Gøtzsche and Johansen³⁷

Strategy	SMD	95% CI	Patients (n)	P-value	I ²
Sojourn high altitude	NA	NA	NA	NA	NA
Total avoidance	NA	NA	NA	NA	NA
Exposure-based	NA	NA	NA	NA	NA
Concurrent bedroom	0.14	-0.02 to 0.29	633	0.08	0%
1 barrier	0.11	-0.11 to 0.33	332	0.32	0%
2-3 barriers	0.17	-0.06 to 0.40	301	0.15	28%
Air purification	0.07	-0.53 to 0.68	42	0.81	0%
Mixed strategies	0.13	-0.02 to 0.29	675	0.09	0%
Gøtzsche & Johansen ^a	0.13	-0.02 to 0.28	675	0.09	0%

^aStandardized mean differences as calculated by Gøtzsche and Johansen³⁷ with a fixed-effect model.

5.2 | On textile-based strategies

A post hoc reanalysis of the dominant meta-analysis by Gøtzsche and Johansen³⁷ suggests that a majority of the trials examined had reported on the use of concurrent bedroom interventions executed in a minimal manner. The exposure-based strategy was not tested in the included trials. This result suggests that it is unknown whether the conclusion by Gøtzsche and Johansen³⁷ is valid for the exposure-based strategy. In our opinion, the choice of the strategy of concurrent bedroom interventions reflects the principals of traditional clinical trial design.⁸⁴ In a clinical experiment, the aim is to test for a possible difference between treatment and no treatment. A secondary aim in a clinical experiment is to minimize the variance in outcomes to discriminate a treatment effect in as unbiased a manner as possible.⁸⁵ Among the many issues playing a role in minimizing variance in a trial, we consider the choice of a predefined simple and homogeneous treatment to be one, for instance, such as the choice

TABLE 4 Standardized mean differences in PC₂₀ related to environmental strategy in the meta-analysis by Gøtzsche and Johansen³⁷

Strategy	SMD	95% CI	Patients (n)	P-value	I ²
Sojourn high altitude	NA	NA	NA	NA	NA
Total avoidance	NA	NA	NA	NA	NA
Exposure-based	NA	NA	NA	NA	NA
Concurrent bedroom	0.05	-0.09 to 0.20	475	0.45	0%
1 barrier	0.05	-0.20 to 0.30	254	0.68	0%
2-3 barriers	0.05	-0.21 to 0.32	221	0.69	0%
Air purification	-0.12	-1.05 to 0.80	18	0.80	0%
Mixed strategies	0.05	-0.13 to 0.22	493	0.61	0%
Gøtzsche & Johansen ^a	0.05	-0.13 to 0.22	493	0.61	0%

^aStandardized mean differences as calculated by Gøtzsche and Johansen³⁷ with a fixed-effect model.

of single bedding covers. However, the opposite of minimizing the variance is the considerable heterogeneity present in personal exposure. Studies on personal airborne exposure⁸⁶⁻⁸⁸ show that relevant average exposure is not necessarily related to the sleeping site. Environmentally, emission sources, emission magnitudes, emission frequencies, and the presence of patients at emission sites may all vary. The considerable variance in exposure in patient practice calls for an exposure-based strategy. Nonetheless, we do not know of any study comparing the (clinical) effectiveness of the frequently tested strategy of concurrent bedroom interventions with the exposure-based strategy. This research question is relevant, as highly skilled health practitioners from France and The Netherlands advise their patients by use of the exposure-based strategy.⁸⁹⁻⁹⁰

5.3 | Recent studies

Additionally, recent studies have not related their findings to a specific strategy. Leas et al⁹¹ systematically reviewed the effectiveness of

TABLE 5 Standardized mean differences in medication usage related to environmental strategy in the meta-analysis by Gøtzsche and Johansen³⁷

Strategy	SMD	95% CI	Patients (n)	P-value	I ²
Sojourn high altitude	NA	NA	NA	NA	NA
Total avoidance	NA	NA	NA	NA	NA
Exposure-based	NA	NA	NA	NA	NA
Concurrent bedroom	-0.04	-0.16 to 0.08	1043	0.49	0%
1 barrier	-0.04	-0.16 to 0.08	1043	0.49	0%
2-3 barriers	NA	NA	NA	NA	NA
Air purification	-0.17	-0.64 to 0.29	72	0.46	0%
Mixed strategies	-0.05	-0.17 to 0.07	1115	0.39	0%
Gøtzsche & Johansen ^a	-0.05	-0.17 to 0.07	1115	0.39	0%

^aStandardized mean differences as calculated by Gøtzsche and Johansen³⁷ with a fixed-effect model.

TABLE 6 Risk ratios for the number of patients improved related to environmental strategy in the meta-analysis by Gøtzsche and Johansen³⁷

Strategy	RR	95% CI	Patients (n)	P-value	I ²
Sojourn high altitude	NA	NA	NA	NA	NA
Total avoidance	NA	NA	NA	NA	NA
Exposure-based	NA	NA	NA	NA	NA
Concurrent bedroom	1.06	0.75-1.50	282	0.82	0%
1 barrier	1.07	0.75-1.53	233	0.77	0%
2-3 barriers	0.85	0.19-3.79	49	0.87	0%
Air purification	0.67	0.24-1.87	56	0.61	0%
Mixed strategies	1.01	0.73-1.40	338	0.96	0%
Gøtzsche & Johansen ^a	1.01	0.80-1.27	338	0.94	0%

^aRisk ratios as calculated by Gøtzsche and Johansen³⁷ with a fixed-effect model.

allergen control by subgrouping the control methods but not the strategies. In the review by Leas et al,⁹¹ the assessment of the effect size remained unclear. Le Cann et al⁹² reviewed the effectiveness of home interventions for the treatment of allergy and respiratory diseases. They subgrouped interventions into three categories: education-based methods, physical methods, and a combination of both. Le Cann et al⁹² reported mixed results of these home interventions, urging further study of a multifaceted approach. Murray et al⁹³ investigated the effect of mite-impermeable covers in a large randomized trial (n = 284) for the treatment of severe asthma exacerbations in children. In this trial, Murray et al⁹³ reported a significant decrease in the primary outcome of hospitalization, which is sparsely studied in this field. We classified their intervention as the strategy of concurrent bedroom interventions using two barriers. From the observations by Murray et al, we assessed the SMD in asthma symptom score as -0.15 (95% CI: -0.41 to +0.12; P = 0.28), which fitted

satisfyingly to our recalculation for the subgroup with two to three barriers.

5.4 | Developing the debate?

What does our reintroduction of strategies add to the debate on allergen control? As stated above, the debate on the effectiveness of mite allergen control for asthma treatment has not been characterized by progress. Our reintroduction of environmental strategies of mite allergen control continues the call for re-thinking avoidance.¹⁷ This call introduces the idea of improved measurement of personal exposure,^{88,94} reflecting the strategy of exposure-based control. Exposure-based control was not the subject of study in any of the trials we analysed post hoc. The post hoc results of the subgroup of air purification are also of interest and have potential to influence the debate. For the concurrent bedroom interventions strategy, a question arises of the effectiveness of an intervention based on the full elaboration of this strategy, as this method has not yet been studied.

5.5 | Other domains

Investigations on other allergic disorders caused by mites seem to show an identical tendency in strategies. Sheikh et al⁹⁵ conducted a Cochrane review on the treatment of rhinitis and concluded that “extensive bedroom-based environmental control programmes may be of some benefit” and “evidence that isolated use of house dust mite impermeable bedding is unlikely to prove effective.” Two trials stand out in this meta-analysis. Terreehorst et al⁹⁶ investigated the effectiveness of mite-impermeable covers, classified by us as the strategy of concurrent bedroom interventions using two barriers. This large trial (n = 279) did not show clinical benefits for the treatment of rhinitis. A small trial on comprehensive exposure-based control showed benefits in the treatment of rhinitis symptom scores and total IgE.⁹⁷ In the field of eczema, Kort et al⁹⁸ showed identical benefits to those found by Kniest et al in a case related to storage mites by use of the exposure-based strategy. These results underline the usefulness of introducing the strategy of mite allergen control in defining meta-analysis protocols.

6 | CONCLUSION

In summary, the clinical effectiveness of mite allergen control for the treatment of asthma is debatable.³⁷ It remains unclear whether the absence of evidence relates to a specific type of environmental strategy for mite allergen control, several of which were introduced in the early 1990s. A post hoc reanalysis suggests that the dominant conclusions by Gøtzsche and Johansen³⁷ relate to the strategy of concurrent bedroom interventions, which were mainly executed in a minimal manner. An evidence-based effectiveness assessment of the exposure-based control strategy, which is used in Western European patient practice, is still needed. Our post hoc findings indicate that future meta-analyses of mite allergen control should a priori define

the environmental strategy under study. Future trials of mite allergen control are warranted to test the exposure-based strategy as well as the sparsely tested strategy of air purification.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Frank E. van Boven  <https://orcid.org/0000-0001-6520-1477>

REFERENCES

- Ferkol T, Schraufnagel D. The global burden of respiratory disease. *Ann Am Thorac Soc*. 2014;11(3):404-406.
- Mincheva R, Ekerljung L, Bossios A, Lundbäck B, Lötvall J. High prevalence of severe asthma in a large random population study. *J Allergy Clin Immunol*. 2018;141(6):2256-2263.
- Del Giacco SR, Bakirtas A, Bel E, et al. Allergy in severe asthma. *Allergy*. 2017;72(2):207-220.
- Abrams EM, Szeffler SJ, Becker AB. Effect of asthma therapies on the natural course of asthma. *Ann Allergy Asthma Immunol*. 2016;117:627-633.
- Gøtzsche PC, Hammarquist C, Burr M. House dust mite control measures in the management of asthma: meta-analysis. *Br Med J*. 1998;317(7166):1105-1110.
- Custovic A, Gerth van Wijk R. The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA2LEN). *Allergy*. 2005;60(9):1112-1115.
- Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008. *Allergy*. 2008;63(S86):8-160.
- Kader R, Kennedy K, Portnoy JM. Indoor environmental interventions and their effect on asthma outcomes. *Curr Allergy Asthma Rep*. 2018;18(3):17.
- Sánchez-Borges M, Fernandez-Caldas E, Thomas WR, et al. International consensus (ICON) on: clinical consequences of mite hypersensitivity, a global problem. *World Allergy Org J*. 2017;10(1):14.
- Masefield S, Edwards J, Hansen K, et al. The future of asthma research and development: a roadmap from the European Asthma Research and Innovation Partnership (EARIP). *Eur Resp J*. 2017;49:1602295.
- Platts-Mills TAE. Allergen avoidance in the treatment of asthma: problems with the meta-analyses. *J Allergy Clin Immunol*. 2008;122(4):694-696.
- De Blay F, Barnig C, Ott M. House dust mite control measures for asthma. *Allergy*. 2009;64(1):189.
- Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med*. 2004;351(11):1068-1080.
- Gøtzsche PC, Hammarquist C, Burr M. Author's reply. *Br Med J*. 1999;318(7187):871 (27 March 1999).
- Wilson JM, Platts-Mills TAE. Home environmental interventions for house dust mite. *J Allergy Clin Immunol Pract*. 2018;6(1):1-7.
- Gøtzsche PC, Johansen HK. Author's reply on: 'house dust mite control measures for asthma'. *Allergy*. 2009;64:1405.
- Tovey ER, Ferro A. Time for new methods for avoidance of house dust mite and other allergens. *Curr Allergy Asthma Rep*. 2012;12(5):465-477.
- Van Bronswijk JEMH. *House Dust Biology for Allergists, Acarologists and Mycologists*. Zoelmond: NIB Publishers; 1981.
- Van Bronswijk JEMH. Prevention and extermination strategies for house dust mites and their allergens in home textiles. In: *Proceedings of the First International Conference of Insect Pests in the Urban Environment*. Exeter, UK: BPC Wheatons Ltd.; 1993:261-266. https://www.researchgate.net/publication/237114148_PREVENTION_AND_EXTERMINATION_STRATEGIES_FOR_HOUSE_DUST_MITES_AND_THEIR_ALLERGENS_IN_HOME_TEXTILES.
- Colloff MJ. Integrated strategies for dust mite control. In: *Proceedings of Mites, Asthma and Domestic Design II*, Sydney, Australia; 1995:37-44. https://www.researchgate.net/publication/278859545_Integrated_strategies_for_dust_mite_control_a_search_for_synergism.
- Barach AL. A room filter for the removal of dust, pollen and air pollutants: preliminary report. *Ann Allergy*. 1969;27(10):519-520.
- Spieksma FTM, Zuidema P, Leupen MJ. High altitude and house-dust mites. *Br Med J*. 1971;5740(1):82-84.
- Crocker DD, Kinyota S, Dumitru GG, et al. Effectiveness of home-based, multi-trigger, multicomponent interventions with an environmental focus for reducing asthma morbidity: a community guide systematic review. *Am J Prev Med*. 2011;41(2 Suppl. 1):S5-S32.
- Platts-Mills TAE, Mitchell EB, Nock P, Tovey E, Moszoro H, Wilkins S. Reduction of bronchial hyperreactivity during prolonged allergen avoidance. *Lancet*. 1982;320(8300):675-678.
- Platts-Mills TAE, de Weck AL, Aalberse RC, et al. Dust mite allergens and asthma—a worldwide problem. *J Allergy Clin Immunol*. 1989;83(2):416-427.
- Platts-Mills TAE, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: report of the Third International Workshop. *J Allergy Clin Immunol*. 1997;100(6):S2-S24.
- Colloff MJ. *Dust Mites*. Collingwood, Vic.: CSIRO Publishing; 2009.
- Bischoff E, Schirmacher W, Schober G. Farbnachweis für allergenhaltigen Hausstaub. *Allergologie*. 1984;11:446-449.
- van Bronswijk JEMH, Pauli G, eds. An update on long-lasting mite avoidance. Dwelling construction, humidity management, cleaning. A symposium at the 1996 Annual congress of the European Respiratory Society in Stockholm/Sweden.
- Kort HSM, Kniest FM. Four-year stability of Der p I in house dust under simulated domestic conditions in vitro. *Allergy*. 1994;49(2):131-133.
- Bornehag CG, Blomquist G, Gyntelberg F, et al. Dampness in buildings and health. Nordic interdisciplinary review of the scientific evidence on associations between exposure to "dampness" in buildings and health effects (NORDDAMP). *Indoor Air*. 2001;11(2):72-86.
- American Society of Mechanical Engineers. ASME AG-1a-2004, "Addenda to ASME AG-1-2003 Code on Nuclear Air and Gas Treatment"; 2004.
- Tovey ER, Chapman MD, Wells CW, Platts-Mills TAE. The distribution of dust mite allergen in the houses of patients with asthma 1-3. *Am Rev Resp Dis*. 1981;124(5):630-635.
- Verrall B, Muir DC, Wilson WM, Milner R, Johnston M, Dolovich J. Laminar flow air cleaner bed attachment: a controlled trial. *Ann Allergy*. 1988;61(2):117-122.
- Antonicelli L, Bilo MB, Pucci S, Schou C, Bonifazi F. Efficacy of an air-cleaning device equipped with a high efficiency particulate air filter in house dust mite respiratory allergy. *Allergy*. 1991;46(8):594-600.
- Warburton CJ, Niven RM, Pickering CAC, Fletcher AM, Hepworth J, Francis HC. Domiciliary air filtration units, symptoms and lung function in atopic asthmatics. *Resp Med*. 1994;88(10):771-776.
- Gøtzsche PC, Johansen HK. House dust mite control measures for asthma review. *Cochrane Database Syst Rev*. 2008;(2):CD001187.
- McDonald E, Cook D, Newman T. Effect of air filtration systems on asthma: a systematic review of randomized trials. *Chest*. 2002;122:1535-1542.
- Macdonald C, Sternberg A, Hunter PR. A systematic review and meta-analysis of interventions used to reduce exposure to house dust and their effect on the development and severity of asthma. *Environ Health Perspect*. 2007;115(12):1691-1695.
- Campbell F, Gibson PG. Feather versus non-feather bedding for asthma. *Cochrane Database Syst Rev*. 2000;(4):CD002154.

41. Singh M, Jaiswal N. Dehumidifiers for chronic asthma. *Cochrane Database Syst Rev*. 2013;(6):CD003563.
42. Arroyave WD, Rabito FA, Carlson JC, Friedman EE, Stinebaugh SJ. Impermeable dust mite covers in the primary and tertiary prevention of allergic disease: a meta-analysis. *Ann Allergy Asthma Immunol*. 2014;112(3):237-248.
43. Van Boven FE. Effectiveness of mite-impermeable covers: a hypothesis-generating meta-analysis. *Clin Exp Allergy*. 2014;44:1473-1483.
44. Huiyan W, Yuhe G, Juan W, et al. The importance of allergen avoidance in high risk infants and sensitized patients: a meta-analysis study. *Allergy Asthma Immunol Res*. 2014;6(6):525-534.
45. Bousquet J, Kiley J, Bateman ED, et al. Prioritised research agenda for prevention and control of chronic respiratory diseases. *Eur Resp J*. 2010;36(5):995-1001.
46. Pingitore G, Pinter E. Environmental interventions for mite-induced asthma: a journey between systematic reviews, contrasting evidence and clinical practice. *Eur Ann Allergy Clin Immunol*. 2013;45(3):74-77.
47. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw*. 2010;36:1-48.
48. Ihaka R, Gentleman R. R: a language for data analysis and graphics. *J Comp Graph Stat*. 1996;5(3):299-314.
49. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn. Hillsdale, NJ: Erlbaum; 1988.
50. Bahir A, Goldberg A, Mekori YA, et al. Continuous avoidance measures with or without acaricide in dust mite allergic asthmatic children. *Ann Allergy Asthma Immunol*. 1997;78:506-512.
51. Burr ML, Dean BV, Merrett TG, Neale E, St Leger AS, Verrier-Jones ER. Effects of anti-mite measures on children with mite-sensitive asthma: a controlled trial. *Thorax*. 1980;35:506-512.
52. Burr ML, Neale E, Dean BV, Verrier-Jones ER. Effect of a change to mite-free bedding on children with mite-sensitive asthma: a controlled trial. *Thorax*. 1980;35:513-514.
53. Carswell F, Birmingham K, Oliver J, Crewes A, Weeks J. The respiratory effects of reduction of mite allergen in the bedrooms of asthmatic children – a double-blind controlled trial. *Clin Exp Allergy*. 1996;26:386-396.
54. Chang JH, Becker A, Ferguson A, et al. Effect of application of benzyl benzoate on house dust mite allergen levels. *Ann Allergy Asthma Immunol*. 1996;77:187-190.
55. Chen CC, Hsieh K-H. Effects of Microstop-treated anti-mite bedding on children with mite-sensitive asthma. *Acta Paediatr Sin*. 1996;37:420-427.
56. Cinti C, Canessa PA, Lavecchia MA, Capocchi V. Efficacia di un coprimaterasso e copricuscino antiacaro nel controllo dell asma dei pazienti allergici al dermatofagoides. *Lotta Contro La Tuberculosis e Le Malattie Polmonari Sociali*. 1996;66:131-138.
57. Cloosterman SG, Schermer TR, Bijl Hofland ID, et al. Effects of house dust mite avoidance measures on Der p 1 concentrations and clinical condition of mild adult house dust mite-allergic asthmatic patients, using no inhaled steroids. *Clin Exp Allergy*. 1999;29:1336-1346.
58. De Vries MP, Van den Bemt L, Aretz K, et al. House dust mite allergen avoidance and self-management in allergic patients with asthma: randomised controlled trial. *Br J Gen Pract*. 2007;57:184-190.
59. Dharmage S, Walters EH, Thien F, et al. Encasement of bedding does not improve asthma in atopic adult asthmatics. *Int Arch Allergy Immunol*. 2006;139:132-138.
60. Dietemann A, Bessot JC, Hoyet C, Ott M, Verot A, Pauli G. A double-blind, placebo controlled trial of solidified benzyl benzoate applied in dwellings of asthmatic patients sensitive to mites: clinical efficacy and effect on mite allergens. *J Allergy Clin Immunol*. 1993;91:738-746.
61. Dorward AJ, Colloff MJ, MacKay NS, McSharry C, Thomson NC. Effect of house dust mite avoidance measures on adult atopic asthma. *Thorax*. 1988;43:98-102.
62. Ehnert B, Lau-Schadendorf S, Weber A, Buettner P, Schou C, Wahn U. Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma. *J Allergy Clin Immunol*. 1992;90:135-138.
63. Fang Z, Cai Y, Wang L. [The efficacy of controlling of house dusts in attacks of mite sensitive asthmatics]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2001;24:685-689.
64. Geller-Bernstein C, Pibourdin JM, Dornelas A, Fondarai J. Efficacy of the acaricide: acaridust for the prevention of asthma and rhinitis due to dust mite allergy, in children. *Allerg Immunol*. 1995;27:147-154.
65. Halcken S, Host A, Niklassen U, et al. Effect of mattress and pillow encasings on children with asthma and house dust mite allergy. *J Allergy Clin Immunol*. 2003;111:169-176.
66. Htut T, Higenbottam TW, Gill GW, Darwin R, Anderson PB, Syed N. Eradication of house dust mite from homes of atopic asthmatic subjects: a double-blind trial. *J Allergy Clin Immunol*. 2001;107:55-60.
67. Huss K, Squire EN, Carpenter GB, et al. Effective education of adults with asthma who are allergic to dust mites. *J Allergy Clin Immunol*. 1992;89:836-843.
68. Kroidl RF, Gobel D, Balzer D, Trendelenburg F, Schwichtenberg U. Clinical effects of benzyl benzoate in the prevention of house-dust-mite allergy. Results of a prospective, double-blind, multicenter study. *Allergy*. 1998;53:435-440.
69. Maesen FPV, Sluysmans FG, Brombacher PJ, Smeets JJ. Ervaringen met het gebruik van luchtfiltratieapparatuur in de woonruimten van voor huisstof overgevoelige atopische patienten. *Acta Tuberc Pneumol Belg*. 1977;68:133-147.
70. Marks GB, Tovey ER, Green W, Shearer M, Salome CM, Woolcock AJ. House dust mite allergen avoidance: a randomized controlled trial of surface chemical treatment and encasement of bedding. *Clin Exp Allergy*. 1994;24:1078-1083.
71. Reiser J, Ingram D, Mitchell EB, Warner JO. House dust mite allergen levels and an anti-mite mattress spray (natamycin) in the treatment of childhood asthma. *Clin Exp Allergy*. 1990;20:561-567.
72. Rijssenbeek-Nouwens LHM, Oosting AJ, de Bruin-Weller MS, Bregman I, De Monchy JG, Postma DS. Clinical evaluation of the effect of anti-allergic mattress covers in patients with moderate to severe asthma and house dust mite allergy: a randomised double blind placebo controlled study. *Thorax*. 2002;57(9):784-790.
73. Sette L, Comis A, Marcucci F, Sensi L, Piacentini GL, Boner AL. Benzylbenzoate foam: effects on mite allergens in mattress, serum and nasal secretory IgE to *Dermatophagoides pteronyssinus*, and bronchial hyperreactivity in children with allergic asthma. *Pediatr Pulmonol*. 1994;18:218-227.
74. Shapiro GG, Wighton TG, Chinn T, et al. House dust mite avoidance for children with asthma in homes of low-income families. *J Allergy Clin Immunol*. 1999;103:1069-1074.
75. Sheikh A, Hurwitz B, Sibbald B, Barnes G, Howe M, Durham S. House dust mite barrier bedding for childhood asthma: randomised placebo controlled trial in primary care. *BMC Fam Pract*. 2002;3:12.
76. Thiam DG, Tim CF, Hoon LS, Lei Z, Bee-Wah L. An evaluation of mattress encasings and high efficiency particulate filters on asthma control in the tropics. *Asian Pac J Allergy Immunol*. 1999;17:169-174.
77. Van der Heide S, Kaufmann HF, Dubois AEJ, De Monchy JGR. Allergen-avoidance measures in homes of house-dust-mite-allergic asthmatic patients: effects of acaricides and mattress encasings. *Allergy*. 1997;52:921-927.
78. Walshaw MJ, Evans CC. Allergen avoidance in house dust mite sensitive adult asthma. *Q J Med*. 1986;58:199-215.
79. Warner JA, Marchant JL, Warner JO. Double blind trial of ionisers in children with asthma sensitive to the house dust mite. *Thorax*. 1993;48:330-333.
80. Woodcock A, Forster L, Matthews E, et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. *N Engl J Med*. 2003;349:225-236.

81. Wright GR, Howieson S, McSharry C, et al. Effect of improved home ventilation on asthma control and house dust mite allergen levels. *Allergy*. 2009;64(11):1671-1680.
82. Zwemer RJ, Karibo J. Use of laminar control device as adjunct to standard environmental control measures in symptomatic asthmatic children. *Ann Allergy*. 1973;31:284-290.
83. Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Chichester, UK: Wiley-Blackwell; 2008.
84. Berry DA. Emerging innovations in clinical trial design. *Clin Pharma Ther*. 2016;99(1):82-91.
85. Evans SR. Fundamentals of clinical trial design. *J Exp Stroke Trans Med*. 2010;3(1):19.
86. O'Rourke SD, Tovey ER, O'meara TJ. Personal exposure to mite and cat allergen. *J Allergy Clin Immunol*. 2002;109(1):S47.
87. Tovey ER, Willenborg CM, Crisafulli DA, Rimmer J, Marks GB. Most personal exposure to house dust mite aeroallergen occurs during the day. *PLoS ONE*. 2013;(8):e69900.
88. Tovey ER, Liu-Brennan D, Garden FL, Oliver BG, Perzanowski MS, Marks GB. Time-based measurement of personal mite allergen bioaerosol exposure over 24 hour periods. *PLoS ONE*. 2016;11(5):e0153414.
89. De Blay F, Fourgaut G, Hedelin G, Vervloet D, Michel FB, Godard P, Scientific Committee of the MIEC study. Medical Indoor Environment Counselor (MIEC): role in compliance with advice on mite allergen avoidance and on mite allergen exposure. *Allergy*. 2003;58(1):27-33.
90. V&VN Longverpleegkundigen. Handleiding saneren bij een huisstofmijtallergie, April 2011, Utrecht, The Netherlands. <https://longverpleegkundigen.venvn.nl/Portals/25/Handleiding%20Saneren%20VenVN%20april%202011%20definitief.pdf?ver=2017-08-24-155238-907>.
91. Leas BF, D'Anci KE, Apter AJ, et al. Effectiveness of indoor allergen reduction in asthma management: a systematic review. *J Allergy Clin Immunol*. 2018;141(5):1854-1869.
92. Le Cann P, Paulus H, Glorennec P, Le Bot B, Frain S, Gangneux JP. Home environmental interventions for the prevention or control of allergic and respiratory diseases: what really works. *J Allergy Clin Immunol Pract*. 2017;5(1):66-79.
93. Murray CS, Foden P, Sumner H, Shepley E, Custovic A, Simpson A. Preventing severe asthma exacerbations in children. A randomized trial of mite-impermeable bedcovers. *Am J Resp Crit Care Med*. 2017;196(2):150-158.
94. Tovey ER. Two ideas to improve mite allergen avoidance. *J Aller Clin Immunol Pract*. 2018;6(4):1435-1436.
95. Sheikh A, Hurwitz B, Nurmatov U, van Schayck CP. House dust mite avoidance measures for perennial allergic rhinitis. *Cochrane Database Syst Rev*. 2010;(7):CD001563.
96. Terreehorst I, Hak E, Oosting AJ, et al. Evaluation of impermeable covers for bedding in patients with allergic rhinitis. *N Eng J Med*. 2003;349(3):237-246.
97. Kniest FM, Young E, Praag MV, et al. Clinical evaluation of a double-blind dust-mite avoidance trial with mite-allergic rhinitic patients. *Clin Exp Allergy*. 1991;21(1):39-47.
98. Kort HSM, Koers WJ, van Nes AMT, et al. Clinical improvement after unusual avoidance measures in the home of an atopic dermatitis patient. *Allergy*. 1993;48(6):468-471.

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