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# House dust mite avoidance measures for perennial allergic rhinitis (Review)

Sheikh A, Hurwitz B, Nurmatov U, van Schayck CP

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[Intervention Review]

# House dust mite avoidance measures for perennial allergic rhinitis

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## ABSTRACT

### Background

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 4, 2001 and previously updated in 2003 and 2007.

It is estimated that in developed countries approximately 30% of the general population suffer from one or more allergic disorders, of which allergic rhinitis is particularly common. Perennial rhinitis is most often due to allergy to the house dust mite. In such patients house dust mite avoidance is logical, but there is considerable uncertainty regarding the efficacy and effectiveness of interventions designed to reduce dust mite exposure.

### Objectives

To assess the benefit (and harm) of measures designed to reduce house dust mite exposure in the management of house dust mite sensitive allergic rhinitis.

### Search methods

Our search included the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials Register (CENTRAL) (*The Cochrane Library* Issue 4, 2009), MEDLINE and EMBASE. The date of the last search was 31 December 2009.

### Selection criteria

Randomised controlled trials, with or without blinding, in which house dust mite control measures have been evaluated in comparison with placebo or other dust mite avoidance measures, in patients with clinician-diagnosed allergic rhinitis and confirmed allergy to dust mite.

### Data collection and analysis

Two authors independently screened titles and abstracts, graded methodological quality using the Cochrane approach and extracted data. Meta-analysis was neither possible nor appropriate due to heterogeneity of the patient groups studied.

### Main results

Nine trials involving 501 participants satisfied the inclusion criteria. Only two studies investigating the effectiveness of mite impermeable bedding covers were of good quality; the remaining seven studies were small and of poor quality. Two trials investigated the efficacy of acaricides, another two trials investigated the role of high-efficiency particulate air (HEPA) filters. One trial, using a factorial design, investigated the efficacy of both acaricide and house dust mite impermeable bedding covers in isolation and combination; the remaining four trials investigated the efficacy of bedroom environmental control programmes involving use of house dust mite impermeable bedding covers. Seven of the nine trials reported that, when compared with control, the interventions studied resulted in significant

reductions in house dust mite load. Of the interventions studied to date, acaricides appear to be the most promising type of intervention, although the findings from these studies need to be interpreted with care because of their methodological limitations. House dust mite impermeable bedding as an isolated intervention is unlikely to offer clinical benefit. No serious adverse effects were reported from any of the interventions.

**Authors' conclusions**

Trials to date have on the whole been small and of poor methodological quality, making it difficult to offer any definitive recommendations on the role, if any, of house dust mite avoidance measures in the management of house dust mite sensitive perennial allergic rhinitis. The results of these studies suggest that use of acaricides and extensive bedroom-based environmental control programmes may be of some benefit in reducing rhinitis symptoms and, if considered appropriate, these should be the interventions of choice. Isolated use of house dust mite impermeable bedding is unlikely to prove effective.

## PLAIN LANGUAGE SUMMARY

**House dust mite avoidance measures for perennial allergic rhinitis**

Perennial allergic rhinitis (all-year hay fever like symptoms) is an allergic disorder which can be triggered by house dust mites and causes a congested, runny nose, nasal itching and sneezing. Avoiding the allergic triggers (such as house dust mites) should in theory help to reduce the symptoms of allergic rhinitis in sensitised individuals.

There is limited evidence that measures to reduce the numbers of house dust mites might improve symptoms of allergic rhinitis, but more research is needed to clarify the effectiveness of acaricides (chemicals which kill mites) both as a single intervention and as part of a more multi-faceted approach incorporating high efficiency particulate air (HEPA) filters, allergy control bedding or both.

Overall, this review of trials found that acaricides and extensive bedroom-based environmental control programmes might reduce symptoms of allergic rhinitis for some people, but the evidence is not strong. More research is needed.

## BACKGROUND

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 4, 2001 and previously updated in 2003 and 2007.

It is estimated that up to 30% of the general population of developed countries suffer from one or more allergic diseases (Anandan 2009; Gupta 2004; Kay 1998; Sibbald 1993), however large cross-sectional studies of adolescents throughout the world have revealed marked geographical variations in the prevalence of rhinitis (ISAAC 1998; ISAAC 2006). The most commonly encountered allergic conditions include allergic rhinitis, asthma and eczema. Almost 3% of all general practitioner consultations in the United Kingdom are for allergic rhinitis (Gupta 2004; McCormick 1995; Simpson 2008). As with other allergic diseases, there is concern that the prevalence of allergic rhinitis has increased in recent decades (Flemming 1987; Simpson 2008) for reasons which are poorly understood.

The main clinical symptoms of rhinitis are nasal irritation, sneezing, watery nasal discharge (rhinorrhoea) and the sensation of a blocked nose (Lund 1994). Rhinitis is responsible for considerable morbidity and significant costs to health services (Scadding 1997; Walker 2007).

Traditionally allergic rhinitis has been managed by advising regular use of topical nasal steroids, or the use of systemic antihistamines. Other agents used include topical anticholinergic agents and topical mast cell stabilisers. In more severe cases systemic steroids or immunotherapy may be used. In some cases, surgical treatment is recommended as a complement to medical therapy. Although allergen avoidance has always occupied a central role in the specialist management of allergic rhinitis, this advice has subsequently also been extended to the general management of allergic rhinitis (Lund 1994; Mackay 1998; MeReC 1998; Woodcock 1998).

Allergic rhinitis can be classified as being seasonal (e.g. hay fever), in which case the major allergen trigger is pollen, or perennial (lasting throughout the year). In some countries, for example the United Kingdom, the commonest allergic trigger for perennial allergic rhinitis is the house dust mite. There are a number of techniques designed to decrease exposure to house dust mite. These can be classified as physical (heating, ventilation, freezing, washing, barrier methods, air filtration, vacuuming and ionisers) or chemical treatments (acaricides), or a combination of these approaches.

Attempts at house dust mite reduction in the management of house dust mite sensitive individuals with perennial allergic rhinitis are logical. However, these approaches have received only patchy uptake (Woodcock 1998) as there are concerns regarding the practicality, feasibility, effectiveness and cost-effectiveness of such interventions. The present review aims to ascertain the value of house dust mite control measures in the management of perennial allergic rhinitis by searching the literature systematically and analysing all evidence arising from randomised controlled trials to ascertain the usefulness of house dust mite control measures in the management of perennial allergic rhinitis.

## OBJECTIVES

To assess the benefit (and harm) of measures designed to control numbers of house dust mites in the management of allergic rhinitis in individuals sensitive to house dust mites.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomised controlled trials, with or without blinding. As some house dust mite control measures are impossible to blind, we accepted trials in which blinding was not undertaken.

#### Types of participants

All patients with a diagnosis of allergic rhinitis made by a qualified physician. Children and adults of all ages and both sexes were included. We stipulated that a diagnosis of house dust mite allergy must have been confirmed by an objective test, such as skin prick testing, allergen specific-IgE concentrations or provocation testing.

#### Types of interventions

These included studies in which house dust mite control measures were compared with placebo, or in which different types of control measures were compared. We considered studies evaluating physical and chemical treatments, or a combination of these approaches.

#### Types of outcome measures

We were interested in both subjective and objective outcome measures.

##### *Primary outcomes*

1. Quality of life, general well-being.
2. Days off/sick leave from school/work.
3. Nasal symptom scores.
4. Any adverse outcome as reported in trials.

##### *Secondary outcomes*

1. Nasal peak inspiratory flow.
2. Nasal provocation tests.
3. Rhinomanometry.
4. Medication usage.
5. Compliance with treatment.
6. Percentage of drop-outs.

If house dust mite avoidance measures were found to confer no benefit, this could be due to a failure to achieve an adequate reduction in house dust mite allergen levels. We therefore considered the following process outcome measure:

Change in house dust mite level achieved, expressed in absolute terms and as a percentage of levels present at the outset of the trial.

### Search methods for identification of studies

We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication

status restrictions. The latest update searches were conducted in April 2009 and December 2009.

### Electronic searches

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials Register (CENTRAL) (*The Cochrane Library* Issue 4, 2009), MEDLINE (2005 to 2009), EMBASE (2005 to 2009), CINAHL, *m*RCT (m*eta*Register of Clinical Trials, including ClinicalTrials.gov), NRR (National Research Register), LILACS, KoreaMed, IndMed, PakMediNet, China Knowledge Network, CAB Abstracts, Web of Science, BIOSIS Previews, *m*RCT (Current Controlled Trials), ICTRP (International Clinical Trials Registry Platform) and Google. There were no language or publication status restrictions.

The search strategies (revised since the previous update) used to search CENTRAL, MEDLINE, EMBASE and CINAHL are shown in Appendix 1. We combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2, Box 6.4.b. (Handbook 2009)).

For the previous update, in May 2005, we searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials Register (CENTRAL) (*The Cochrane Library*, Issue 2, 2005), MEDLINE (1950 to May 2005) and EMBASE (1974 to May 2005), CINAHL, AMED, LILACS, KoreaMed, IndMed, MedCarib, National Research Register (NRR), *m*RCT (*meta*Register of Controlled Trials) and ISRCTN , ZETOC Conference Proceedings, Cambridge Scientific Abstracts (CSA), Science Citation Index (via ISI Web of Science) and ISI Proceedings. The search strategies used to search CENTRAL, MEDLINE, EMBASE and CINAHL in 2005 are shown in Appendix 2.

### Searching other resources

For the 2009 update, we scanned the reference lists of identified publications for additional trials and contacted trial authors where necessary. In addition we searched PubMed, TRIPdatabase, NHS Evidence - ENT & Audiology and Google to retrieve existing systematic reviews relevant to this systematic review, so that we could scan their reference lists for additional trials.

The bibliography of each paper identified in the 2005 update was also checked for further references. The primary authors of each study were contacted in an attempt to ascertain additional trials, whether published or unpublished.

## Data collection and analysis

### Selection of studies

Two independent authors checked titles and abstracts identified from the searches. We obtained the full texts of all studies of possible relevance for assessment. We decided which trials satisfied the inclusion criteria and graded their methodological quality. Any disagreement was resolved by discussion between the authors.

### Data extraction and management

One author performed data extraction (UN) using a standardised form; this process was checked by the second author (AS).

### Assessment of risk of bias in included studies

We assessed the quality of each trial following the Cochrane approach using the methods detailed in Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2009). We focused on the following domains to assess the quality of included studies.

1. Adequate sequence generation.
2. Allocation concealment.
3. Blinding (of subjects, investigators, outcome assessors or data analysts).
4. Incomplete outcome data adequately addressed.
5. Free of selective reporting.
6. Free of other bias.

Each parameter was given a judgement as follows:

- 'Yes' - a low risk of bias;
- 'No' - a high risk of bias;
- 'Unclear' - uncertain risk of bias.

We also documented the methodological quality of studies with regards to the following criteria: baseline differences between experimental groups, diagnostic criteria used and length of follow up.

### Data synthesis

Due to the relatively few trials uncovered, trialists' failure to present their results fully and the clinical heterogeneity of the patient groups studied, meta-analysis was not considered appropriate. We therefore summarised results in a narrative overview. We had planned to perform quantitative analyses of outcomes on an intention-to-treat basis, where relevant, considering data in terms of changes from baseline.

In the event of further trial data being made available we intend to express summary results as relative risk (RR) or odds ratio (OR) for dichotomous outcomes and weighted mean differences (WMD) for continuous data. Risk differences (RD) will be used to ascertain numbers needed to treat (NNT) to achieve significant changes in symptom scores or quality of life measures. Separate analyses will be performed for trials showing evidence of mite antigen reduction and for trials not showing reduction. The mite assessment methods that will be considered acceptable are: mite counts, immunochemical assays for mite allergen and guanine determination. Sub-sets of trials will be analysed depending on the technique employed to reduce house dust mite levels (i.e. physical, chemical or combination) and on the presence or absence of blinding.

# RESULTS

## Description of studies

Of the 161 abstracts retrieved, we considered 12 randomised controlled trials to be possibly relevant. Four of the papers reported data from the same two trials (Kniest 1991 - see sub-reference to

Kniest 1992; Terreehorst 2003 - see sub-reference to Terreehorst 2005). One trial (Kim 2005) was available only in abstract format (we made a request for the full-text report to the lead author, but no response was received and so this will not be considered in detail below). All nine trials identified, which have been reported in full, satisfied the inclusion criteria (Antonicelli 1991; Bernstein 1995; Brehler 2006; Ghazala 2004; Incorvaia 2008; Kniest 1991; Moon 1999; Reisman 1990; Terreehorst 2003). The study by Ghazala 2004 required translating into English. Searching the bibliographies of these papers did not reveal any further trials.

**Studies of high efficiency particulate air filters**

Reisman 1990

Forty patients with symptoms of perennial rhinitis (nasal stuffiness, postnasal drainage, rhinorrhoea) and/or asthma, all of whom showed 4 mm or more wheal reaction to intradermal skin test of house dust mite (1:10,000 wt/vol) or house dust mite extract (1:1000 wt/vol), were recruited from two centres into a cross-over trial and randomly allocated to one of two possible groups for bedroom use of a high efficiency particulate air filter (HEPA) for eight weeks (filtering at 300 cu ft/min):

- Group 1 participants received HEPAs loaded with an active Enviracaire® filter for the first four weeks, followed by placebo filters for four weeks;
- Group 2 were given the same HEPAs and filters, but the order in which they were fitted to the HEPAs was reversed.

The outcome measures studied were as follows.

1. Particulate counts >/= 0.3 um in bedroom air (measured by Climet model 208C light-scattering particle counter).
2. Symptoms scaled by a) duration: 1 to 3 (1 = 30 minutes; 3 = > 2 hours) and b) severity: 1 to 3 (1 = mild; 3 = severe) during each 12-hour day and night-time period over the eight-week study period for: sneezing, nasal discharge, nasal congestion, itchy eyes, ears, nose, throat and asthma. These scores were added to patient medication use scores for the same intervals as follows: 1 = antihistamine or decongestant tablets; 2 = theophylline tablet; and 3 = nasal or systemic steroid, and totalled to yield a symptom medication score (SMS). When divided by the number of days studied, the resulting specific SMS was used to compare filter effects upon disease. Only the results of the last two weeks of treatment in each four-week period were compared, however, to lessen the spill-over effects of treatment prior to the four weeks allocated for use of each filter.
3. Patients' subjective response were evaluated at the end of each four-week period.

Antonicelli 1991

This study involved studying nine young patients (10 to 20 years) affected by perennial allergic rhinitis and mild asthma with a positive skin positive test to Der p1 and Der f1, defined as having a wheal 4 mm greater in diameter than the control using a skin prick test. The patients recruited were allocated to a four-month cross-over randomised trial. The recruited subjects were allocated to one of two groups for use of a HEPA filter 24 hours a day for at least eight weeks, as well as routine house cleaning. The other group in the same period carried out only routine house cleaning. Exposure to the HEPA filter was reversed after the first study period.

The outcome measures studied included the following.

1. Daily symptom score (rhinitis, cough, dyspnoea): subjective severity of patients' symptoms was scored on a visual analogue scale from 0 (asymptomatic) to 3 (maximum symptoms).
2. Medication scores: the days on which drugs were used were totalled and divided by the number of trial days to obtain each medication score.
3. Allergen quantification by monthly collection of dust samples from the bedroom floor the day after usual room cleaning using the same vacuum cleaner for 30 minutes.

**Studies of isolated use of acaricides**

Kniest 1991

Twenty subjects aged 12 to 36 years with a long-standing history of house dust mite perennial rhinitis and sensitivity to Pyroglyphid mites (12 participants also sensitive to stored product mites) were selected from a sample of 60 outpatients. Selection aimed to ensure identification of 10 matched patient pairs (matched by age, house dust mite, IgE and skin testing results, guanine exposure value, severity of complaints, hyperreactivity, type of dwelling and number of inhabitants). Subjects were allocated to 12 months of intensive home cleaning either with or without addition of acaricide (solidified benzyl benzoate).

Outcome measures were the three-month median of summed daily patient symptom scores (for itching of eye and/or nose, sneezing, nose secretion, nose bleeding, eye irritation and nasal blockage) for each two-week period; use of medication score for use of steroid nasal sprays, cromoglycate nasal sprays and antihistamine tablets after the second, third and fourth three-month period of the study; and physicians' assessments of whether each patient's overall condition had improved (which were informed by patient diary entries). In each patient, total IgE, mite-specific IgE, the intracutaneous test for house dust mite and histamine were measured at the end of the 12-month study and the levels of blood and nose eosinophils, and guaninine exposure measured every three months.

Bernstein 1995

Thirty-five children aged four to 12 suffering from allergic asthma, rhinitis or both were recruited. Entry criteria stipulated documented allergy to house dust mite, requirement for regular rhinitis medication and a bedroom with a heavy load of house dust mite. All bedrooms were cleaned regularly throughout the study period; in addition participants were allocated to their bedrooms being cleaned and sprayed on day 0 and day 90 with either acaricide (Acardust®) or placebo.

Each child completed an individual daily score card (0 to 3) for asthma and rhinitis symptoms, medication taken and additional symptoms. Peak flow was recorded twice weekly and all children examined monthly for peak expiratory flow (PEF) and forced expiratory volume in one second (FEV1). Doctors' and patients' opinion of clinical symptoms were recorded according to the same scales (0 to 3), and dust samples from bedrooms examined for house dust mite antigen content. At days 0, 90 and 180 total IgE and dust mite specific antigen were estimated for each patient.

**Studies involving isolated use of barrier bedding**

Moon 1999

Thirty patients attending a university hospital allergy clinic were recruited. Inclusion criteria were physician-diagnosed allergic

rhinitis, positive skin prick tests and RAST to house dust mite, negative skin prick tests to all other common aero-allergens and lack of knowledge and practice of environmental control measures to decrease house dust mite exposure. Subjects were aged between six and 31 years with a mean age of 15.6 years. None had a carpet or air-conditioner in their bedroom. Subjects were randomly assigned to experimental group or control group; all subjects continued to use existing rhinitis treatment throughout the four-week trial period. Active intervention was confined to the subject's bedroom and consisted of the following measures provided by the researcher: wrapping the mattress with a vinyl cover, hot washing (55 °C) the top bedding cover fortnightly, removing soft furnishings and wet cleaning the bedroom floor every day. The control group, however, received only verbal instructions regarding ways of reducing house dust mite exposure.

Outcome measures were changes in nasal symptom scores 0 to 9 (0 = no symptoms; 9 = severe) and changes in house dust mite load measured from the bedroom floor, bedding and mattress.

Terreehorst 2003
This randomised, double-blind, placebo-controlled trial involved 279 subjects aged eight to 50 years with a clinical history of perennial allergic rhinitis and a positive nasal allergen provocation test to house dust mite allergen; RAST class 2 or more and/or a skin test index of 0.7 or more to house dust mite. Subjects were allocated to 12 months of receiving impermeable or non-impermeable (control) covers for their mattress, pillow, and duvet or blanket.

The primary endpoint was the score on the rhinitis specific visual analogue scale. Secondary end points included the daily symptom score (nasal obstruction, nasal discharge and nasal itching) and the score on nasal allergen provocation testing. Concentrations of Der p1 and Der f1 in the dust samples from mattresses, bedroom floors and living-room floors were also measured.

Ghazala 2004
This trial involved 30 patients (mean age of 30 years) with perennial allergic rhinitis (17 of whom also had asthma) due to house dust mite allergy. All subjects displayed positive skin prick tests to house dust mite, had RAST class 2 or greater to Der p1 or Der f1 and had a positive conjunctival provocation test to house dust mite extract. The intervention group received allergen impermeable mattress covers (VrioProtect encasings) and this was compared with placebo mattress covers in a double-blind cross-over trial.

The primary endpoints were measurement of rhinitis and asthma quality of life, medication scores and mattress Der p1/ Der f1 concentration. Also measured were serum eosinophil cationic protein (ECP), to assess the underlying allergic inflammation and sleeping comfort with active and placebo covers.

Brehler 2006

This one-year, double-blind, randomised, placebo-controlled, parallel-group trial involved 32 mite-allergic individuals (11 females and 21 males with a mean age of 37.2 years). The inclusion criteria were a positive skin prick test and RAST to house dust mite allergen and a history indicative of clinically relevant house dust mite allergy manifesting with rhinoconjunctivitis.

The intervention group received allergen impermeable mattress, pillow, duvet or blanket covers (Allergopharma, Reinbek, Germany) and the control group was provided with placebo covers of loosely woven cotton produced by the same company.

The primary endpoints for the trial were symptom scores and use of anti-allergic drugs.

**Studies involving use of barrier bedding and acaricides**

Incorvaia 2008

This small randomised controlled trial with a factorial design involved 25 participants (12 in the intervention group, 13 in the placebo group). The age range of participants was not given. Inclusion criteria were the presence of physician-diagnosed persistent rhinitis for at least two years, and a positive skin prick test to house dust mite allergens. Participants were randomised either to receive the active interventions, comprising of polypropylene bed cover (Aclobed, Lofarma, Milan, Italy) and/or an acaricide containing 2.5% benzyl-benzoate as the main ingredient (Aclocid, Lofarma, Milan, Italy), or placebos comprising a cotton bed cover and/or an aerosol similar to the active one, but without the active ingredient.

The primary outcome was the impact of the interventions on disease-specific quality of life, assessed using the Rhinitis Quality of Life Questionnaire (RQLQ). Change in house dust mite load was also assessed.

## Risk of bias in included studies

**Studies of high efficiency particulate air filters**

Reisman 1990
Patients and investigators were both blinded to the order in which filters were deployed in the HEPAs, however the randomisation technique in this trial was not described. The authors failed to provide details about the criteria used to categorise symptom severity raising the likelihood of significant misclassification bias with significant inter-patient variability. Furthermore, it was unclear whether the decision to only compare data from the last two weeks of each intervention period was decided a priori or whether this constituted a post-hoc analysis. Follow up was short and there were difficulties in disaggregating rhinitis and asthma responses.

Antonicelli 1991
This cross-over study was of small size (nine participants) and short duration (two phases, each one lasting for two months). The authors did not provide any details about the randomisation process. There was no blinding of participants or investigators.

**Studies of isolated use of acaricides**

Kniest 1991
This study had an unusual trial design in which matched pairs were identified and then individuals within each pair arbitrarily allocated to one or other treatment in a double-blind manner; no further details of the randomisation technique were provided. Symptoms were classified as present/absent and if present their duration recorded.

Bernstein 1995

This was a double-blind randomised controlled trial, however the technique of randomisation was not described. Analysis appears not to have been performed on an intention-to-treat basis. Tabulated symptom scores were not disaggregated for asthma and rhinitis and no side effects of treatment were reported.

### Studies involving isolated use of barrier bedding

Moon 1999
Randomisation technique was not described in this open trial. To minimise chances of bias, clinical evaluation was performed according to a pre-defined protocol which is not described but reference is made to a paper by Okuda 1984. It is not clear from the report whether the nurse assessing clinical outcome or the entomologist measuring dust mite load were blinded to the treatment group assigned. It is also unclear whether any changes were made to the medical treatment received by subjects during the course of the trial and, if so, how this may have impacted on post-intervention rhinitis symptom scores.

Terreehorst 2003
Patients, investigators and persons responsible for outcome were all double-blinded to the assignment process. The randomisation process was well-described. However, the analysis was not intention-to-treat.

Ghazala 2004
This was a small study involving 26 patients who were studied in a double-blind, placebo-controlled, cross-over study with two phases which each lasted nine to 11 weeks; the washout period lasted between two and 10 weeks. Independent randomisation took place and a study independent person also collected dust samples for the evaluation of allergen content. The primary outcome of quality of life was studied using quality of life measures that have been validated in English (although whether or not these had formally been validated in German is unclear).

Brehler 2006

This small study, involving 32 patients, employed a one-year double-blind, randomised, placebo-controlled trial design. Details of the randomisation technique were difficult to ascertain, other than the fact that bedding covers were distributed in numbered packages. The study protocol stipulated that the randomisation code was to be broken for volunteers who developed severe asthma symptoms during the study period and in such cases these patients were to be withdrawn from the study. Eleven patients were lost to follow up and analysis was not intention-to-treat. Analysis was flawed as only within-group changes were reported.

### Studies involving use of barrier bedding and acaricides

Incorvaia 2008

The authors did not provide any details of the randomisation technique employed in this small (n = 29) factorial design study. The study employed a double-blind design. Four patients were lost to follow up; analysis was not intention-to-treat. The analysis appears also to have been within-group, rather than between-group and so is difficult to interpret. Quality of life was studied using a validated instrument, but there are no details of whether the Italian version of the instrument used in this study had been formally validated.

## Effects of interventions

### Studies of high efficiency particulate air filters

Reisman 1990
Of the 40 patients recruited, there were eight drop-outs (three from one site and five from the other). Reasons for dropping out were inadequate record keeping (n = 3), poor compliance (n = 3), severe concurrent respiratory infection (n = 1) and inappropriate selection (n = 1).

Outcomes:

1. Particulate counts: average reduction (from baseline) in particulate counts >/= 0.3 um in bedroom air after active filtration was 73.4% whereas average count increased by 3.6% with placebo filtration.
2. Aggregated rhinitis and asthma symptom/medication scores: over the last two weeks of treatment symptom/medication scores were lower after active filtration than after placebo filtration (day 8.79 versus 10.38, night 8.28 versus 9.90) with Wilcoxon matched pair rank sum test suggesting active filtration resulted in significant reduction of symptom/medication scores for 24-hour nasal congestion and discharge, eye irritation and upper airway scores.
3. Patients' subjective response: 11 subjects reported improvement with active filtration, seven with placebo and 14 reported no change in symptoms.

Antonicelli 1991
All patients completed the study with only one complaint (by one patient) concerning excessive night-time noise produced by the Enviracaire®. A comparison between the floor allergen levels showed no significant differences associated with HEPA use. The intervention failed to have any significant impact on rhinitis symptom scores.

### Studies involving isolated use of acaricides

Kniest 1991
All subjects completed the study and reported no toxic effects. Twelve months after treatment three-month symptom scores (0 to 3 months versus 9 to 12 months) were lower in the acaricide cleaner group as compared with the control group (matched pairs P = 0.025). Absolute values were not reported but categorised as improved, no change or worse, based upon the ratio of medians in each of the last three quarters of the study to the median value of patient symptom scores in the first quarter of the study. Physicians' assessments showed more patients in the acaricide group improved (start to end) than in the control group (start to end, P = 0.05) but comparison in matched pairs showed no difference. Four of the 10 patients in the acaricide group reported using medication on a daily basis compared with six of the 10 patients in the placebo group. Total IgE dropped in the acaricide group as compared to the control group (matched pairs P = 0.005) but there was no difference in specific IgE to *D. Pteronyssinus* levels. In each of the four patients of the acaricide group with raised baseline eosinophil levels the count fell below 200 after 12 months of treatment, compared with a similar fall in one out of three patients with raised baseline levels in the placebo group. Guaninine exposure dropped in the acaricide group (matched pairs P = 0.005) on comparing start to finish, but dust exposure did not change. Guaninine levels decreased constantly in the acaricide

group reaching 70% of the starting value by the end of the study (P = 0.001) whereas in the control group exposure fell by 3%.

### Bernstein 1995

Of 35 children recruited, three dropped out due to poor compliance. Of the 32 children remaining in the study, 17 were in the Acardust® group and 15 in the placebo group. Treatment and controls were comparable as regards sex ratio, duration of disease, proportion with asthma and rhinitis and age (average age of active group 9.7 years (SD 2.6) compared with 8.1 years (SD 2.6) in placebo group, P = 0.09).

Determination of Der fI antigen in dust samples showed a fall over six months in the mean allergen levels (micrograms/gram dust) in the Acardust® treated group from 10.05 (SD 13.74) to 4.15 (SD 6.51) compared with 6.01 (SD 8.01) to 3.01 (SD 4.33) in the placebo treated group (P = 0.02). Tabulated symptom scores are not disaggregated for asthma and rhinitis, but mean symptom scores decreased more in the Acardust® group than in the placebo group over the six-month period on the following aggregated symptom dimensions:

- Daily activity disruption (Acardust® 117 to 13 compared with placebo 94 to 27).
- Patient's overall evaluation of symptoms (Acardust® 3483 to 547 compared with placebo 2988 to 660).
- Doctor's evaluation of symptoms (Acardust® 3456 to 420 compared with placebo 2965 to 600).

Symptoms of nasal secretion, the symptom complex sneezing/lacrimation/itching and rhinitis medication use all reduced more quickly on a log time scale in the Acardust® treated group than in the placebo group.

**Studies involving isolated use of barrier bedding**

### Moon 1999

Both groups were comparable at baseline with respect to key demographic variables and had similar disease severity. Of the 30 subjects recruited, only one subject from the control group was lost to follow up. There were no adverse effects reported. Mean dust mite loads were significantly reduced in the active group compared with the control group over the four-week study period (-32.5 versus +15.8; 95% CI of difference not presented; P = 0.03).

Mean daily rhinitis symptom scores fell in the experimental group from 5 at baseline to 2.1 (SD not presented) after four weeks of active treatment (mean difference -2.9; P = 0.001), compared with a change from a mean of 4.2 at baseline to 3.9 (SD not presented) at the end of the trial (mean difference -0.3; P > 0.05). Comparison of change in nasal symptom scores between active and control groups showed the bedroom environmental measures undertaken conferred significant benefit (-2.9 versus -0.3; 95% CI of difference not presented; P = 0.026).

### Terreehorst 2003

Of 279 patients recruited, there were 47 drop-outs (25 from one intervention group and 22 from control group). Reasons for drop-out included pregnancy (n = 4), patients having moved (n = 11), protocol violation (n = 7), study took too much time (n = 2), losing contact (n = 1), study was too bothersome (n = 3), covers were too hot (n = 3), unable to stop nasal medication (n = 1), unrelated illnesses (n = 3), missed medication too often (n = 1), lack of co-operation (n = 1), no reason given (n = 3), unknown (n = 3) and no data on the primary outcome (n = 4).

The geometric mean concentration of Derp1 and Derf1 in the mattress sample was significantly lower in the impermeable cover group when compared with the control group (P < 0.001). The ratio of the level 12 months after the covers were put on to the level before the covers were put on was 0.31 (0.21 to 0.46) in the intervention group, as compared with 0.82 (0.58 to 1.15) in the control group.

There was, however, no significant difference between groups in the score on specific visual analogue scale, the nasal allergen-provocation testing, or the daily symptom score. The mean change of symptoms on the rhinitis specific visual analogue scale (VAS) was -10.86 (-16.64 to -50.09) in the control group and -9.83 (-15.28 to -4.39) in the intervention group (P = 0.8). Mean change in the nasal allergen provocation test was also comparable between the two arms: -0.33 (-1.42 to 0.76) in the control group and -0.23 (-1.28 to 0.81) in the intervention group (P = 0.90), as was mean change of daily symptom scores: -0.33 (-0.63 to -0.02) in the control group and -0.18 (-0.45 to 0.10) in the intervention group (P = 0.48)

### Ghazala 2004

Of 30 patients recruited, 26 completed the study. A statistically significant reduction of allergen content from 1.4 mug/$m^2$/2 min to 0.065 mug/$m^2$/2 min was found after using the active cover (P = 0.006), but not after using the placebo cover (1.49 mug/$m^2$/2 min) (exact P value not specified). The general comfort using the active cover was good with the exception of some rustling.

There was a statistically significant decrease in the subjective rhinitis and ocular symptom scores in all 26 patients receiving either placebo (P = 0.025) or active (P = 0.02) treatments In eight patients with an elevated eosinophil cationic protein level (> 16 mug/L), an amelioration of rhinitis could be seen in the active phase compared to the placebo phase where six out of eight patients had a lower level of eosinophil cationic protein in the active group while six patients had a higher level of eosinophil cationic protein at the placebo group (P < 0.025). However, this finding needs to be interpreted with care as it arose from a post-hoc analysis. Medication intake declined in both active and placebo groups, but no difference between the reductions achieved was found.

### Brehler 2006

Of the 32 participants enrolled in this trial, 21 participants completed the study. Reasons for dropping out included volunteers who moved (n = 4), incorrect/inadequate use of covers (n = 4), problems with recording symptoms (n = 1), mould allergy (n = 1) and one patient who withdrew informed consent. One further participant developed a significant mould allergy after nine months of entering the study necessitating continuous asthma therapy before the study ended.

The authors only undertook within-arm trial comparisons, both for symptom scores and use of anti-allergic drugs, these revealing a statistically significant reduction in symptom scores when compared to baseline in the intervention arm, but not in the placebo arm. There was no reduction in the use of anti-allergic drugs in either the intervention or placebo arms.

These analyses are, however, potentially very biased and we therefore reanalysed the reported data (per protocol analysis) comparing the outcomes of interest between the trial arms. This revealed a non-significant reduction in symptom scores (mean difference (MD) -2.34, 95% CI -5.68 to 1.18) and anti-allergic drug use (MD -0.41; 95% CI -2.50 to 1.68).

**Studies involving use of barrier bedding and acaricides**

Incorvaia 2008

Twenty-nine subjects with mite-induced rhinitis and asthma were divided into four groups using a factorial design: 1) both active mattress encasement and acaricide; 2) active encasement and placebo acaricide; 3) placebo encasement and active acaricide; and 4) both placebo treatments. Four patients were lost to follow up; reasons for dropping out included two patients who moved to another house, one who refused to continue and one for unspecified reasons. Thus, 25 patients were evaluated for changes in quality of life; 12 allocated to active treatment and 13 to placebo treatment.

The main trial results were difficult to interpret, but the analysis appeared to be mainly within-group rather than between groups. Thus, although the two active treatments resulted in a significant improvement compared with baseline, the difference relative to the placebo interventions is unclear.

## DISCUSSION

Trials to date have on the whole been small and of poor methodological quality, making it difficult to offer any definitive recommendations on the role, if any, of house dust mite avoidance measures in the management of house dust mite sensitive perennial allergic rhinitis. The results of these studies suggest that the use of acaricides and extensive bedroom-based environmental control programmes may be of some benefit in reducing rhinitis symptoms. There is now reasonably strong evidence that isolated use of house dust mite impermeable bedding is unlikely to prove effective.

With the exception of the Terreehorst 2003 trial, all studies conducted to date have been small and omit presentation of power calculations. Furthermore, these nine studies provide insufficient information to allow retrospective power calculations to be performed. This makes it difficult to be sure that sample sizes studied have been adequate to exclude the possibility of false negative results (Type II errors) confidently. All the trials identified included both children and adults, but it is unclear how representative the population groups studied are of house dust mite allergic perennial rhinitis sufferers in the general population. In particular, none appear to have recruited from a community care setting, which suggests that the groups of patients being studied had greater disease severity then those routinely seen in a primary care setting.

The studies by Bernstein 1995, Kniest 1991, Moon 1999 and Reisman 1990 all suggest that the interventions employed can result in some reduction in rhinitis symptoms, though it is not possible to estimate the magnitude or clinical significance of this likely reduction reliably because of various limitations in their study design, rendering them at moderate or high risk of bias. Also noteworthy is that in the study by Moon et al (Moon 1999), routine provision of advice on measures to reduce exposure to house dust mite failed either to decrease house dust mite load or (more importantly) to reduce clinical symptoms of rhinitis, which raises important questions about the generalisability of this environmental intervention in routine clinical care.

Neither of the two fully reported studies newly included in this update (Brehler 2006; Incorvaia 2008) provided convincing evidence of clinical benefit associated with the interventions studied. Only one small study (Kim 2005), which is at present only available in abstract format suggested that house dust mite impermeable bed covers may be associated with improvement in rhinitis symptoms.

Of the interventions studied to date, acaricides still appear to be the most promising and further pragmatic randomised controlled trials to determine the effectiveness of this mono-intervention are warranted in patients not receiving concomitant medical therapy, in order to allow the effectiveness of the control measures to be determined reliably. Such trials need to be adequately powered (and may therefore need to be multi-centred), generalisable, use validated outcome measures, and have long enough follow up (more than six months) to allow clinically meaningful results to be obtained. In the context of the management of a chronic disease such as rhinitis, a broad range of outcome measures should be studied including quality of life measures, school/work absences and other medication usage. Detailed health economic analysis should also be built into future trials. Although house dust mite barrier bedding and HEPA filter use are unlikely to be of much benefit when used individually, studies of more multi-faceted interventions incorporating these interventions are still warranted.

## AUTHORS' CONCLUSIONS

### Implications for practice

We found very limited evidence to suggest that the use of acaricides to reduce house dust mite exposure in patients with house dust mite allergic perennial rhinitis may be beneficial in reducing rhinitis symptoms. Interventions involving isolated use of house dust mite impermeable bedding are unlikely to be effective.

### Implications for research

There is a need for high-quality trials designed to determine the effectiveness of acaricides as a mono-intervention and also more multi-faceted interventions incorporating HEPA filters and allergy control bedding. Future trials need to be pragmatic, adequately powered, have uniform inclusion criteria, and should ensure long enough follow up (more than six months) to allow detection of clinically meaningful outcomes. In the context of the management of a chronic disease such as rhinitis, a broad range of outcomes need to be studied including changes in validated generic and disease-specific quality of life measures, school/work absences, other medication usage, satisfaction and data on the cost-effectiveness of treatments.

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* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

**Antonicelli 1991**

| | |
|---|---|
| Methods | Randomised cross-over study |
| Participants | 9 participants aged 10 to 28 years with either allergic rhinitis or asthma |
| Interventions | Using an air-cleaning device equipped with HEPA |
| Outcomes | House dust mite (Der p1, Der f1 and Der m1) allergen level<br>Rhinitis and asthma symptom score |
| Notes | — |
| ***Risk of bias*** | |

**Antonicelli 1991** *(Continued)*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Unclear risk | "Patients were randomly divided into two groups of five and four subjects in each"<br>The use of random sequences is not stated |
| Allocation concealment? | Unclear risk | Insufficient information |
| Blinding? | High risk | No blinding of participants or investigators |
| Incomplete outcome data addressed?<br>All outcomes | Low risk | No evidence of incomplete data |
| Free of selective reporting? | Low risk | No evidence of selective reporting |
| Free of other bias? | High risk | Very small study group |

**Bernstein 1995**

| | |
|---|---|
| Methods | Double-blind randomised controlled trial |
| Participants | 32 children aged 4 to 12 years with either allergic rhinitis or asthma or both and confirmed mono-allergy to house dust mite |
| Interventions | Bedroom sprayed with either Acardust acaricide or placebo on days 0 and 90 |
| Outcomes | Daily rhinitis and asthma symptom scores<br>Medication use<br>Twice weekly PEF<br>Monthly clinical assessment<br>Dust house dust mite antigen concentration at days 0, 90 and 180 |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Unclear risk | "The study was double-blind, randomised, comparative, versus placebo"<br>With respect to the use of random sequences, the technique of randomisation is not described |
| Allocation concealment? | Low risk | "At this entry visit, each child got the first canister (numbered with a consecutive number), containing either Acardust or Placebo - both looking perfectly identical, in a randomized manner" |
| Blinding? | Low risk | "The study had a double-blind, controlled manner versus placebo" design |

**Bernstein 1995** *(Continued)*

| | | |
|---|---|---|
| Incomplete outcome data addressed?<br>All outcomes | Unclear risk | "Out of the 35 children there were 3 drop-outs for lack of compliance (1 in the Acardust group, 2 in the placebo group)". However, they appear not to have undertaken an intention-to-treat analysis |
| Free of selective reporting? | Low risk | No evidence of selective reporting |
| Free of other bias? | Low risk | No evidence of other bias |

**Brehler 2006**

| | |
|---|---|
| Methods | Randomised, placebo-controlled, double-blind, parallel-group design |
| Participants | 32 patients of mean age 37.2 years with proven sensitivity to house dust mite and symptoms of rhinoconjunctivitis |
| Interventions | House dust mite impermeable bedding |
| Outcomes | Symptom scores<br>Use of anti-allergic medication |
| Notes | — |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Adequate sequence generation? | Unclear risk | "... the volunteers were randomised to receive either active or placebo encasings" |
| Allocation concealment? | Unclear risk | "... the covers for mattresses, pillows, and duvets or blankets were handed out in numbered packages" |
| Blinding? | Unclear risk | Insufficient information |
| Incomplete outcome data addressed?<br>All outcomes | High risk | 11 of the 32 patients enrolled did not complete the study; an intention-to-treat analysis was not undertaken |
| Free of selective reporting? | Low risk | — |
| Free of other bias? | High risk | The authors compared the outcome measures within the 2 arms not between them as required |

**Ghazala 2004**

| | |
|---|---|
| Methods | Randomised cross-over study |
| Participants | 30 subjects with mean age 29.8 years complaining of allergic rhinitis or asthma |
| Interventions | Using encasings that were impermeable to mite allergens |

**Ghazala 2004** *(Continued)*

| | |
|---|---|
| Outcomes | Allergen (Der p1, Der f1 and mite group 2) content<br>Subjective clinical complaint |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Low risk | "The randomisation of the patients was conducted by an independent person" |
| Allocation concealment? | Low risk | Independent allocation |
| Blinding? | Low risk | "A double-blind placebo-controlled crossover study" |
| Incomplete outcome data addressed?<br>All outcomes | High risk | "Of the 30 patients who fulfilled the entry criteria, 4 fell out due to non compliance (non attendance of appointments and not filling in of diary)". They appear not to have undertaken an intention-to-treat analysis. |
| Free of selective reporting? | Low risk | All of the study's pre-specified outcomes are reported |
| Free of other bias? | Unclear risk | The primary outcome of quality of life was studied using quality of life measures that have been validated in English (although whether or not these had formally been validated in German is unclear) |

**Incorvaia 2008**

| | |
|---|---|
| Methods | Randomised, placebo-controlled, 2 x 2 factorial trial |
| Participants | 29 patients (age range not given) with proven sensitivity to house dust mite and allergic rhinitis |
| Interventions | Participants were divided into 4 groups: 1) both active mattress encasement and acaricide; 2) active encasement and placebo acaricide; 3) placebo encasement and active acaricide; 4) placebo bedding and placebo acaricide |
| Outcomes | Disease-specific quality of life using the RQLQ |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | High risk | No evidence of adequate sequence generation |
| Allocation concealment? | High risk | No evidence of allocation concealment |
| Blinding? | High risk | No evidence of blinding |
| Incomplete outcome data addressed? | High risk | Whilst the reasons for withdrawals are noted, an intention-to-treat analysis was not performed |

**Incorvaia 2008** *(Continued)*

All outcomes

| | | |
|---|---|---|
| Free of selective reporting? | Low risk | No evidence of selective reporting |
| Free of other bias? | High risk | Within-group reporting of findings rather than between-group |

**Kniest 1991**

| | |
|---|---|
| Methods | Double-blind, matched pair controlled trial |
| Participants | 20 subjects aged 12 to 36 with house dust mite rhinitis. Divided into matched pairs on clinical and environmental parameters and then arbitrarily allocated to one of the 2 interventions. |
| Interventions | 12 months of intensive home cleaning either with or without the addition of acaricide (solidified benzyl benzoate) |
| Outcomes | Daily symptoms and medication scores<br>Physician assessment<br>Total and mite-specific IgE<br>Blood and nose eosinophils<br>Guanine exposure |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Unclear risk | "From each subject group, one member was arbitrarily allocated to acaricidal cleaning treatment and the other to control treatment". No further details of the randomisation technique were provided |
| Allocation concealment? | Unclear risk | Insufficient information |
| Blinding? | Low risk | "The allocation was unknown to both experimenters and subjects until the end of the study" |
| Incomplete outcome data addressed?<br>All outcomes | Low risk | All outcome data reported |
| Free of selective reporting? | Unclear risk | Use of an unusual trial design in which matched pairs were identified and use of unusual statistical tests to modify data |
| Free of other bias? | Unclear risk | Patients were selected from outpatients file, so may not represent the standard population |

**Moon 1999**

| | |
|---|---|
| Methods | Open randomised controlled trial |
| Participants | 30 subjects aged 6 to 31 with confirmed house dust mite rhinitis and no other concomitant allergy to common aero-allergens |
| Interventions | All subjects continued normal rhinitis treatment. In addition, they received either verbal advice on allergen avoidance or provision of the following bedroom-based intervention for 4 weeks: vinyl mattress cover, daily wet cleaning of floor, fortnightly boil washing of top bedding cover and removal of soft furnishings. |
| Outcomes | Change in house dust mite load and daily rhinitis symptom scores from baseline and between groups |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Unclear risk | Randomisation technique was not described in this open trial |
| Allocation concealment? | Unclear risk | Insufficient information |
| Blinding? | Unclear risk | It is not clear from the report whether the nurse assessing clinical outcome or the entomologist measuring dust mite load were blinded to the treatment group assigned |
| Incomplete outcome data addressed?<br>All outcomes | Low risk | "Total subjects consisted of 29 patients because one subject in the control group failed to complete the study". The reason is not given. In addition, they appear not to have undertaken an intention-to-treat analysis. |
| Free of selective reporting? | Low risk | All of the study's pre-specified outcomes are reported |
| Free of other bias? | Unclear risk | It is unclear whether any changes were made to the medical treatment received by subjects during the course of the trial and, if so, how this may have impacted on post-intervention rhinitis symptom scores |

**Reisman 1990**

| | |
|---|---|
| Methods | Double-blind, cross-over, randomised controlled trial |
| Participants | 40 subjects with perennial allergic rhinitis and/or asthma and confirmed allergy to house dust mite |
| Interventions | Group 1: HEPA loaded with an active Enviracaire filter for 4 weeks followed by placebo for 4 weeks<br>Group 2: same as Group 1 but order of active and placebo filters reversed |
| Outcomes | Particulate counts in bedroom air<br>Symptom and medication scores<br>Patients' subjective response to treatment |
| Notes | — |

**Reisman 1990** *(Continued)*

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Unclear risk | The randomisation technique in this trial was not described |
| Allocation concealment? | Low risk | "A double-blind study" |
| Blinding? | Low risk | Patients and investigators were both blinded to the order in which filters were deployed in the HEPAs |
| Incomplete outcome data addressed?<br>All outcomes | Low risk | The drop-outs in both groups were described fully and intention-to-treat analysis was performed |
| Free of selective reporting? | Low risk | No evidence of selective reporting |
| Free of other bias? | High risk | It was unclear whether the decision to only compare data from the last 2 weeks of each intervention period was decided a priori or whether this constituted a post-hoc analysis. Follow up was short and there were difficulties in disaggregating rhinitis and asthma responses |

**Terreehorst 2003**

| | |
|---|---|
| Methods | Double-blind randomised controlled trial |
| Participants | 279 participants aged 8 to 50 years with history of allergic rhinitis and/or asthma |
| Interventions | Using bed covers that were impermeable to mite allergens |
| Outcomes | Score on the rhinitis-specific VAS, daily symptom score, the score on nasal allergen-provocation testing, and concentrations of Der p1 and Der f1 |
| Notes | — |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Adequate sequence generation? | Low risk | "Central randomisation was used" |
| Allocation concealment? | Low risk | Adequate |
| Blinding? | Low risk | "A randomised, double-blind, placebo-controlled trial" |
| Incomplete outcome data addressed?<br>All outcomes | Low risk | Loss to follow up is described fully in Figure 1. "Intention-to-treat analysis was performed with the use of data all 232 patients from whom valid scores on the visual-analogue scale could be obtained after 12 months" |
| Free of selective reporting? | Low risk | No evidence of selective reporting of outcomes |

**Terreehorst 2003** *(Continued)*

| | | |
|---|---|---|
| Free of other bias? | Low risk | No evidence of other bias |

HDM = house dust mite
PEF = peak expiratory flow
RQLQ = rhinoconjunctivitis quality of life questionnaire
VAS = visual analogue scale

### Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Lee 2003 | House dust mite and asthma outcomes not allergic rhinitis |
| Skulberg 2005 | No physician-diagnosed rhinitis |

### Characteristics of studies awaiting assessment *[ordered by study ID]*

**Kim 2005**

| | |
|---|---|
| Methods | Randomised, placebo-controlled trial |
| Participants | 35 patients with house dust mite-sensitive allergic rhinitis (age range not given) |
| Interventions | House dust mite impermeable bedding |
| Outcomes | The concentration of HDM major allergen in dust from patients' bedding<br>Symptom score for previous week<br>Visual analogue scale for rhinitis<br>Methacholine challenge test |
| Notes | Only reported in abstract format currently |

HDM = house dust mite

## APPENDICES

### Appendix 1. Updated search strategies 2009

| CENTRAL | MEDLINE | EMBASE | CINAHL |
|---|---|---|---|
| #1 RHINITIS ALLERGIC PERENNIAL single term (MeSH)<br>#2 RHINITIS single term (MeSH)<br>#3 RHINITI*<br>#4 ALLERG*<br>#5 ((#2 OR #3) AND #4)<br>#6 ALLERGENS single term (MeSH)<br>#7 MITES explode all trees (MeSH) | #1 Search RHINITIS,ALLERGIC,PERENNIAL[MH]<br>#2 Search RHINITIS[MH] OR RHINITI*[TIAB]<br>#3 Search ALLERG*[TIAB]<br>#4 Search #2 AND #3<br>#5 Search #1 OR #4<br>#6 Search MITES[MH] | 1 House Dust Allergy/<br>2 allergic rhinitis/ or perennial rhinitis/<br>3 exp Rhinitis/<br>4 rhiniti*.tw.<br>5 4 or 3<br>6 allerg*.tw.<br>7 6 and 5 | S1 (MH "Rhinitis, Allergic, Perennial")<br>S2 (MH "Rhinitis")<br>S3 TX rhiniti*<br>S4 S2 or S3<br>S5 TX allerg*<br>S6 S4 and S5<br>S7 S1 or S6 |

(Continued)

#8 ANTIGENS single term (MeSH)
#9 AIR POLLUTION INDOOR single term (MeSH)
#10 DUST single term (MeSH)
#11 ANTIGENS DERMATOPHAGOIDES single term (MeSH)
#12 MITE* OR DUST* OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA ADJ TROPICALIS OR NORISEN OR PHARMALGEN
#13 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 (#1 OR #5) AND #13
#15 PRIMARY PREVENTION single term (MeSH)
#16 BEDDING AND LINENS single term (MeSH)
#17 FLOORS AND FLOORCOVERINGS single term (MeSH)
#18 ENVIRONMENTAL EXPOSURE [pc] single term (MeSH)
#19 MITE* NEAR PROOF OR MITE* NEAR IMPERMEABLE OR MITE* NEAR REDUC* OR MITE* NEAR ELIMINAT* OR MITE* NEAR DESTROY* OR MITE* NEAR EXTERMINAT* OR MITE* NEAR ERADICAT* OR MITE* NEAR REMOV* OR MITE* NEAR KILL* OR MITE* NEAR SPRAY*
#20 CEDAR OR ACARICID* OR ACARACID* OR NEEM ADJ OIL OR NEEMOIL OR MARGOSA OR MITICIDE
#21 BENZYL ADJ BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN ADJ MP ADJ '100' OR NIMBASA
#22 DWELLING* OR HOUSE* OR UPHOLSTER* OR PILLOW* OR MATTRESS* OR BED* OR CUSHION* OR COVER* OR ENCAS* OR SOFT ADJ FURNISHING* OR CARPET* OR FLOOR* OR CURTAIN*
#23 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24 #14 AND #23
#25 RHINITIS ALLERGIC PERENNIAL [pc] single term (MeSH)
#26 #24 OR #25

#7 Search ALLERGENS[MH]
#8 Search ANTIGENS[MH]
#9 Search ANTIGENS,DERMATOPHAGOIDES[MH]
#10 Search DUST[MH]
#11 Search "Air Pollution, Indoor"[MH]
#12 Search (MITE* OR DUST* OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA TROPICALIS OR NORISEN OR PHARMALGEN)
#13 Search #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 Search #5 AND #13
#15 Search PRIMARY PREVENTION[MH]
#16 Search ("Bedding and Linens"[Mesh] OR "Floors and Floorcoverings"[Mesh]) OR ("Environmental Exposure"[Mesh] OR "Environmental Exposure/prevention and control"[Mesh])
#17 Search MITE* AND (PROOF OR IMPERMEABLE OR REDUC* OR ELIMINAT* OR DESTROY* OR EXTERMINAT* OR ERADICAT* OR REMOV* OR KILL* OR SPRAY*)
#18 Search CEDAR OR ACARICID* OR ACARACID* OR NEEM OIL OR NEEMOIL OR MARGOSA OR MITICIDE
#19 Search BENZYL BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN MP 100 OR TNMP100 OR NIMBASAN
#20 Search DWELLING* OR HOUSE* OR UPHOLSTER* OR PILLOW* OR MATTRESS* OR BED OR BEDS OR BEDDING OR CUSHION* OR COVER* OR ENCAS* OR SOFT FURNISHING* OR CARPET* OR FLOOR* OR CURTAIN
#21 Search #15 OR #16 OR #17 OR #18 OR #19 OR #20
#22 Search #14 AND #21

8 7 or 2
9 allergen/ or house dust allergen/
10 exp blomia/ or exp mite/
11 exp Antigen/
12 Indoor Air Pollution/
13 Dust Exposure/
14 house dust/
15 Environmental Exposure/
16 environmental factor/
17 (MITE* or DUST* or HDM or PYROGLYPHIDAE or EUROGLYPHUS or DERMATOPHAGOIDES or BLOMIA or NORISEN or PHARMALGEN).tw.
18 primary prevention/
19 exp bed/
20 clothing/
21 building/ or furniture/
22 dust control/
23 cleaning/
24 avoidance behavior/
25 insect control/
26 prophylaxis/
27 (MITE* and (Avoid* or PROOF or IMPERMEABLE or REDUC* or ELIMINAT* or DESTROY* or EXTERMINAT* or ERADICAT* or REMOV* or KILL* or SPRAY*)).tw.
28 (CEDAR or ACARICID* or ACARACID* or "NEEM OIL" or NEEMOIL or MARGOSA or MITICIDE or "BENZYL BENZOATE" or BENZYLBENZOATE or BIOMAL or MILBIOL or NEEMOL or SPINNRAD or "TN MP 100" or NIMBASAN).tw.
29 (DWELLING* or HOUSE* or UPHOLSTER* or PILLOW* or MATTRESS* or BED* or CUSHION* or COVER* or ENCAS* or "SOFT FURNISHING" or "SOFT FURNISHINGS CARPET*" or FLOOR* or CURTAIN*).tw.
30 ACARICIDE/
31 NEEM OIL/
32 Perennial Rhinitis/pc [Prevention]
33 26 or 24 or 31 or 27 or 20 or 25 or 19 or 21 or 29 or 23 or 18 or 22 or 30 or 28
34 11 or 9 or 17 or 12 or 15 or 14 or 10 or 13 or 16
35 8 and 34
36 35 or 1
37 33 and 36
38 32 or 37

S8 (MH "Mites")
S9 (MH "Dust")
S10 (MH "Allergens+")
S11 (MH "Antigens+")
S12 (MH "Air Pollution, Indoor")
S13 TX MITE* OR DUST* OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA OR NORISEN OR PHARMALGEN
S14 S8 or S9 or S10 or S11 or S12 or S13
S15 S7 and S14
S16 (MH "Bedding and Linens")
S17 (MH "Floors and Floorcoverings")
S18 (MH "Environmental Exposure+/PC")
S19 TX Avoid* or PROOF or IMPERMEABLE or REDUC* or ELIMINAT* or DESTROY* or EXTERMINAT* or ERADICAT* or REMOV* or KILL* or SPRAY*
S20 TX CEDAR or ACARICID* or ACARACID* or "NEEM OIL" or NEEMOIL or MARGOSA or MITICIDE or "BENZYL BENZOATE" or BENZYLBENZOATE or BIOMAL or MILBIOL or NEEMOL or SPINNRAD or "TN MP 100" or NIMBASAN
S21 TX DWELLING* or HOUSE* or UPHOLSTER* or PILLOW* or MATTRESS* or BED* or CUSHION* or COVER* or ENCAS* or "SOFT FURNISHING" or CARPET* or FLOOR* or CURTAIN*
S22 S16 or S17 or S18 or S19 or S20 or S21
S23 S15 and S22

## Appendix 2. Update search strategies 2005

| CENTRAL | MEDLINE (DataStar) | EMBASE (DataStar) | CINAHL (DataStar) |
|---|---|---|---|
| #1 RHINITIS ALLERGIC PERENNIAL single term (MeSH)<br>#2 RHINITIS single term (MeSH)<br>#3 RHINITI*<br>#4 ALLERG*<br>#5 ((#2 OR #3) AND #4)<br>#6 ALLERGENS single term (MeSH)<br>#7 MITES explode all trees (MeSH)<br>#8 ANTIGENS single term (MeSH)<br>#9 AIR POLLUTION INDOOR single term (MeSH)<br>#10 DUST single term (MeSH)<br>#11 ANTIGENS DERMATOPHAGOIDES single term (MeSH)<br>#12 MITE* OR DUST* OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA ADJ TROPICALIS OR NORISEN OR PHARMALGEN<br>#13 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12<br>#14 #5 AND #13<br>#15 PRIMARY PREVENTION single term (MeSH)<br>#16 BEDDING AND LINENS single term (MeSH)<br>#17 FLOORS AND FLOORCOVERINGS single term (MeSH)<br>#18 ENVIRONMENTAL EXPOSURE [pc] single term (MeSH)<br>#19 MITE* NEAR PROOF OR MITE* NEAR IMPERMEABLE OR MITE* NEAR REDUC* OR MITE* NEAR ELIMINAT* OR MITE* NEAR DESTROY* OR MITE* NEAR EXTERMINAT* OR MITE* NEAR ERADICAT* OR MITE* NEAR REMOV* OR MITE* NEAR KILL* OR MITE* NEAR SPRAY*<br>#20 CEDAR OR ACARICID* OR ACARACID* OR NEEM ADJ OIL OR NEEMOIL OR MARGOSA OR MITICIDE<br>#21 BENZYL ADJ BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN ADJ MP ADJ '100' OR NIMBASA | 1. RHINITIS-ALLERGIC-PERENNIAL.DE.<br>2. RHINITIS.DE. OR RHINITI $1.TI,AB.<br>3. ALLERG$3.TI,AB.<br>4. 2 AND 3<br>5. 1 OR 4<br>6. MITES#.DE.<br>7. ALLERGENS.DE.<br>8. ANTIGENS.DE.<br>9. ANTIGENS-DERMATOPHAGOIDES.DE.<br>10. DUST.DE.<br>11. AIR-POLLUTION-INDOOR.DE.<br>12. (MITE$1 OR DUST$1 OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA ADJ TROPICALIS OR NORISEN OR PHARMALGEN).TI,AB.<br>13. 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12<br>14. 5 AND 13<br>15. PRIMARY-PREVENTION.DE.<br>16. BEDDING-AND-LINENS.DE.<br>17. FLOORS-AND-FLOORCOVERINGS.DE.<br>18. ENVIRONMENTAL-EXPOSURE-PC.DE.<br>19. (MITE$1 NEAR PROOF OR MITE$1 NEAR IMPERMEABLE OR MITE$1 NEAR REDUC$4 OR MITE NEAR ELIMINAT$3 OR MITE$1 NEAR DESTROY $3 OR MITE$1 NEAR EXTERMINAT$3 OR MITE$1 NEAR ERADICAT$3 OR MITE$1 NEAR REMOV$3 OR MITE$1 NEAR KILL$3 OR MITE$1 NEAR SPRAY$3).TI,AB.<br>20. (CEDAR OR ACARICID $2 OR ACARACID$2 OR NEEM ADJ OIL OR NEEMOIL OR MARGOSA OR MITICIDE).TI,AB.<br>21. (BENZYL ADJ BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN ADJ MP ADJ '100' OR NIMBASAN).TI,AB. | 1. HOUSE-DUST-ALLERGY.DE.<br>2. PERENNIAL-RHINITIS.DE. OR ALLERGIC-RHINITIS.DE.<br>3. RHINITIS.DE. OR RHINITI$.TI,AB.<br>4. ALLERG$3.TI,AB.<br>5. 3 AND 4<br>6. 2 OR 5<br>7. HOUSE-DUST-ALLERGEN.DE. OR ALLERGEN.DE.<br>8. MITE#.DE. OR BLOMIA#.DE.<br>9. ANTIGEN.DE.<br>10. INDOOR-AIR-POLLUTION.DE.<br>11. DUST-EXPOSURE.DE. OR HOUSE-DUST.DE.<br>12. ENVIRONMENTAL-EXPOSURE.DE. OR ENVIRONMENTAL-FACTOR.DE.<br>13. (MITE$1 OR DUST$1 OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA OR NORISEN OR PHARMALGEN).TI,AB.<br>14. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13<br>15. 6 AND 14<br>16. 1 OR 15<br>17. PRIMARY-PREVENTION.DE.<br>18. BED.DE. OR CLOTHING.DE.<br>19. BUILDING.DE. OR FURNITURE.DE.<br>20. DUST-CONTROL.DE. OR CLEANING.DE.<br>21. AVOIDANCE-BEHAVIOR.DE. OR INSECT-CONTROL.DE.<br>22. PROPHYLAXIS.DE.<br>23. (MITE$1 NEAR PROOF OR MITE $1 NEAR IMPERMEABLE OR MITE $1 NEAR REDUC$4 OR MITE NEAR ELIMINAT$3 OR MITE$1 NEAR DESTROY$3 OR MITE$1 NEAR EXTERMINAT$3 OR MITE$1 NEAR ERADICAT$3 OR MITE$1 NEAR REMOV$3 OR MITE$1 NEAR KILL$3 OR MITE$1 NEAR SPRAY$3).TI,AB.<br>24. ACARICIDE#.DE. OR NEEMOIL.DE.<br>25. (CEDAR OR ACARICID$2 OR ACARACID$2 OR NEEM ADJ OIL OR NEEMOIL OR MARGOSA OR MITICIDE).TI,AB.<br>26. (BENZYL ADJ BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN ADJ MP ADJ '100' OR NIMBASAN).TI,AB. | 1. ALLERGIC-RHINITIS.DE.<br>2. RHINITIS.DE. OR RHINITI $1.TI,AB.<br>3. ALLERG$3.TI,AB.<br>4. 2 AND 3<br>5. 1 OR 4<br>6. MITES#.DE.<br>7. ALLERGENS.DE.<br>8. ANTIGENS.DE.<br>9. DUST.DE.<br>10. AIR-POLLUTION-INDOOR.DE.<br>11. (MITE$1 OR DUST$1 OR HDM OR PYROGLYPHIDAE OR EUROGLYPHUS OR DERMATOPHAGOIDES OR BLOMIA ADJ TROPICALIS OR NORISEN OR PHARMALGEN).TI,AB.<br>12. 6 OR 7 OR 8 OR 9 OR 10 OR 11<br>13. 5 AND 12<br>14. BEDDING-AND-LINENS.DE.<br>15. FLOORS-AND-FLOORCOVERINGS.DE.<br>16. ENVIRONMENTAL-EXPOSURE-PC.DE.<br>17. (MITE$1 NEAR PROOF OR MITE$1 NEAR IMPERMEABLE OR MITE$1 NEAR REDUC$4 OR MITE NEAR ELIMINAT$3 OR MITE$1 NEAR DESTROY$3 OR MITE $1 NEAR EXTERMINAT$3 OR MITE$1 NEAR ERADICAT$3 OR MITE$1 NEAR REMOV$3 OR MITE$1 NEAR KILL$3 OR MITE$1 NEAR SPRAY$3).TI,AB.<br>18. (CEDAR OR ACARICID $2 OR ACARACID$2 OR NEEM ADJ OIL OR NEEMOIL OR MARGOSA OR MITICIDE).TI,AB.<br>19. (BENZYL ADJ BENZOATE OR BENZYLBENZOATE OR BIOMAL OR MILBIOL OR NEEMOL OR SPINNRAD OR TN ADJ MP ADJ '100' OR NIMBASAN).TI,AB.<br>20. (DWELLING$1 OR HOUSE$1 OR UP- |

*(Continued)*

| | | | |
|---|---|---|---|
| #22 DWELLING* OR HOUSE* OR UPHOLSTER* OR PILLOW* OR MATTRESS* OR BED* OR CUSHION* OR COVER* OR ENCAS* OR SOFT ADJ FURNISHING* OR CARPET* OR FLOOR* OR CURTAIN*<br>#23 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22<br>#24 #14 AND #23<br>#25 RHINITIS ALLERGIC PERENNIAL [pc] single term (MeSH)<br>#26 #24 OR #25 | 22. (DWELLING$1 OR HOUSE$1 OR UPHOLSTER$2 OR PILLOW$1 OR MATTRESS$2 OR BED$3 OR CUSHION$1 OR COVER$4 OR ENCAS$4 OR SOFT ADJ FURNISHING$1 OR CARPET$3 OR FLOOR$3 OR CURTAIN$1).TI,AB.<br>23. 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22<br>24. 14 AND 23<br>25. RHINITIS-ALLERGIC-PERENNIAL-PC.DE.<br>26. 24 OR 25 | 27. (DWELLING$1 OR HOUSE$1 OR UPHOLSTER$2 OR PILLOW$1 OR MATTRESS$2 OR BED$3 OR CUSHION$1 OR COVER$4 OR ENCAS$4 OR SOFT ADJ FURNISHING $1 OR CARPET$3 OR FLOOR$3 OR CURTAIN$1).TI,AB.<br>28. 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27<br>29. 16 AND 28<br>30. PERENNIAL-RHINITIS-PC.DE.<br>31. 29 OR 30 | HOLSTER$2 OR PILLOW$1 OR MATTRESS$2 OR BED $3 OR CUSHION$1 OR COVER$4 OR ENCAS$4 OR SOFT ADJ FURNISHING$1 OR CARPET$3 OR FLOOR $3 OR CURTAIN$1).TI,AB.<br>21. 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20<br>22. 13 AND 21<br>23. ALLERGIC-RHINITIS-PC.DE.<br>24. 22 OR 23 |

## WHAT'S NEW

| Date | Event | Description |
|---|---|---|
| 20 April 2010 | New citation required but conclusions have not changed | Review updated. Two new studies included. No changes to review conclusions.<br><br>Two new review authors. |
| 31 December 2009 | New search has been performed | New searches run 31 December 2009. |

## HISTORY

Protocol first published: Issue 2, 1999
Review first published: Issue 4, 2001

| Date | Event | Description |
|---|---|---|
| 22 October 2008 | Amended | Converted to new review format. |
| 3 November 2006 | New citation required and conclusions have changed | Substantive amendment. New search conducted May 2005. Three new studies included. |
| 1 February 2003 | New search has been performed | Minor update. New searches run - no new studies identified. |

## CONTRIBUTIONS OF AUTHORS

AZIZ SHEIKH: Lead author, protocol development, searching for trials, quality assessment of trials, data analysis and writing of final review.

BRIAN HURWITZ: Protocol development, quality assessment of trials, data extraction, data analysis and writing of final review.

ULUGBEK NURMATOV: Quality assessment of trials, data extraction and updating of review.

ONNO CP VAN SCHAYCK: Contributed to reviewing drafts of the report.

## DECLARATIONS OF INTEREST

Aziz Sheikh has previously received a small travel grant from Allerayde, manufacturers and distributors of allergy control bedding.

## SOURCES OF SUPPORT

### Internal sources

- CAPHRI, University of Maastricht, Netherlands.

### External sources

- No sources of support supplied

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the 2010 update of this review, we adopted the new 'Risk of bias' method (the domain-based evaluation described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2009)).

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Mites; Acaricides; Bedding and Linens [parasitology] [standards]; Dust; Randomized Controlled Trials as Topic; Rhinitis, Allergic, Perennial [parasitology] [*prevention & control]; Tick Control [*methods]

### MeSH check words

Animals; Humans