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[Intervention Review]

House dust mite control measures for asthma

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Editorial note: This 2011 review predates current reporting standards and methodological expectations for Cochrane Reviews. It should not be used for clinical decision-making.

ABSTRACT

Background

The major allergen in house dust comes from mites. Chemical, physical and combined methods of reducing mite allergen levels are intended to reduce asthma symptoms in people who are sensitive to house dust mites.

Objectives

To assess the effects of reducing exposure to house dust mite antigens in the homes of people with mite-sensitive asthma.

Search methods

We searched PubMed and the Cochrane Airways Group Register (last search July 2011). No restrictions were placed on language of publication.

Selection criteria

We included randomised trials of mite control measures versus placebo or no treatment in people with asthma known to be sensitive to house dust mites.

Data collection and analysis

Two authors applied the trial inclusion criteria and evaluated the data. We contacted trial authors to clarify information.

Main results

We included 55 trials (3121 patients). Thirty-seven trials assessed physical methods, including 26 trials employing mattress encasings. Ten trials involved chemical methods and eight trials involved a combination of chemical and physical methods. Despite the fact that many trials were of poor quality and would be expected to exaggerate the reported effect, we did not find an effect of the interventions. For the most frequently reported outcome, peak flow in the morning (1665 patients), the standardised mean difference (SMD) was 0.01 (95% confidence interval (CI) -0.08 to 0.11). There were no statistically significant differences either in number of patients improved (risk ratio 1.01, 95% CI 0.80 to 1.27), asthma symptom scores (SMD -0.06, 95% CI -0.16 to 0.05), or in medication usage (SMD -0.05, 95% CI -0.17 to 0.07).

Authors' conclusions

Chemical and physical methods aimed at reducing exposure to house dust mite allergens cannot be recommended. It is doubtful whether further studies, similar to the ones in our review, are worthwhile. If other types of studies are considered, they should be methodologically rigorous and use other methods than those used so far, with careful monitoring of mite exposure and relevant clinical outcomes.

PLAIN LANGUAGE SUMMARY

Does controlling exposure to house dust mites improve asthma?

Asthma is a chronic inflammatory disease of the airways. The prevalence of asthma has increased and it is now the commonest chronic disease among children. Asthma is triggered by allergens (substances that cause an allergic reaction) and house dust presents a problem in some people with asthma. The major allergen in house dust comes from mites and it is hypothesised that controlling exposure to house dust mites will reduce asthma symptoms in people who are sensitive to house dust mites.

We included 55 randomised trials on 3121 people with asthma. There are both chemical (10 trials) and physical methods such as mattress encasings (37 trials) of reducing mite allergen levels and we included both types in this review. There were also eight trials that used both physical and chemical methods. Many trials were of poor quality and would therefore be expected to exaggerate the reported effect, but we did not find an effect of the interventions. There was no difference in peak flow (a measure of lung function), asthma symptoms and medication scores, or the number of patients reporting an improvement in their asthma symptoms.

While reducing exposure to house dust mites is recommended in guidelines, we did not find an effect of control measures to reduce the exposure to mites or their products. .

BACKGROUND

Asthma is a chronic inflammatory disorder of the airways. The prevalence of asthma has increased and it is now the commonest chronic disease among children. The treatment of asthma is both pharmacological, including immunotherapy (Vervloet 1990; Abramson 1995), and non-pharmacological. Non-pharmacological treatment often involves environmental procedures such as elimination of allergens in the patient's surroundings (Colloff 1992).

Exposure to different allergens can trigger asthma attacks in sensitised individuals. House dust is a mixture containing many different allergens, but the major allergen is derived from mites, especially the species *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. A common site for house dust mites is the bed, where pillows, quilts and mattresses often serve as reservoirs for the allergen. Carpets and upholstered furniture may also contain high mite levels (Platts-Mills 1989; Tovey 1992). It appears very reasonable, and is usually recommended, that environmental control of allergens, although difficult, should be an integral part of the overall management of sensitised patients. However, some of the evidence behind these recommendations is derived from observational studies, including some in which patients were moved to high altitudes or hospitals, whereupon their symptoms improved (Custovic 1998). These measures are not feasible for most patients, and it is not clear whether the allergen levels that can be obtained in the patients' homes are large enough to lead to improvements in the asthma.

Different methods for reducing mite exposure have been tried, for example chemical methods, physical methods and combinations of these (Platts-Mills 1989). We published a systematic review of these methods in 1998 (Gøtzsche 1998; Hammarquist 1998) and the current review is the most recent update.

OBJECTIVES

To study whether patients with asthma who are sensitised to house dust mites benefit from measures designed to reduce their exposure to mite antigen in the home.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised trials. Since some mite control measures are impossible to blind, we accepted non-blinded trials.

Types of participants

We included participants with physician-diagnosed bronchial asthma. We included participants who had their mite sensitisation assessed by either skin testing, bronchial provocation tests or serum assays for specific IgE antibodies.

Types of interventions

Intervention

a) Chemical (acaricides).
b) Physical (for example mattress covers, vacuum-cleaning, heating, ventilation, freezing, washing, air-filtration and ionisers).
c) Combinations of these.

Control

Placebo or no treatment.

Types of outcome measures

- Subjective well-being
- Asthma symptom scores
- Medication usage
- Days of sick-leave from school or work
- Number of unscheduled visits to a physician or a hospital
- FEV1 (forced expiratory volume in one second)
- PEFR (peak expiratory flow rate)
- PC20 (provocative concentration that causes a 20% fall in FEV1)

Search methods for identification of studies

We identified trials from the Cochrane Airways Group Specialised Register of trials (CAGR), which is derived from systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED and PsycINFO, and handsearching of respiratory journals and meeting abstracts (please see Appendix 1 for further details). We searched all records in the CAGR coded as 'asthma' with the terms: mite* or dust* or "house dust" or house-dust or acari*. We searched the CAGR in June 2011.

We also searched PubMed from 1966 onwards with the terms mite* AND asthma*, combined with one or more of the following: random* OR control* OR blind* (last search July 2011).

There was no language restriction.

Data collection and analysis

Selection of studies

The authors independently selected the trials for inclusion. We resolved ambiguities by discussion. When necessary we contacted the trial authors for clarification

Data extraction and management

When it was not stated at what time of the day the peak flow had been recorded, we assumed it was in the morning. We resolved ambiguities by discussion. When necessary we contacted the trial authors for clarification.

Assessment of risk of bias in included studies

Assessment of the risk of bias and extraction of data was primarily done by one author (PCG) and checked by another (HKJ for the current version of the review). All assessments were open. We judged the adequacy of the allocation concealment according to the guidelines laid out in the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2008).

Measures of treatment effect

When continuous data presented on different scales, for example peak expiratory flow rate (PEFR) and forced expiratory volume in one second (FEV1), could be given either as absolute values or as percent of predicted values, we used the standardised mean difference. With this method, the difference in effect between two treatments is divided by the standard deviation of the measurements. By that transformation, the effect measures

become dimensionless and outcomes from trials which have used different scales may therefore often be combined. Data on well-being and asthma symptom scores were reported in a number of different ways, but as these two outcome measures were closely related or even equivalent, we summarised categorical data in the well-being category (number of patients who improved) and continuous data (which mostly concerned asthma symptoms) in the asthma symptoms score category. The authors had usually analysed the provocative concentration that causes a 20% fall in FEV1 (PC20) after logarithmic transformation, since the data were highly skewed. We analysed the data accordingly and when the authors had converted their means and standard deviations from the logarithmic scale to the arithmetic scale, we converted them back again (Bland 1996). We excluded PC20 data that had not been analysed after logarithmic transformation.

Unit of analysis issues

Since the results from cross-over trials were usually reported by the authors in summary form, as if they had come from a group comparative trial, we analysed these data accordingly, assuming that no important carry-over effects had occurred. We decided not to enter paired data from cross-over trials using the generic inverse variance method, since rather few data were reported in this format and since it would require that all other data should also be so analysed in order to present summary estimates for each outcome. Paired data were only available for some of the cross-over trials and not for all the recorded variables.

When several options were available for medication, we used bronchodilators. When data were recorded at several points in time, we used the longest observation period during which the patients were still on randomised treatment, unless performance bias occurred, for example by a planned reduction in dose of inhaled steroids.

We did not adjust for baseline differences, since inequalities occurring despite the randomisation would be expected to equal each other out in a large sample of trials. Furthermore, baseline recordings were not always available. If we had made adjustments when possible, we would have risked biasing the review, since investigators are inclined to show baseline differences and adjust for them when this procedure favours the experimental treatment (Gøtzsche 2006). It has also been shown that bias occurring during data analysis is very common and almost without exception favours the new treatment over the control treatment (Gøtzsche 1990).

To avoid double-counting of the control group when there was more than one active group in a trial, we pooled the active groups when feasible. This was not possible for one very small trial in which a chemical method was used in one group and a combination of methods in another group (Ehnert 1992). For this trial, we split the seven patients in the control group into four patients for one comparison and three for the other.

Assessment of heterogeneity

We tested heterogeneity with the Chi^2 test and assessed its magnitude with the I^2 statistic (that gives the amount of between-trial variation in relation to the total variation). When we encountered heterogeneity ($P < 0.10$), we explored the reasons.

Data synthesis

We calculated 95% confidence intervals (CI) with a fixed-effect model.

RESULTS

Description of studies

We included 55 trials involving 3121 patients. This represents an addition of one trial since the last update of our review (Gøtzsche 2008). The potential for outcome reporting bias, i.e. the omission or incomplete reporting of outcomes that were not statistically significant (Chan 2004), was very large. Eleven trials did not contain any usable data for meta-analysis (Korsgaard 1983; Charpin 1990; Sooltangos 1992; Howarth 1992; Manjra 1994; Jooma 1995; van der Heide 1997B; Frederick 1997; Shapiro 1999; van der Heide 1999; Ghazala 2004). In the remaining trials, many outcomes were reported in a way that did not allow us to use them in a meta-analysis and it was often unclear how many patients contributed values to the various analyses (see Characteristics of included studies table). The most frequently reported outcome was PEFR in the morning (1665 patients in our meta-analysis). Length of the intervention and follow-up varied from two weeks to two years.

All trials but six had used skin prick testing for diagnosis of mite sensitivity. Extracts used were *Dermatophagoides pteronyssinus* and/or *Dermatophagoides farinae* apart from two trials where subjects were tested with unspecified 'house dust extract' (Zwemer 1973; Maesen 1977). In three trials, sensitivity was established by specific serum IgE (van der Heide 1999; Luczynska 2003; Woodcock 2003), in two trials by either skin prick testing or IgE (Thiam 1999; Rijssenbeek 2002), and in one trial published only as an abstract the means of diagnosis was not given (Howarth 1992).

Thirty-seven trials used physical methods to reduce exposure to mites, 10 used chemical methods and eight used a combination of chemical and physical methods (see Characteristics of included studies table). Twenty-six of the trials used mattress encasings (Burr 1976; Burr 1980B; Walshaw 1986; Gillies 1987; Howarth 1992; Ehnert 1992; Marks 1994; Jooma 1995; Carswell 1996; Chen 1996; Cinti 1996; van der Heide 1997B; Frederick 1997; Shapiro 1999; Thiam 1999; Cloosterman 1999; Sheikh 2002; Rijssenbeek 2002; Halken 2003; Luczynska 2003; Lee 2003; Woodcock 2003; Ghazala 2004; van den Bemt 2004; Dharmage 2006; de Vries 2007). Mite reduction occurred in 17 trials, according to the authors' own judgements (Walshaw 1986; Dorward 1988; Charpin 1990; Huss 1992; Warner 1993; Carswell 1996; Frederick 1997; Shapiro 1999; Cloosterman 1999; Htut 2001; Fang 2001; Rijssenbeek 2002; Halken 2003; Woodcock 2003; van den Bemt 2004; Dharmage 2006; de Vries 2007), mite reduction was unsuccessful in 25 and was not measured or reported in the remaining 13 trials.

Risk of bias in included studies

The randomisation method was rarely described and even using rather broad criteria only eight trials reported adequate concealment of allocation: sealed, opaque envelopes (Cinti 1996; Shapiro 1999), computer program (Halken 2003; Wright 2009), sealed envelopes with consecutive numbers (Kroidl 1998), centralised, using numbers generated from a random numbers table (Sheikh 2002), computer using minimisation (van der Heide 1997B; van der Heide 1999) and co-ordination centre, using minimisation (Woodcock 2003). All eight trials with adequate

concealment of allocation were also reported to have been blinded, although in at least one trial, the attempted blinding was not perfect (Gøtzsche 2003; Halken 2003) and in another the intervention frequency differed between the groups (Shapiro 1999). One trial maintained the blinding during data analysis (Sheikh 2002). A summary of our risk of bias judgements can be found in Figure 1.

Figure 1. 'Risk of bias' summary: review authors' judgements about allocation concealment for each included study.

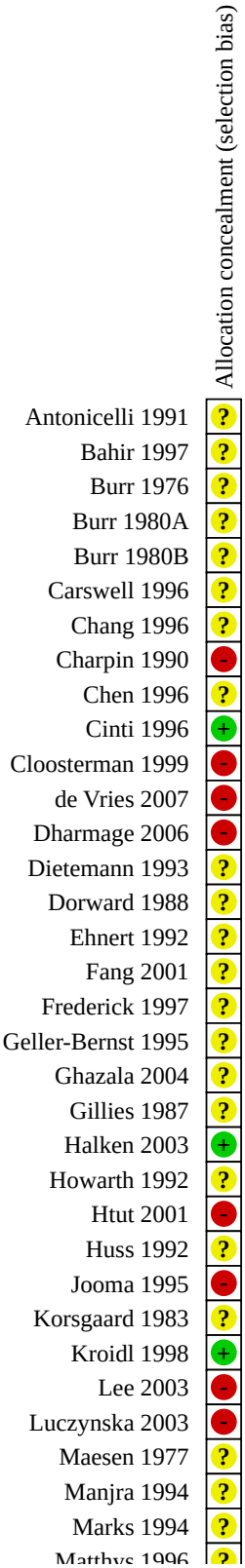

Figure 1. (Continued)

Twelve trials had a cross-over design (Zwemer 1973; Burr 1976; Maesen 1977; Burr 1980B; Mitchell 1980; Verrall 1988; Antonicelli 1991; Warner 1993; Warburton 1994; Matthys 1996; Frederick 1997; van der Heide 1999). The remaining were group comparative trials.

Effects of interventions

We did not find an effect of control measures to reduce the exposure to mites or their products in the 55 trials we reviewed.

The total number of patients who improved after the experimental interventions was very similar to the corresponding number in the control groups, risk ratio 1.01 (95% confidence interval (CI) 0.80 to 1.27; Analysis 1.1) (data available for seven trials in 143 participants).

Asthma symptom scores were very heterogeneous (P = 0.0002 for test of heterogeneity, I^2 = 61%) (20 trials on 1485 people). The heterogeneity was caused by two small trials of poor quality that were the only ones that reported a significantly positive effect (Zwemer 1973; Thiam 1999). The standardised mean difference (SMD) for all trials was -0.06 (95% CI -0.16 to 0.05; Analysis 1.2). After exclusion of the two trials of poor quality, the SMD was -0.02 (95% CI -0.12 to 0.08).

Medication usage was very similar in the experimental and control groups (11 trials in 1115 participants). The SMD was -0.05 (95% CI -0.17 to 0.07; Analysis 1.3). Data for chemical methods were given in only one trial (Dietemann 1993) in which medication usage was significantly larger in the experimental group than in the control group (0.89, 95% CI 0.02 to 1.75). This finding is of doubtful value, however, since the standard deviation was unusually low and may have been erroneous. If this trial is excluded, the SMD is -0.07 (95% CI -0.19 to 0.05).

For FEV1, the SMD was 0.13 (95% CI -0.02 to 0.28; Analysis 1.4) (15 trials in 675 participants). In one trial, unusually large variations in FEV1 from visit to visit were reported which indicates that the data may not have been reliable (Thiam 1999). If this trial is excluded, the SMD is 0.11 (95% CI -0.05 to 0.26).

For peak flow in the morning, the standardised mean difference was 0.01 (95% CI -0.08 to 0.11; Analysis 1.5) (24 trials in 1665 participants). For peak flow in the evening, the SMD was 0.06 (95% CI -0.13 to 0.24; Analysis 1.6) (13 trials).

For PC20 the SMD was 0.05 (95% CI -0.13 to 0.22; Analysis 1.7) (13 trials in 493 participants).

Only two trials reported on unscheduled visits to a physician or hospital, or on missed work or school days. In the largest trial included in our review, 38 patients required a hospital visit or a course of oral steroids in the intervention group and 27 in the control group; number of days of work missed was 0.10 versus 0.23 (95% CI for difference -0.28 to 0.01) (Woodcock 2003). A small cross-over trial of poor quality reported that none of 12 participants missed school during the treatment period, as opposed to three during the control period; however, there was no mention of

reasons for missing school or data on another six randomised patients (Zwemer 1973).

DISCUSSION

Summary of main results

We were unable to demonstrate any clinical benefit to mite-sensitive patients with asthma of measures designed to reduce mite exposure. It is not likely that we missed a clinically relevant effect, since the total number of patients in the trials was quite large. The most commonly used outcome, morning peak flow, is related to the severity of the asthma and peak flow measurements did not suggest any worthwhile effect. This can be seen more clearly if the difference in morning peak flow is translated into the most commonly used unit, L/min. With a standard deviation of 100 L/min (in accordance with the meta-analysis graph) and a control group peak flow of 300 L/min, the experimental group peak flow would be 301 L/min, with a 95% confidence interval that ranges from 292 to 311 (L/min). A similarly narrow confidence interval around no effect was seen for asthma symptoms.

When there is no indication of an effect of an intervention, subgroup analyses should not be performed, since they would be expected to be seriously misleading. We discuss below, however, strengths and limitations of the trials.

Adherence to the applied measures was rarely evaluated, but successful mite reduction was obtained in several trials, including the biggest one (Woodcock 2003) that contributed 628 patients of a total of 1665 to the measurements of morning peak flow. It should be noted, however, that mite reduction was determined in different ways in the various studies. Some recorded mite counts and some measured antigen levels, using dust samples from different sources, and the reductions reported do not necessarily correspond to a similar reduction in the patients' exposure. For example, removing mites from the surface of mattresses and pillows does not affect the mite content of blankets or duvets, and merely killing the mites does not necessarily reduce airborne mite antigen, if nothing is done to remove the faecal particles that contain it. A potential reservoir for mites is the scalp and it has been suggested that neglect of this source may explain the failure of many trials of mite eradication (Naspitz 1997). In a previous version of our review, we were asked to do a subgroup analysis according to whether or not mite reduction was achieved (Gøtzsche 2001). We did not find any difference.

It seems unlikely that the initial mite levels were already too low for any reduction to be effective. It has been shown that quite low allergen concentrations can affect bronchial responsiveness (Ihre 1988; Ihre 1993) and the concentrations were such as would usually be considered to represent a risk to mite-sensitive asthmatics. Allergen levels varied between the studies and there was a wide range of concentrations in each study, so that some participants' exposure may have been very low, but this was uncommon.

Potential sources of bias should be considered. The randomisation methods were rarely described. It is likely that some studies were not truly randomised, or that the allocation was not adequately concealed, which are defects that would be expected to lead to bias in favour of a treatment effect. Most trials were very small and our sample of trials may therefore have been influenced by publication bias, which also tends to exaggerate the effect of treatment. The reporting of the data was often poor, for example many trials only reported that there were no significant differences between the intervention and the control groups. This lack of proper reporting would also be expected to lead to bias in favour of a treatment effect. In a comparison of 102 trial protocols with subsequent publications, it was shown that the chance that an outcome was fully reported was twice as high if the result was statistically significant (Chan 2004). It should also be noted that on a few occasions it was necessary to correct the originally reported data, for example in one trial we could not confirm a reported significant effect on mite allergen level (Geller-Bernst 1995).

Physical interventions may need to be applied repeatedly before the reduction in allergen levels is sufficient to be effective. However, the lack of effect was also apparent in the subgroup of trials with long treatment duration or follow-up. Furthermore, if the interventions were effective, one would expect to see at least some effect also in short-term trials as mite allergen causes a Type 1 hypersensitivity reaction.

The house dust mite is the allergen to which asthmatics are most frequently sensitive, and the acute effects of exposure on the symptoms of asthma are well established. The explanation that we find most plausible for the lack of effect of the interventions is therefore that the methods we have reviewed do not adequately reduce mite antigen levels as it seems inherently implausible to suggest that complete removal of a major provoking agent would be ineffective. It is important to remember, however, that mite-sensitive asthmatic patients are usually sensitive to other allergens, so that successful elimination of only one allergen may have limited benefit, whatever its success. We excluded a large trial of multiple interventions in 937 patients with multiple allergies that is interesting in this respect (Morgan 2004). This trial reported positive effects on clinically relevant outcomes, such as number of days with symptoms, night awakenings and missed school days. However, the study was not blinded and the positive results for these subjective outcomes were obtained through telephone interviews. Furthermore, the intervention group received more home visits than the control group, results for objective outcomes such as forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR) were very similar for the two groups, and the allergen levels decreased by less than 50%, compared with the control group, which is far too little to be expected to have any effect. A meta-analysis that compared multifaceted with mono-faceted interventions for preventing the development of asthma in newborns suggested that multifaceted interventions might be more effective, but as the comparisons were indirect, the authors also recommended comparing these modalities directly in randomised trials (van Schayck 2007).

We conclude that the trials of current chemical and physical methods aimed at reducing exposure to house dust mite allergens failed to find an effect. Reviews and guidelines should reflect the facts.

Potential biases in the review process

We tried carefully to avoid bias during data extraction, for example by making blinded decisions when several options were available. On a few occasions, however, we could not select the data in a neutral fashion but had to choose data which favoured the hypothesis that interventions were effective, for example in the trials by Carswell and Reiser (see table Characteristics of included

studies). For the biggest trial (Woodcock 2003), we selected data after six rather than 12 months, in accordance with the authors' power calculation, since this part investigated the effects of allergen reduction on asthma symptoms and was not biased by the planned reduction of steroids (there was also significant allergen reduction after six months, but not after 12 months). Further, there was no indication that we had excluded trials with positive results (see table Characteristics of excluded studies). We therefore believe that we have not favoured the null hypothesis of no treatment effect in our meta-analysis; if anything, we have favoured the alternative hypothesis.

Agreements and disagreements with other studies or reviews

Reviews and guidelines do not reflect the fact that measures designed to reduce the patients' exposure to mite antigen in the home are ineffective. In fact, they usually recommend several measures as being effective, and provide a highly selected and biased sample of references in support of such claims. The most quoted trial in 70 reviews had only seven patients per group, its claimed significant result was probably erroneous, and it did not report a clinical outcome (Schmidt 2005). Furthermore, recommendations were often based on non-randomised studies and the most quoted non-randomised study had included only 10 patients per group but claimed very positive results (Schmidt 2005).

The 2007 extensive US guidelines for asthma control (US Guidelines 2007) were also misleading. On page 171 the expert panel recommends various interventions, including encasing the mattress in an allergen-impermeable cover. The panel quotes 10 papers in support of this, but one is an editorial, one is a review, one is a before-after study, one is about rhinitis, one was excluded from our review as only some of the patients were allergic to mites and no outcome data were provided for this group, and one is not relevant as it involved multiple interventions and allergens (Gøtzsche 2008a). What remains are only five trials and these did not show an effect of mattress encasings.

In 2008, guidelines endorsed by the American Academy of Allergy, Asthma, and Immunology and the European Academy of Allergology and Clinical Immunology (US/Europe Guidelines 2008) were described as being evidence-based and one of the authors was quoted as saying: "We tried very hard to make these recommendations evidence-based and tried to avoid expert opinion as the basis for recommendations" (Mitka 2008). However, the guidelines recommend several interventions against house dust mites, none of which are evidence-based, and all three references offered in their support are irrelevant. These guidelines were published in *Allergy*, which made the editor-in-chief ask us to co-publish our Cochrane Review in his journal to bring more rigour to the field, which we did (Gøtzsche 2008b).

AUTHORS' CONCLUSIONS

Implications for practice

Chemical and physical methods aimed at reducing exposure to house dust mite allergens cannot be recommended.

Implications for research

It is doubtful whether further studies, similar to the ones in our meta-analysis, are worthwhile. In particular, it should be noted that several of the trials had used very extensive mite eradication and avoidance schemes, involving many different measures applied simultaneously. If other types of studies are considered, we suggest that they should be methodologically rigorous and use other methods than those used so far, with careful monitoring of mite exposure and relevant clinical outcomes.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Antonicelli 1991

Study characteristics	
Methods	Cross-over trial Randomisation method: not described Not blind (apart from PD20) Physical
Participants	N = 9 (9 in analyses) Mean age 16 years (range 10 to 28) Skin positive to D pter and D far
Interventions	Test: HEPA-filter (Enviracaire) in bedroom for 8 weeks Control: none Each period lasted 8 weeks
Outcomes	Daily symptom score (scale 0 to 3), medication score, FEV1, PEFR morning and evening, PD20
Notes	No reduction in mite allergens (ELISA). Additional data from author. For asthma symptoms, we selected daytime wheeze blindly as the most relevant variable (other variables yielded closely similar results). Medication usage: salbutamol. FEV1 and PEFR from Table 2.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Bahir 1997

Study characteristics	
Methods	Randomisation method: not described Double-blind

Bahir 1997 *(Continued)*

	Chemical
Participants	N = 40 children (30 in analyses) Age range 6 to 17 years Skin positive to D pter and/or D far
Interventions	Test: acaricide (esdepallethin 0.9% and piperonyl butoxide 7.2%) Control: placebo (and a third control group) 6 months
Outcomes	Daily symptom score, use of beta-2 agonists, FEV1, morning and evening PEFR, Acarex test
Notes	No reduction in mite allergens (guanine determination). The authors' fig. 3 indicates SEM which must be an error, should have been SD as for other data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Burr 1976

Study characteristics

Methods	Cross-over trial Randomisation method: not described Not blind Physical
Participants	N = 32 (32 in analyses) Mean age: 33 years Positive skin tests to D pter
Interventions	Test: initial vacuum-cleaning of the bed and laundering; enclosure of the mattress with a plastic cover for 6 weeks Control: no such interventions
Outcomes	Medication used during the past 24 hours, morning PEFR
Notes	No assessment of mite reduction. Data from Table II

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Burr 1980A

Study characteristics

Burr 1980A *(Continued)*

Methods	Randomisation method: not described Blind assessment Physical
Participants	N = 55 children (53 in analyses) Age range 5 to 14 years Skin positive to D pter
Interventions	Test: visited by a nurse, extensive scheme with vacuum-cleaning, laundering, beating in open air, removal of toys, etc. Placebo: visited by a nurse, given a placebo treatment that consisted mainly of removal of dust in the living-room 8 weeks
Outcomes	Numbers improved, PEFR morning and evening
Notes	No reduction in mite counts or mite antigen. Numbers improved: much better or better from Table 3. Peak flow was measured as coefficient of variation and was therefore omitted (very similar results were obtained in test and control groups).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Burr 1980B

Study characteristics

Methods	Cross-over Randomisation method: not described Not blind Physical
Participants	N = 21 children from trial Burr 1980A who still complained of symptoms
Interventions	Test: new sleeping bag, pillow and blanket, mattress enclosed in an impervious plastic bag, other bedding enclosed or renewed, vacuum-cleaning of carpets in the bedroom Control: as in Burr 1980A Each period lasted 1 month
Outcomes	Mothers asked whether the patients were better during test or control period, PEFR morning and evening
Notes	No reduction in mite counts. Peak flow was measured as coefficient of variation and therefore omitted (very similar results were obtained in test and control period).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Carswell 1996

Study characteristics	
Methods	Randomisation method: not described Double-blind Combination
Participants	N = 70 children (49 in analyses) Mean age 9.9 years Positive skin test D pter
Interventions	Test: Acarosan powder and foam, Medivac filter vacuum cleaner, allergen exclusion covers, bed linen washed weekly at 60 degrees C Control: chalk dust and water spray, cotton placebo covers, bed linen washed weekly at 40 degrees C 24 weeks
Outcomes	Numbers improved (no. randomised minus no. with symptoms in Fig. 5 minus no. without symptoms at baseline), asthma symptoms, medication usage, PEFR measured in 4 different 2-week periods, FEV1 (only reported after 24 weeks), PC20
Notes	Mite antigen level (ELISA) fell in bedding. Data reported after 2, 6 and 24 weeks. FEV was only reported after 24 weeks. We used 6 weeks data for PEFR which was only reported accurately at this time (house dust mite removal was most effective after 6 weeks and there was a significant effect in bronchial sensitivity after 6 weeks, but not after 24 weeks).

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Chang 1996

Study characteristics	
Methods	Randomisation method: not described Not blind Chemical
Participants	N = 26 (11 children and 15 adults, 26 in analyses) Positive skin test to mite allergen
Interventions	Test: acaricide (Acarosan) to mattresses and carpets in bedroom Control: no acaricide 3 months
Outcomes	Daily symptoms, medication, FEV1, morning and evening PEFR, PC20
Notes	No mite antigen reduction (ELISA)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Chang 1996 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Information not available

Charpin 1990

Study characteristics	
Methods	Randomisation method: table provided by laboratory Double-blind Chemical
Participants	N = 42 (11 only had rhinitis) Numbers in analyses not clear Mean age 27 years Positive skin prick test
Interventions	Test: Acardust (synthetic pyrethrinoid + piperonyl butoxide) sprayed once on bed linen and in room Control: no acaricide 3 months
Outcomes	Global assessment by patient and doctor, morning and evening PEFR, number of attacks
Notes	Reduction in mite allergen. No data on dispersion (PEFR in the morning was 435 in the test group, 437 in the control group; doctor's global assessment was 3.1 versus 2.8 on a 10 cm analogue scale).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	High risk	Table provided by laboratory

Chen 1996

Study characteristics	
Methods	Randomisation method: not described. Double-blind Physical
Participants	N = 56 (35 in analyses) Age range 5 to 14 years Positive to DP1
Interventions	Test: Microstop (impermeable polyurethane-coated nylon ticking) Control: new, conventional polyurethane mattresses (there was a second control group as well) 12 months
Outcomes	Asthma symptoms and morning and evening PEFR
Notes	No reduction in mite counts. Odd that randomisation leads to 29, 29 and 15 patients. Two exclusions unclear, we allocated one to each group.

Chen 1996 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Cinti 1996

Study characteristics

Methods	Randomisation method: sealed opaque envelopes Double-blind Physical
Participants	N = 20 (20 in analyses) Mean age 30 years (range 10 to 69) RAST or skin test positive for D pter or D far
Interventions	Test: "mite-proof" mattress and pillow covers Placebo: covers of cotton 12 weeks
Outcomes	Daily symptom scores, number of acute episodes, medications, eosinophil cationic protein, PEFR
Notes	No assessment of mite counts. Additional data supplied by author.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes

Cloosterman 1999

Study characteristics

Methods	Randomisation method: statistician informed investigators, open list of random numbers, open to investigators Blind to patient and technician Combination
Participants	N = 204 (157 in analyses) Mean age 33 years (range 16 to 60) Mite sensitivity diagnosed at an allergy laboratory
Interventions	Test: Acarosan and mite impermeable covers for mattresses Control: water and cotton covers 20 weeks
Outcomes	Asthma symptoms, medication use, FEV1, morning and evening PEFR, PC20

Cloosterman 1999 *(Continued)*

Notes	Mite antigen reduction achieved (ELISA). Table 2 and fig 4 and 5 used for data on symptoms and peak flow.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Statistician informed investigators, open list of random numbers, open to investigators

de Vries 2007

Study characteristics

Methods	Randomisation method: "randomisation list", "patients were assigned according to the number on the list, in sequence of inclusion" Double-blind: placebo covers were indistinguishable Physical Intention-to-treat (last observation carried forward)
Participants	N = 143 (105 completed 2 years) Mean age 42 years (SD 12) Mite sensitivity: RAST
Interventions	Test: impermeable mattress, duvet and pillow covers Placebo: permeable covers 2 years
Outcomes	Asthma symptoms, medication use, morning and evening PEFR
Notes	Mite antigen reduction achieved, down to about 10% of placebo group levels (ng allergen per square metre). No data for PEFR provided, only P = 0.52 for difference. Funded partly by 2 drug companies.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	"randomisation list","patients were assigned according to the number on the list, in sequence of inclusion"

Dharmage 2006

Study characteristics

Methods	Randomisation method: "permuted blocks of size two", "randomized...by the toss of a coin" Double-blind: "identically-appearing " placebo covers Physical
Participants	N = 32 (30 in analyses) Mean age 32 years (SD 6.3) Positive skin test
Interventions	Test: impermeable mattress, doona and pillow covers

Dharmage 2006 *(Continued)*

	Placebo: permeable covers 6 months
Outcomes	Asthma symptoms, medication use, FEV1, PEFR morning and evening, quality of life, time spent home, log PD20
Notes	Reduction in mite allergens. Only data after 3 months, and none for FEV1 or PEFR. Data reported inadequately for meta-analysis, apart from log PD20.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Coin toss

Dietemann 1993

Study characteristics

Methods	Randomisation method: not described Double-blind Chemical
Participants	N = 26 (23 in analyses) Mean age 35 years (range 13 to 58) Positive skin test to D pter, RAST positive
Interventions	Test: solidified benzyl benzoate and tenside agents at the beginning and after 6 months Control: placebo powder 1 year
Outcomes	Asthma symptoms (VAS 0 to 10), medication score (0 to 3), FEV1, FVC, FEF25-75, PEFR morning and evening, clinical score (0 to 4)
Notes	No reduction in mite allergens (guanine determination and ELISA). Values after treatment calculated from percentage change and baseline values. SDs calculated from confidence intervals at baseline, assuming they were the same after treatment, which is reasonable, based on other trials.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Dorward 1988

Study characteristics

Methods	Randomisation method: not described Blinded assessment Combination

Dorward 1988 *(Continued)*

Participants	N = 21 (18 in analyses) Age range 13 to 53 years Positive skin tests to D pter
Interventions	Test: liquid nitrogen, vacuum-cleaning, other cleaning, washing, airing, damp dusting; plants, soft toys, cushions and upholstered furniture removed Control: normal cleaning activities 8 weeks
Outcomes	Asthma symptom score (VAS 0 to 10), daily number of puffs of salbutamol, PEFR morning and evening, PC20, S-IgE.
Notes	Mite counts significantly reduced. For PC20, we used the logarithmic values for the means from Table 2 and calculated their SDs from Fig. 2.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Ehnert 1992

Study characteristics

Methods	Randomisation method: not described Test 1: double-blind, chemical Test 2: not blind, combination
Participants	N = 24, 8 in each group (21 in analyses) Age range 7 to 15 years Skin positive D pter and D far positive serum IgE
Interventions	Test 1: mattresses treated with benzyl benzoate, carpets treated with powder on day 0 and after 4 and 8 months. Vacuum-cleaning after 4 hours Test 2: polyurethane mattress covers and tannic acid 3% on carpets Control: placebo foam 1 year
Outcomes	PC20
Notes	No reduction in mite allergens (ELISA). A within-group significant change was reported for the encasing group for PC20, but the time trends for the 3 groups were not compared. As the control group was used for both comparisons in the meta-analysis graph, its number of patients were split in half, one half being used in each analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Fang 2001

Study characteristics	
Methods	Randomisation method: not described Not blind Physical
Participants	N = 43 (not clear whether more were randomised) Age 37 (SD 20) Skin positive for *Dermatophagoides*
Interventions	Test: washing bedclothes and clothes, sun exposure and ventilation Control: untreated 2 years
Outcomes	Asthma symptoms, medication use, PEFR morning and evening
Notes	Mite reduction claimed (P < 0.001). Reduction in IgE also claimed (P < 0.001) which is surprising.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Frederick 1997

Study characteristics	
Methods	Cross-over Randomisation method: not described Single-blind Physical
Participants	N = 31 Children aged 5 to 15 years Positive skin prick test and/or IgE
Interventions	Test: covers (Intervent) for mattress, duvet and pillow, wiped down weekly Control: polycotton covers Each period lasted 3 months
Outcomes	Asthma symptoms, medication use (bronchodilators), FEV1, PEFR morning and evening, PC20
Notes	Reduction in mite allergens. No useful data (medians and ranges), PEFR in the morning was 257 versus 282.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Geller-Bernst 1995

Study characteristics	
Methods	Randomisation method: not described Double-blind Combination
Participants	N = 32 (14 in most analyses) Age range 4 to 12 years Positive skin tests only to house dust mites
Interventions	Test: change of bed sheet and blanket, dust removal with damp cloth, vacuuming of carpets and furniture, sprays on day 0 and 90 with Acardust Control: placebo spray 6 months
Outcomes	Asthma symptoms (0 to 3), medication use, FEV1, PEFR, doctor's and patient's opinion of clinical symptoms, serum IgE
Notes	No reduction in mite allergens. No useful data.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Ghazala 2004

Study characteristics	
Methods	Randomisation method: not described, "Studienunabhängige Person" Double-blind, no details Physical
Participants	N = 17 (12 in analyses) Cross-over trial Age not stated for asthma patients Positive skin prick test and positive IgE
Interventions	Test: covers (VarioProtect) for mattress, washed weekly Control: cotton covers Each period lasted 9 to 11 weeks
Outcomes	Asthma symptoms, medication use
Notes	Unclear whether reduction in mite allergens. No data on medication use. Figure shows exactly the same asthma score, but authors claim that P = 0.025. Not clear what the box plot symbols mean. Data unusable for meta-analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Ghazala 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Information not available

Gillies 1987

Study characteristics	
Methods	Randomisation method: not described Not blind Physical
Participants	N = 26 (25 in analyses) Age range 6 to 16 years Skin positive D pter
Interventions	Test: enclosing of mattresses and pillows, pets and soft toys excluded from bedroom, synthetic bedding employed, damp dusting, vacuum-cleaning Control: no such measures 6 weeks
Outcomes	Asthma symptoms, medication requirements, PEFR morning and evening, PC20, serum IgE
Notes	No reduction in mite counts PC20 values omitted since they were calculated arithmetically. No useful data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Halken 2003

Study characteristics	
Methods	Randomisation method: computer program, stratified by 4 factors Described as double-blind, but the covers were different Physical
Participants	N = 60 (47 in analyses) Children aged 5 to 15 years Positive skin prick test
Interventions	Test: mattress and pillow encasings coated with semi-permeable polyurethane (Allergy Control) Controls: placebo encasings. 12 months
Outcomes	Medication usage, FEV1, PEFR, asthma symptoms, PC20. Dose of inhaled steroids was reduced during the trial at lowest effective dose.
Notes	Reduction in mite allergens. Complicated randomisation, but no baseline imbalances according to individual patient data obtained from author. Symptom scores not used, as distribution was very far from being Gaussian.

Halken 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Computer program, stratified by 4 factors.

Howarth 1992

Study characteristics

Methods	Randomisation method: not described Double-blind Physical
Participants	N = 35 (number in analyses not reported, some had rhinitis) Age 13 to 23 years Positive skin prick test
Interventions	Test: covers of mattress, duvet and pillow Control: placebo covers 6 weeks
Outcomes	Asthma symptoms
Notes	Very promising abstract, but never published and author did not respond to our letters

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Htut 2001

Study characteristics

Methods	Randomisation method: open table of random numbers Double-blind Physical
Participants	N = 30 in trial report, N = 33 in previous abstract (23 in analyses) Age 18 to 45 years Positive skin prick test
Interventions	Test 1: steam-cleaning once of mattresses and duvets, and new pillows Test 2: same treatment, but in addition, a ventilation system (Nuaire) was installed in bedrooms Control: sham steam cleaning 1 year
Outcomes	PD20

Htut 2001 *(Continued)*

Notes	Reduction in mite allergens. We combined the 2 test groups for meta-analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Open table of random numbers

Huss 1992

Study characteristics

Methods	Randomisation method: not described Not blind Physical
Participants	N = 52 (52 in analyses) Age range 18 to 75 years Skin positive to D far or D pter
Interventions	Test: computer-assisted instruction in addition to conventional mite avoidance instruction (encasing mattresses, box springs and pillows, removing carpeting and upholstered furniture, laundering bedding, controlling indoor temperature (< 70 degrees F) and humidity (< 45% RH)) Control: verbal and written guidance 12 weeks
Outcomes	Asthma symptoms, medication usage (inhaled bronchodilator use), FEV1
Notes	Reduction in mite allergens (ELISA). Authors report that there was no difference for FEV1, but give no data

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Jooma 1995

Study characteristics

Methods	Randomisation method: open table of random numbers Not blind Combination
Participants	N = 60 (not all included in analyses, numbers not stated) Children aged 6 to 14 years Positive skin prick test
Interventions	Test 1: mattress and pillow covers (Allergy Control Products) + tannic acid to carpets every 8 weeks Test 2: acaricide (benzyl benzoate + bromopol) applied to carpets and mattresses

Jooma 1995 *(Continued)*

	Control: none 6 months
Outcomes	PC20
Notes	No reduction in mite allergens. No useable data, no significant changes in PC20.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Open table of random numbers

Korsgaard 1983

Study characteristics

Methods	Randomisation method: not described Not blind Physical
Participants	N = 51 (46 in analyses) Median age 30 years Positive skin prick test and IgE, and bronchial provocation test for mite extract
Interventions	Test: vacuum-cleaning and wash of bed linen twice-weekly, new synthetic quilts and pillows, bedroom aired for 20 minutes daily and permanently half-open window Control: none 12 weeks
Outcomes	PEFR morning and evening, use of bronchodilator, asthma symptoms
Notes	No reduction in mite counts on mattress, but reduction on bedroom floor. Data presented as medians and interquartile ranges. Morning PEFR 490 versus 460 (P = 0.33), evening PEFR 490 for both groups (P = 0.82); less symptoms in test group (P = 0.02).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Kroidl 1998

Study characteristics

Methods	Randomisation method: sealed envelopes with consecutive numbers Double-blind Chemical
Participants	N = 118 (78 in analyses) Age range 8 to 50 years

Kroidl 1998 *(Continued)*

	Skin test and RAST positive to D pter
Interventions	Test: acaricide, benzyl benzoate (Acarosan) Control: cleaning product without acaricide 1 year
Outcomes	Well-being, PC20, RAST, changes in skin prick test
Notes	No assessment of mite reduction. Drop-outs not described per group but provided by author: 18 versus 22 patients.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Sealed envelopes with consecutive numbers

Lee 2003

Study characteristics

Methods	Randomisation method: "assigned at random by coin tossing" Not blind Physical
Participants	Conflicting information, see Notes N = 42 in analyses Age: most were above 30 years Positive skin prick test and RAST
Interventions	Test: outer cotton bed covers, boiled 10 minutes, 3 hours sunlight every 14 days Control: no intervention 4 weeks
Outcomes	PEFR morning and evening, frequency of 6 different asthma symptoms
Notes	Two partly conflicting trial reports, the most recent does not quote the earlier one. No reduction in mite allergens. Frequency of 6 different asthma symptoms not used in our meta-analysis due to lack of a severity score and of an acceptable way of combining the data (SD far bigger than mean for most symptoms, i.e. a gross violation of the Gaussian assumption).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Coin toss

Luczynska 2003

Study characteristics

Luczynska 2003 *(Continued)*

Methods	Randomisation method: statistical program generated a list of 1s and 2s where patient number were written; not adequately concealed as blinding could be broken Double-blind Physical
Participants	N = 58, only 45 started the trial, and only 31 in analyses Age 18 to 54 Serum IgE > 0.7 kU/L specific for mite antigen in all patients
Interventions	Test: allergen-impermeable Micro fibre bedcovers (Allerguard) on bed, blankets and pillows Control: sham bedcovers 1 year
Outcomes	PEFR morning and evening, number of days with chest tightness, quality of life, asthma attacks and medication use
Notes	No reduction in mite allergens. Data not shown for medication use and asthma attacks. No significant differences in number of days with chest tightness and quality of life (the former favoured the test, the latter the control); data not entered in our meta-analysis as it is not straightforward how these 2 measures of asthma symptoms should be combined.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	Statistical program generated a list of 1s and 2s where patient number were written; not adequately concealed as blinding could be broken

Maesen 1977

Study characteristics

Methods	Cross-over trial Randomisation method: unclear, a table of random numbers was used Double-blind Physical
Participants	N = 30 (28 in analyses) 25 adults (15 to 55 years) and 5 children (7 to 14 years) Positive skin test and bronchial provocation test to house dust
Interventions	Test: air-filtration apparatus Control: placebo (the filter was covered with plastic) Each period lasted 1 month
Outcomes	Subjective improvement, medication usage, PEFR morning and evening
Notes	No assessment of mite reduction

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Manjra 1994

Study characteristics	
Methods	Randomisation method: unclear, "system of random numbers" after matching for 3 factors Not blind Chemical
Participants	N = 60 (59 in analyses) Children aged 5 to 12 years Positive skin prick test
Interventions	Test 1: detergent (Metsan) for carpets and bedding Test 2: Metsan + acaricide (Acarosan) for carpets and bedding Control: none 3 months
Outcomes	PC20
Notes	No mite reduction in mattresses. PC20 given as medians, no difference between the groups. Patients not divided on treatment groups. The first author did not answer our letter.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Marks 1994

Study characteristics	
Methods	Randomisation method: not described Blinded participants Combination
Participants	N = 39 (35 in analyses) Age range 13 to 60 years All but 2 subjects had a positive skin test to D pter
Interventions	Test: tannic acid/acaricide solution (Allersearch) + impermeable covers on mattress, pillows and duvets Control: inactive placebo spray 6 months
Outcomes	Symptom score (0 to 10), FEV1, PEFR morning and evening, PD20
Notes	No reduction in mite allergens (ELISA). Values after treatment calculated from percentage change and baseline values. SDs calculated from confidence intervals at baseline, assuming they were the same after treatment, which is reasonable, based on other trials.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Marks 1994 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Information not available

Matthys 1996

Study characteristics	
Methods	Cross-over trial Randomisation method: not described Single-blind (according to thesis) Physical
Participants	N = 14 (10 to 14 in analyses) Positive skin prick test
Interventions	Test: air-dryer in bedroom with water filter Control: air-dryer in bedroom without water filter Each period lasted 4 weeks
Outcomes	Medication usage, PEFR, symptoms
Notes	Significant difference with Acarex-test. Published only as an abstract. Data exist in a thesis, but significant carry-over and period effects for medication usage and PEFR precludes usage of the data.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Information not available

Mitchell 1980

Study characteristics	
Methods	Cross-over trial Randomisation method: not described Not blind Physical
Participants	N = 10 (10 in analyses) Age range 7 to 14 years Positive skin test to D pter and D far
Interventions	Test: electrostatic precipitator plus standard mite-avoidance measures Control: standard mite-avoidance measures Each period lasted 2 weeks
Outcomes	Medication usage, PEFR 3 times a day
Notes	No assessment of mite reduction. Percent expected PEFR calculated from Table II. Numbers improved are omitted, since they are unclear.

Mitchell 1980 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Popplewell 2000

Study characteristics

Methods	Randomisation method: not described Not blind Physical
Participants	N = 60 (51 in analyses) Age: 5 to 15 years for 21 children and 22 to 63 years for 39 adults Positive skin prick test
Interventions	Test: high efficiency vacuum cleaner (Electrolux Z1730 and Z5028) Control: standard efficiency vacuum cleaner (Z1501 and Z2630) 1 year
Outcomes	Medication usage, FEV1, PEFR morning and evening, PC20
Notes	No reduction in mite allergens. First author funded by Electrolux. Non-parametric analysis was used but it is not clear what the reported data mean, i.e. whether they are medians, and the authors have only tested the data within groups which also hampers the interpretation. No useful data could be extracted for our meta-analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Reiser 1990

Study characteristics

Methods	Randomisation method: not described Double-blind Chemical
Participants	N = 51 (46 in analyses) Age range 5 to 16 years Positive skin test to D pter
Interventions	Test: mattresses sprayed every 2 weeks for 3 months with natamycin Control: sprayed with placebo 3 months

Reiser 1990 *(Continued)*

Outcomes	Asthma symptoms, medication usage, FEV1, PEFR 3 times a day, histamine bronchial provocation test
Notes	No reduction in mite allergens (ELISA). We used 3 months data, since the intervention was stopped at 3 months (the effect on PC20 was larger after 3 months than after 6 months).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Rijssenbeek 2002

Study characteristics

Methods	Randomisation method: Zelen design with consent after randomisation; method not described Double-blind Physical
Participants	N = 38 (30 in analyses; however, a separate publication from the same year describes only 27 patients in total) Age range 11 to 44 years Positive skin prick test or IgE
Interventions	Test: allergen-impermeable covers for mattress, pillow and bedding (Allergy Control) Control: matching placebo covers 1 year
Outcomes	PEFR morning and evening, FEV1, asthma symptoms, medication use, PC20, quality of life
Notes	Reduction in mite allergens. The study was published twice, both in 2002, with almost the same outcome measures and population, with no cross-references between the articles. Data exist on FEV1, but not published.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Sette 1994

Study characteristics

Methods	Randomisation method: not described Double-blind Chemical
Participants	N = 24 (24 in analyses) Mean age 13 years Skin positive to D pter

Sette 1994 *(Continued)*

Interventions	Test: treatment of mattresses with benzyl benzoate foam (Acarosan) Control: placebo foam Ca 2 weeks
Outcomes	PC20, serum IgE
Notes	No reduction in mite allergens (Acarex test). PC20 read from Fig. 2, weighted averages of the 2 exposure periods were used (1 was added to zero values to get a logarithmic value of zero).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Shapiro 1999

Study characteristics

Methods	Randomisation method: random number generation, sealed and opaque envelopes Double-blind, but intervention frequency differs between the groups Combination
Participants	N = 44 (36 in analyses) Children 6 to 16 years Positive skin prick test
Interventions	Test: dust-mite impermeable covers (Allergen Control Products), delivery of clean blankets and 4 sets of bed linens every month, tannic acid application to the bedroom and living room every month Control: placebo tannic acid every 4 months and phone call reminders 1 year
Outcomes	FEV1, PEFR morning and evening, asthma symptoms, PD20, emergency department visits and admission to hospital, steroid courses
Notes	Reduction in mite allergens. Author provided data on FEV1, but data for symptoms and peak flow were not useable.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Random number generation, sealed and opaque envelopes

Sheikh 2002

Study characteristics

Methods	Randomisation method: centralised, using numbers generated from a random numbers table Double-blind, with blinded data analysis Physical

Sheikh 2002 *(Continued)*

Participants	N = 47 (43 in analyses) Children, aged 5 to 14 years Positive skin prick test
Interventions	Test: mite impermeable covers (Allerayde Perfect) Control: placebo covers 6 months
Outcomes	PEFR, asthma symptoms, night-time waking, use of medication, unscheduled visits to doctor, emergency department visits and admission to hospital (there were none), steroid courses
Notes	Mite antigen levels were not measured. After 2 months, dosage of inhaled steroids could be reduced by 50%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Centralised, using numbers generated from a random numbers table

Sooltangos 1992

Study characteristics

Methods	Randomisation method: "randomly divided into 2 age, sex and symptom-matched groups" Not blind Chemical
Participants	N = 33 (no information on possibly missing recordings) Mean age 34 years Positive skin prick test
Interventions	Test: cleaning and spraying mattresses with acaricide (benzyl benzoate + tannic acid) every 3 months Control: none 8 months
Outcomes	Asthma symptoms, PEFR, FEV1, medication usage
Notes	Abstract only, authors could not be traced

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Thiam 1999

Study characteristics

Methods	Randomisation method: not described

Thiam 1999 *(Continued)*

	Not blind Physical
Participants	N = 24 (24 in analyses) Children, aged 6 to 14 years Positive skin prick test or IgE
Interventions	Test 1: Allergen Control Covers (ACC) and Vellux blankets if own blankets not washed regularly Test 2: HEPA filters (Enviracaire) Control: none 4 months
Outcomes	FEV1, PEFR morning and evening, asthma symptoms, exercise broncho-provocation test
Notes	No reduction in mite allergens. Sponsored by Honeywell. No data shown for PEFR ("did not improve significantly"). We lumped the 2 active groups for the meta-analyses. The corresponding author did not answer our letters.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

van den Bemt 2004

Study characteristics

Methods	Randomisation method: not described ("randomly allocated") Double-blind Physical Intention-to-treat (as long as the patients participated)
Participants	N = 52 (51 in some of the analyses) Positive RAST
Interventions	Test: impermeable mattress, duvet and pillow covers Placebo: permeable covers 9 weeks
Outcomes	Asthma symptoms, PEFR morning and evening, medication use
Notes	Mite antigen reduction of 87%. No useful data in trial report but data obtained from author on PEFR. Very few symptoms in both groups and skewed distribution precluded use in meta-analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

van der Heide 1997A

Study characteristics	
Methods	Randomisation method: not clear whether randomised Double-blind Chemical
Participants	N = 59 (40 in analyses) Mean age 31 years SPT positive to D pter
Interventions	Test: Acarosan powder and foam on textile floors and mattresses Control: Sapur (detergent) on textile floors and Groupriem (detergent) on mattresses 1 year
Outcomes	FEV1, PC20, serum total IgE
Notes	No reduction in mite allergens

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

van der Heide 1997B

Study characteristics	
Methods	Randomisation method: computer using minimisation (2 factors) Double-blind Physical
Participants	N = 30 (for relevant comparison; no information on possibly missing recordings) Age range 18 to 45 years Positive skin prick test
Interventions	Test 1: air-cleaners Test 2: air-cleaners + mattress and pillow covers Control: placebo air-cleaners + mattress and pillow covers 6 months
Outcomes	FEV1, PEFR morning and evening, PC20
Notes	No reduction in mite allergens. Supported by maker of air-cleaners. No data on FEV1 and PEFR and no useable data on PC20.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Computer using minimisation (2 factors)

van der Heide 1999

Study characteristics	
Methods	Cross-over Randomisation method: computer using minimisation (2 factors) Double-blind Physical
Participants	N = 22 (20 in analyses) Mean age 12 years Positive IgE
Interventions	Test: air-cleaners Control: placebo air-cleaners Each period lasted 3 months
Outcomes	Asthma symptoms, FEV1, PEFR morning and evening, PC20
Notes	No data on mite reduction. Supported by maker of air-cleaners. No data on FEV1 and PEFR and no useable data on PC20. Author provided additional data but only at baseline.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	Computer using minimisation (2 factors)

Verrall 1988

Study characteristics	
Methods	Cross-over trial Randomisation method: not described Double-blind Physical
Participants	N = 16 (13 in analyses) Mean age 14 years, range 7 to 27 Positive skin test to D pter
Interventions	Test: HEPA-filter in the bedroom at night Control: non-use of HEPA-filter (foam plug) There were 4 controlled trial phases of 3 weeks each
Outcomes	Asthma symptoms, medication usage (analysed for the final 2 weeks of each 3-week period, allowing 1-week washout for each period), PEFR
Notes	No mite assessment. Medication use read from Fig. 5; no data on symptoms apart from average scores without SD (which did not favour the experimental treatment).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Verrall 1988 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Information not available

Walshaw 1986

Study characteristics	
Methods	Randomisation method: not described Not blind Physical
Participants	N = 50 (42 in analyses) Mean age 34 years Positive skin test to D pter (but only 38 of the 50 were allergic)
Interventions	Test: plastic mattress and pillow covers, vacuum-cleaning, damp dusting of the covers, synthetic or cotton blankets, washing and shaking, linoleum carpets Control: no such measures 1 year
Outcomes	Asthma symptom score, medication use, FEV1, PEFR, PC20, serum immunoglobulins, RAST to D pter
Notes	Mite counts reduced

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Warburton 1994

Study characteristics	
Methods	Cross-over trial Randomisation method: not described Double-blind Physical
Participants	N = 13 (12 in analyses) Mean age 46 years (range 19 to 64) Positive skin test to D pter
Interventions	Test: air filtration unit in the main living room Control: placebo air filtration unit Each period lasted 4 weeks
Outcomes	Asthma symptom score (VAS), medication usage, frequency of nocturnal wakening, FEV1, PEFR twice daily, PD20
Notes	No reduction in mite allergens (ELISA)

Warburton 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Warner 1993

Study characteristics

Methods	Cross-over trial Randomisation method: not described Double-blind Physical
Participants	N = 20 (14 in analyses) Age range 3 to 11 years Positive skin test
Interventions	Test: ioniser (Clean Air) Control: placebo Each period lasted 6 weeks
Outcomes	Asthma symptom score, medication usage, PEFR morning and evening
Notes	Reduction in mite allergens (ELISA)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Warner 2000

Study characteristics

Methods	Randomisation method: not described Double-blind Physical
Participants	N = 40 27 children aged 4 to 16 years and 13 adults aged 20 to 67 years Positive skin prick test
Interventions	Test 1: mechanical ventilation system with heat recovery and high-efficiency vacuum cleaner Test 2: mechanical ventilation system with heat recovery Test 3: high-efficiency vacuum cleaner Control: no intervention 12 months

Warner 2000 *(Continued)*

Outcomes	PEFR morning and evening, FEV1, PC20, asthma symptoms, medication usage
Notes	No reduction in mite allergens. Ten homes that were unsuitable for ventilation system were randomised to test 3 or control. Numbers in each group not stated. No useable data in article.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

Woodcock 2003

Study characteristics

Methods	Randomisation method: co-ordination centre, using minimisation within each practice (3 factors) Double-blind Physical
Participants	N = 1122, N = 732 were mite sensitive (628 of these in analyses) Mean age 36 years Mite sensitisation: serum IgE
Interventions	Test: allergen-impermeable covers for mattress, pillow and quilt (Allergy Control Products) Control: non-impermeable polyester-cotton covers Duration 1 year, after 6 months, controlled reduction in steroid therapy. Dust sampled for mite allergens in a 10% random sample of participants.
Outcomes	PEFR morning and evening, medication usage (beta-agonists), asthma symptoms, exacerbations and hospital visits, days of work missed, quality of life
Notes	Reduction in mite allergens after 6 months. In accordance with the authors who used 6-month data for their power calculation, we used 6-month data for our meta-analysis as this part-investigated the effects of allergen reduction on asthma symptoms and was not confounded by the planned reduction of steroids.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Co-ordination centre, using minimisation within each practice (3 factors)

Wright 2009

Study characteristics

Methods	Random number generator, sequential blocks of 4, automated telephone-answering system
Participants	N = 119 (100 in analyses) Age range 16 to 60 years Positive skin test

Wright 2009 *(Continued)*

Interventions	Test: mechanical heat recovery ventilation system Control: placebo mechanical heat recovery ventilation system Allergen eradication was carried out in all homes. Carpets were cleaned, new pillows, duvets and mattress covers were supplied to all participants.
Outcomes	Peak flow, asthma symptoms, medication usage, visits to hospital
Notes	18 major protocol violators (machine inadvertently turned on)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	See above

Zwemer 1973

Study characteristics

Methods	Cross-over trial Randomisation method: not described Double-blind Physical
Participants	N = 18 (12 in analyses) Age range 6 to 16 years Positive skin tests to house dust
Interventions	Test: active laminar air flow system (Pure-zone system) Control: dummy filter Each period lasted 4 weeks
Outcomes	Asthma symptoms Three patients had sick days in the control group, none in the experimental group
Notes	No assessment of mite reduction. Daytime wheeze was selected blindly as the most relevant variable (other variables yielded closely similar results). Since the data were extremely skewed, the logarithm of the scores was used.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

D pter: *Dermatophagoides pteronyssinus*; D far: *Dermatophagoides farinae*; DP1: D(2) receptor type 1; ELISA: enzyme-linked immunosorbent assay; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; HEPA: high-efficiency particulate air; PD20 provocative dose producing a 20% fall in FEV1; PEFR: peak expiratory flow rate; RAST: radioallergosorbent test; SD: standard deviation; SEM: standard error of the mean; SPT: skin prick test; VAS: visual analogue scale

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

Study	Reason for exclusion
Bowler 1985	Not a RCT against no treatment, N = 12
Brown 1991	Not a RCT
Burr 1988	No clinical data
Carswell 1999	No clinical data
Carter 2001	Only some (exact number not stated) of 104 enrolled patients were allergic to mites; no outcome data or number of patients provided for this group
Chew 1996	No clinical data
Cloosterman 1997	Not asthma
de Blay 2003	No clinical data
Elixmann 1988	Not a RCT
Gallardo 1994	Some patients did not have asthma, but rhinitis (N = 17 in whole trial)
Glasgow 2011	Compares active interventions and co-interventions are not the same in the 2 randomised groups
Griffin 1989	Only published as abstract, author cannot be traced. Acaricide versus placebo (N = 60), FEV 1.86 in both groups after treatment
Hannaway 1993	Not relevant comparison: acaricide + encasings versus carpet cleaner + placebo encasings (N = 23)
Harving 1994	Not a RCT
Hayden 1997	Only 15 of 23 patients were sensitive to mites
Hegarty 1995	Not clear whether randomised and how sensitivity to mites was assessed. No response to letter. Small trial (N = 23), published only as an abstract.
Huss 1991	No clinical data
Huss 1994	No clinical data, authors did not respond to our letters
Hyndman 2000	No clinical data
Joseph 2003	No clinical data, not fully randomised
Korsgaard 1982	Not a RCT
Krieger 2005	Multifactor intervention trial, 274 children. No clear how many were allergic to mites
Lau 2002	No clinical data
Lau-Schadendorf 1991	No clinical data
Leclercq 1985	Unknown whether trial was randomised, authors did not respond to our letters

Study	Reason for exclusion
Massey 1993	No clinical data
Medina 1994	No clinical data, mixture of patients with rhinitis and/or asthma, N = 17
Morgan 2004	Multiple interventions and multiple allergies, 937 children. Furthermore, the intervention group received more home visits than the control group; the study was not blinded and the only positive effects were found on subjective outcomes obtained through telephone interviews; no effect was found on FEV1 or on PEFR. Allergen levels decreased by less than 50%, compared with the control group.
Mosbech 1988	No clinical data
Munir 1993	No clinical data
Murray 1983	Not a RCT
Nambu 2008	Data on asthma symptoms only for 9 of 20 randomised patients
Nishioka 2006	Not a RCT
Olaguibel 1994	No clinical data
Owen 1990	No clinical data
Peroni 1994	Not a RCT
Quek 1994	Not a RCT
Rebmann 1996	Study of mattresses, not patients
Reisman 1990	Only 11 of the 32 patients had asthma (results were quite similar in the 2 groups)
Sarsfield 1974	Not a RCT
Scherr 1977	No information on mite sensitisation. Aimed more generally at filtrating air
Shedd 2007	Failed trial (many missing data, the report describes only 177 of 902 randomised patients) and not clear whether patients were allergic to mites
Sporik 1998	No clinical data
Terreehorst 2005	Only 111 of 224 enrolled patients had asthma; no data for asthma patients separately, and none of the data we included, only modelled quality of life data (SF-36) were available
Tobias 2004	No clinical data and mixture of 24 patients with asthma, rhinitis and atopic dermatitis
Villaveces 1977	13 patients took part, but 15 measurements were made, since 2 patients were measured twice. Authors did not respond to our letters.
Warner 1993B	Not a RCT
Weeks 1995	No clinical data, duplicate publication with Carswell 1999 (see above in this table)
Williams 2006	Multifactor intervention trial and only 93 of the 161 patients were allergic to mites. Trial lasted 14 months; no significant difference in asthma severity scores.

FEV1: forced expiratory volume in 1 second; PEFR: peak expiratory flow rate; RCT: randomised clinical trial.

DATA AND ANALYSES

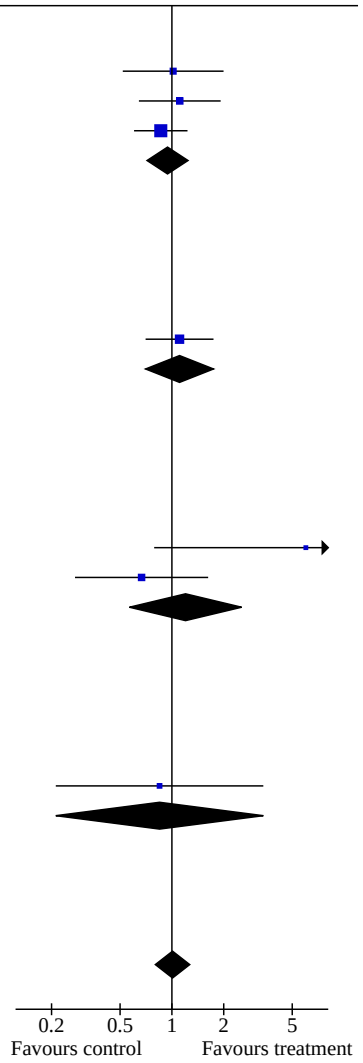
Comparison 1. House dust mite reduction versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Numbers improved	7	338	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.80, 1.27]
1.1.1 Chemical methods	3	138	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.72, 1.24]
1.1.2 Physical methods - parallel-group studies	1	53	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.70, 1.74]
1.1.3 Physical methods - crossover studies	2	98	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.57, 2.54]
1.1.4 Combination methods	1	49	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.21, 3.40]
1.2 Asthma symptoms score	20	1485	Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.16, 0.05]
1.2.1 Chemical methods	4	125	Std. Mean Difference (IV, Fixed, 95% CI)	0.39 [0.04, 0.75]
1.2.2 Physical methods - parallel-group studies	11	1098	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.21, 0.03]
1.2.3 Physical methods - crossover studies	3	70	Std. Mean Difference (IV, Fixed, 95% CI)	-0.48 [-0.97, 0.01]
1.2.4 Combination methods	2	192	Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.29, 0.28]
1.3 Medication usage	11	1115	Std. Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.17, 0.07]
1.3.1 Chemical methods	1	23	Std. Mean Difference (IV, Fixed, 95% CI)	0.89 [0.02, 1.75]
1.3.2 Physical methods - parallel-group studies	7	1020	Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.19, 0.06]
1.3.3 Physical methods - crossover studies	3	72	Std. Mean Difference (IV, Fixed, 95% CI)	-0.17 [-0.64, 0.29]
1.4 FEV1 (forced expiratory volume in one second)	15	675	Std. Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.02, 0.28]
1.4.1 Chemical methods	4	125	Std. Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.41, 0.30]
1.4.2 Physical methods - parallel-group studies	5	249	Std. Mean Difference (IV, Fixed, 95% CI)	0.25 [-0.00, 0.51]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4.3 Physical methods - crossover studies	2	42	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.53, 0.68]
1.4.4 Combination methods	4	259	Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [-0.12, 0.36]
1.5 PEFR morning (Peak Expiratory Flow Rate)	24	1665	Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.08, 0.11]
1.5.1 Chemical methods	4	125	Std. Mean Difference (IV, Fixed, 95% CI)	-0.21 [-0.56, 0.15]
1.5.2 Physical methods - parallel-group studies	12	1162	Std. Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.10, 0.13]
1.5.3 Physical methods - crossover studies	5	154	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.26, 0.37]
1.5.4 Combination methods	3	224	Std. Mean Difference (IV, Fixed, 95% CI)	0.09 [-0.18, 0.35]
1.6 PEFR evening (Peak Expiratory Flow Rate)	13	467	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.13, 0.24]
1.6.1 Chemical methods	2	53	Std. Mean Difference (IV, Fixed, 95% CI)	-0.49 [-1.05, 0.07]
1.6.2 Physical methods - parallel-group studies	6	306	Std. Mean Difference (IV, Fixed, 95% CI)	0.15 [-0.08, 0.37]
1.6.3 Physical methods - crossover studies	4	90	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.35, 0.47]
1.6.4 Combination methods	1	18	Std. Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.96, 0.89]
1.7 PC20 (provocative concentration for 20% fall in FEV1)	13	493	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.13, 0.22]
1.7.1 Chemical methods	5	147	Std. Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.43, 0.23]
1.7.2 Physical methods, parallel-group studies	4	130	Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.27, 0.43]
1.7.3 Physical methods - crossover studies	1	18	Std. Mean Difference (IV, Fixed, 95% CI)	-0.12 [-1.05, 0.80]
1.7.4 Combination methods	4	198	Std. Mean Difference (IV, Fixed, 95% CI)	0.15 [-0.13, 0.43]

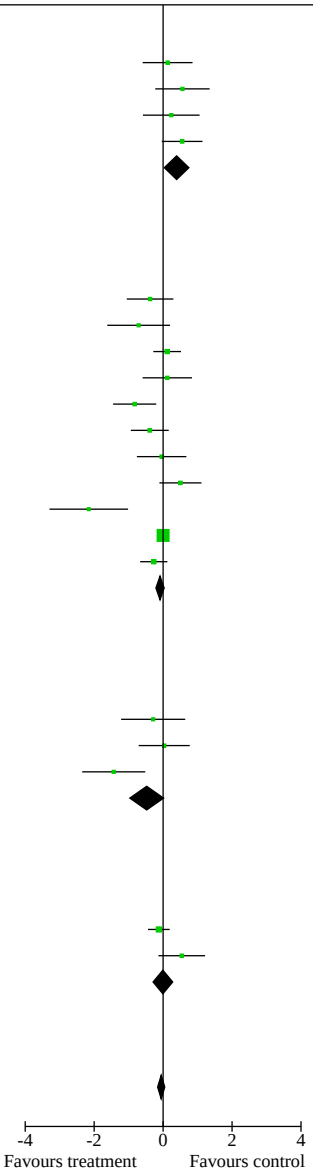
Analysis 1.1. Comparison 1: House dust mite reduction versus control, Outcome 1: Numbers improved

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Chemical methods						
Bahir 1997	7	13	9	17	11.0%	1.02 [0.52 , 2.00]
Geller-Bernst 1995	10	15	9	15	12.7%	1.11 [0.64 , 1.92]
Kroidl 1998	21	37	27	41	36.1%	0.86 [0.60 , 1.23]
Subtotal (95% CI)		**65**		**73**	**59.8%**	**0.94 [0.72 , 1.24]**
Total events:	38		45			
Heterogeneity: Chi² = 0.64, df = 2 (P = 0.73); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.68)						
1.1.2 Physical methods - parallel-group studies						
Burr 1980A	16	26	15	27	20.8%	1.11 [0.70 , 1.74]
Subtotal (95% CI)		**26**		**27**	**20.8%**	**1.11 [0.70 , 1.74]**
Total events:	16		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.44 (P = 0.66)						
1.1.3 Physical methods - cross-over studies						
Burr 1980B	6	21	1	21	1.4%	6.00 [0.79 , 45.63]
Maesen 1977	6	28	9	28	12.7%	0.67 [0.27 , 1.62]
Subtotal (95% CI)		**49**		**49**	**14.1%**	**1.20 [0.57 , 2.54]**
Total events:	12		10			
Heterogeneity: Chi² = 4.09, df = 1 (P = 0.04); I² = 76%						
Test for overall effect: Z = 0.48 (P = 0.63)						
1.1.4 Combination methods						
Carswell 1996	3	23	4	26	5.3%	0.85 [0.21 , 3.40]
Subtotal (95% CI)		**23**		**26**	**5.3%**	**0.85 [0.21 , 3.40]**
Total events:	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.23 (P = 0.82)						
Total (95% CI)		**163**		**175**	**100.0%**	**1.01 [0.80 , 1.27]**
Total events:	69		74			
Heterogeneity: Chi² = 4.89, df = 6 (P = 0.56); I² = 0%						
Test for overall effect: Z = 0.07 (P = 0.94)						
Test for subgroup differences: Chi² = 0.65, df = 3 (P = 0.88), I² = 0%						



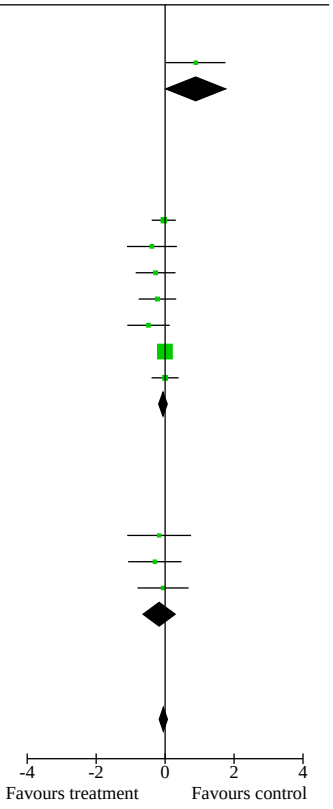
Analysis 1.2. Comparison 1: House dust mite reduction versus control, Outcome 2: Asthma symptoms score

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.2.1 Chemical methods								
Bahir 1997	1.6	1.5	13	1.4	1.5	17	2.0%	0.13 [-0.59 , 0.85]
Chang 1996	1.1	1.7	12	0.4	0.5	14	1.7%	0.56 [-0.23 , 1.35]
Dietemann 1993	1.4	1.24	11	1.18	0.36	12	1.6%	0.24 [-0.58 , 1.06]
Reiser 1990	5.5	4.3	23	3.3	3.5	23	3.0%	0.55 [-0.04 , 1.14]
Subtotal (95% CI)			**59**			**66**	**8.3%**	**0.39 [0.04 , 0.75]**
Heterogeneity: Chi² = 1.10, df = 3 (P = 0.78); I² = 0%								
Test for overall effect: Z = 2.16 (P = 0.03)								
1.2.2 Physical methods - parallel-group studies								
Chen 1996	0.5	0.66	20	0.82	1.01	15	2.3%	-0.38 [-1.05 , 0.30]
Cinti 1996	0.3	0.68	10	1	1.15	10	1.3%	-0.71 [-1.62 , 0.20]
de Vries 2007	1.23	0.86	48	1.13	0.83	48	6.6%	0.12 [-0.28 , 0.52]
Dharmage 2006	-0.02	0.15	15	-0.04	0.17	15	2.1%	0.12 [-0.60 , 0.84]
Fang 2001	10	6.8	22	17.3	10.3	21	2.7%	-0.83 [-1.45 , -0.20]
Huss 1992	8.8	10.7	26	13.1	11.2	26	3.5%	-0.39 [-0.94 , 0.16]
Rijssenbeek 2002	2.25	2.24	16	2.37	3.17	14	2.1%	-0.04 [-0.76 , 0.67]
Sheikh 2002	-3.4	29.5	23	-18.1	27.8	20	2.9%	0.50 [-0.11 , 1.11]
Thiam 1999	0.8	0.5	18	1.8	0.18	6	0.8%	-2.16 [-3.30 , -1.02]
Woodcock 2003	1.03	0.7	315	1.03	0.73	310	43.1%	0.00 [-0.16 , 0.16]
Wright 2009	1.5	1.1	53	1.8	1.1	47	6.8%	-0.27 [-0.67 , 0.12]
Subtotal (95% CI)			**566**			**532**	**74.1%**	**-0.09 [-0.21 , 0.03]**
Heterogeneity: Chi² = 28.61, df = 10 (P = 0.001); I² = 65%								
Test for overall effect: Z = 1.46 (P = 0.14)								
1.2.3 Physical methods - cross-over studies								
Antonicelli 1991	0.16	0.32	9	0.26	0.34	9	1.2%	-0.29 [-1.22 , 0.64]
Warner 1993	0.2	0.26	14	0.19	0.34	14	1.9%	0.03 [-0.71 , 0.77]
Zwemer 1973	0.7	0.51	12	1.4	0.43	12	1.3%	-1.43 [-2.35 , -0.52]
Subtotal (95% CI)			**35**			**35**	**4.4%**	**-0.48 [-0.97 , 0.01]**
Heterogeneity: Chi² = 6.17, df = 2 (P = 0.05); I² = 68%								
Test for overall effect: Z = 1.91 (P = 0.06)								
1.2.4 Combination methods								
Cloosterman 1999	5.5	6.1	76	6.3	6.7	81	10.8%	-0.12 [-0.44 , 0.19]
Marks 1994	0.98	0.57	17	0.67	0.55	18	2.3%	0.54 [-0.14 , 1.22]
Subtotal (95% CI)			**93**			**99**	**13.1%**	**-0.01 [-0.29 , 0.28]**
Heterogeneity: Chi² = 3.06, df = 1 (P = 0.08); I² = 67%								
Test for overall effect: Z = 0.05 (P = 0.96)								
Total (95% CI)			**753**			**732**	**100.0%**	**-0.06 [-0.16 , 0.05]**
Heterogeneity: Chi² = 48.25, df = 19 (P = 0.0002); I² = 61%								
Test for overall effect: Z = 1.05 (P = 0.29)								
Test for subgroup differences: Chi² = 9.31, df = 3 (P = 0.03), I² = 67.8%								



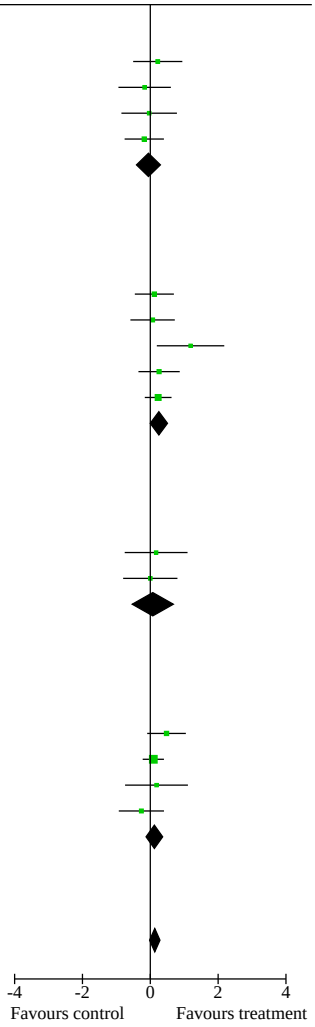
Analysis 1.3. Comparison 1: House dust mite reduction versus control, Outcome 3: Medication usage

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.3.1 Chemical methods								
Dietemann 1993	2	0.55	11	1.54	0.45	12	1.9%	0.89 [0.02 , 1.75]
Subtotal (95% CI)			**11**			**12**	**1.9%**	**0.89 [0.02 , 1.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.01 (P = 0.04)								
1.3.2 Physical methods - parallel-group studies								
de Vries 2007	473	441	63	490	420	63	11.4%	-0.04 [-0.39 , 0.31]
Dharmage 2006	-0.36	0.48	15	-0.2	0.32	15	2.7%	-0.38 [-1.10 , 0.34]
Halken 2003	227	193	26	291	266	21	4.2%	-0.28 [-0.85 , 0.30]
Huss 1992	4.38	3.71	26	5.23	3.79	26	4.7%	-0.22 [-0.77 , 0.32]
Walshaw 1986	2.18	1.8	22	3.56	3.61	20	3.7%	-0.48 [-1.10 , 0.13]
Woodcock 2003	2.23	2.03	312	2.24	1.81	311	56.2%	-0.01 [-0.16 , 0.15]
Wright 2009	3.5	2.8	53	3.5	3.4	47	9.0%	0.00 [-0.39 , 0.39]
Subtotal (95% CI)			**517**			**503**	**91.7%**	**-0.06 [-0.19 , 0.06]**
Heterogeneity: Chi² = 4.02, df = 6 (P = 0.67); I² = 0%								
Test for overall effect: Z = 0.99 (P = 0.32)								
1.3.3 Physical methods - cross-over studies								
Antonicelli 1991	0.02	0.05	9	0.03	0.06	9	1.6%	-0.17 [-1.10 , 0.75]
Verrall 1988	6.81	6.73	13	9.13	8.23	13	2.3%	-0.30 [-1.07 , 0.47]
Warner 1993	0.48	0.67	14	0.53	0.94	14	2.5%	-0.06 [-0.80 , 0.68]
Subtotal (95% CI)			**36**			**36**	**6.5%**	**-0.17 [-0.64 , 0.29]**
Heterogeneity: Chi² = 0.19, df = 2 (P = 0.91); I² = 0%								
Test for overall effect: Z = 0.73 (P = 0.46)								
Total (95% CI)			**564**			**551**	**100.0%**	**-0.05 [-0.17 , 0.07]**
Heterogeneity: Chi² = 9.02, df = 10 (P = 0.53); I² = 0%								
Test for overall effect: Z = 0.86 (P = 0.39)								
Test for subgroup differences: Chi² = 4.81, df = 2 (P = 0.09), I² = 58.4%								



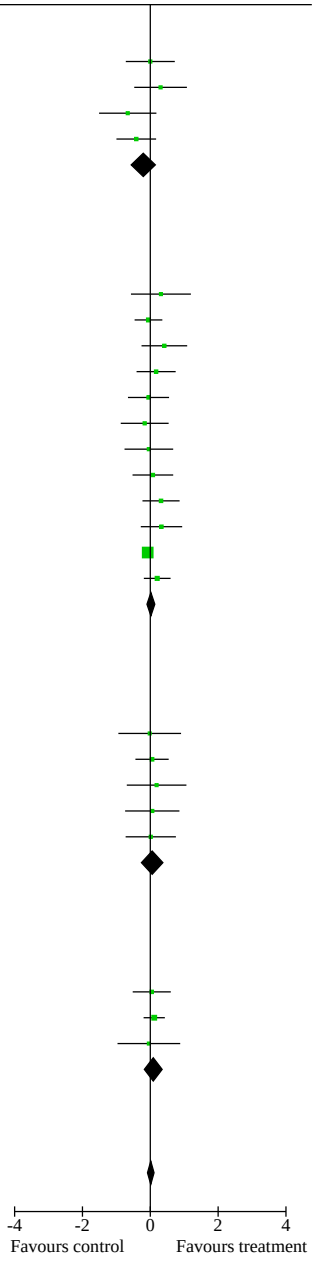
Analysis 1.4. Comparison 1: House dust mite reduction versus control, Outcome 4: FEV1 (forced expiratory volume in one second)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.4.1 Chemical methods								
Bahir 1997	80	8.8	13	77.5	12.5	17	4.4%	0.22 [-0.50 , 0.94]
Chang 1996	87	20	12	90	15	14	3.9%	-0.17 [-0.94 , 0.61]
Dietemann 1993	72.33	11.87	11	72.79	14.78	12	3.5%	-0.03 [-0.85 , 0.79]
Reiser 1990	76	12.5	23	78.5	15	23	6.9%	-0.18 [-0.76 , 0.40]
Subtotal (95% CI)			**59**			**66**	**18.7%**	**-0.05 [-0.41 , 0.30]**
Heterogeneity: Chi² = 0.81, df = 3 (P = 0.85); I² = 0%								
Test for overall effect: Z = 0.30 (P = 0.76)								
1.4.2 Physical methods - parallel-group studies								
Halken 2003	2.51	0.77	26	2.42	0.7	21	7.0%	0.12 [-0.46 , 0.70]
Shapiro 1999	2.11	1.03	19	2.05	0.62	17	5.4%	0.07 [-0.59 , 0.72]
Thiam 1999	1.7	0.3	18	1.3	0.4	6	2.4%	1.19 [0.19 , 2.18]
Walshaw 1986	77.4	9.18	22	74.7	11.25	20	6.3%	0.26 [-0.35 , 0.87]
Wright 2009	86.6	18.1	53	82.5	16.9	47	15.0%	0.23 [-0.16 , 0.63]
Subtotal (95% CI)			**138**			**111**	**36.1%**	**0.25 [-0.00 , 0.51]**
Heterogeneity: Chi² = 3.91, df = 4 (P = 0.42); I² = 0%								
Test for overall effect: Z = 1.95 (P = 0.05)								
1.4.3 Physical methods - cross-over studies								
Antonicelli 1991	3.27	0.73	9	3.13	0.82	9	2.7%	0.17 [-0.75 , 1.10]
Warburton 1994	1.88	0.78	12	1.88	0.77	12	3.6%	0.00 [-0.80 , 0.80]
Subtotal (95% CI)			**21**			**21**	**6.3%**	**0.07 [-0.53 , 0.68]**
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.24 (P = 0.81)								
1.4.4 Combination methods								
Carswell 1996	105	10.2	23	98.6	15.3	26	7.2%	0.48 [-0.09 , 1.05]
Cloosterman 1999	81.3	10.9	76	80.2	13.5	81	23.7%	0.09 [-0.22 , 0.40]
Dorward 1988	2.74	0.81	9	2.61	0.51	9	2.7%	0.18 [-0.74 , 1.11]
Marks 1994	90.3	17.8	17	96.2	25.2	18	5.2%	-0.26 [-0.93 , 0.40]
Subtotal (95% CI)			**125**			**134**	**38.8%**	**0.12 [-0.12 , 0.36]**
Heterogeneity: Chi² = 2.85, df = 3 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.96 (P = 0.34)								
Total (95% CI)			**343**			**332**	**100.0%**	**0.13 [-0.02 , 0.28]**
Heterogeneity: Chi² = 9.63, df = 14 (P = 0.79); I² = 0%								
Test for overall effect: Z = 1.70 (P = 0.09)								
Test for subgroup differences: Chi² = 1.99, df = 3 (P = 0.58), I² = 0%								



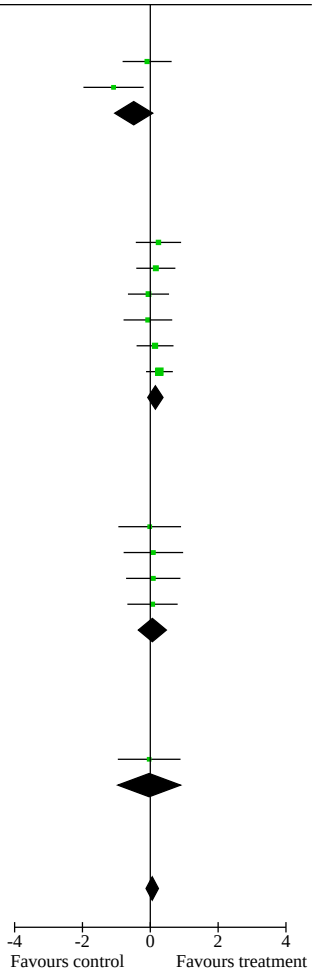
Analysis 1.5. Comparison 1: House dust mite reduction versus control, Outcome 5: PEFR morning (Peak Expiratory Flow Rate)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.5.1 Chemical methods								
Bahir 1997	262	82	13	262	82	17	1.8%	0.00 [-0.72 , 0.72]
Chang 1996	411	75	12	383	100	14	1.5%	0.30 [-0.47 , 1.08]
Dietemann 1993	67.88	11.28	11	75.37	10.46	12	1.3%	-0.66 [-1.51 , 0.18]
Reiser 1990	92	20	23	100	18	23	2.7%	-0.41 [-1.00 , 0.17]
Subtotal (95% CI)			**59**			**66**	**7.3%**	**-0.21 [-0.56 , 0.15]**
Heterogeneity: Chi² = 3.58, df = 3 (P = 0.31); I² = 16%								
Test for overall effect: Z = 1.14 (P = 0.25)								
1.5.2 Physical methods - parallel-group studies								
Cinti 1996	98.2	22.7	10	91.8	15.8	10	1.2%	0.31 [-0.57 , 1.20]
de Vries 2007	457	145	47	464	111	45	5.6%	-0.05 [-0.46 , 0.36]
Fang 2001	349	96	19	304	117	16	2.0%	0.41 [-0.26 , 1.09]
Halken 2003	358	96	26	342	86	21	2.8%	0.17 [-0.40 , 0.75]
Lee 2003	88.6	13.66	22	89.43	17.33	20	2.5%	-0.05 [-0.66 , 0.55]
Luczynska 2003	367	156	16	388	75	15	1.9%	-0.17 [-0.87 , 0.54]
Rijssenbeek 2002	435	115	16	440	115	14	1.8%	-0.04 [-0.76 , 0.68]
Sheikh 2002	16.38	25.62	23	13.68	43.14	20	2.6%	0.08 [-0.52 , 0.68]
van den Bemt 2004	431	115	26	395	109	26	3.1%	0.32 [-0.23 , 0.86]
Walshaw 1986	407	112	22	369	114	20	2.5%	0.33 [-0.28 , 0.94]
Woodcock 2003	429.3	91.7	313	436.2	88.8	315	37.9%	-0.08 [-0.23 , 0.08]
Wright 2009	419.2	127.9	53	395.8	96	47	6.0%	0.20 [-0.19 , 0.60]
Subtotal (95% CI)			**593**			**569**	**69.9%**	**0.02 [-0.10 , 0.13]**
Heterogeneity: Chi² = 6.93, df = 11 (P = 0.80); I² = 0%								
Test for overall effect: Z = 0.30 (P = 0.77)								
1.5.3 Physical methods - cross-over studies								
Antonicelli 1991	443	106	9	445	117	9	1.1%	-0.02 [-0.94 , 0.91]
Burr 1976	335	111	32	329	118	32	3.9%	0.05 [-0.44 , 0.54]
Mitchell 1980	67	15	10	64.3	12.7	10	1.2%	0.19 [-0.69 , 1.06]
Warburton 1994	350	101	12	344	97	12	1.4%	0.06 [-0.74 , 0.86]
Warner 1993	232.6	88	14	231.3	97	14	1.7%	0.01 [-0.73 , 0.75]
Subtotal (95% CI)			**77**			**77**	**9.3%**	**0.06 [-0.26 , 0.37]**
Heterogeneity: Chi² = 0.12, df = 4 (P = 1.00); I² = 0%								
Test for overall effect: Z = 0.34 (P = 0.73)								
1.5.4 Combination methods								
Carswell 1996	99.6	17.8	23	98.9	14.5	26	2.9%	0.04 [-0.52 , 0.60]
Cloosterman 1999	544	132	76	529	126	81	9.5%	0.12 [-0.20 , 0.43]
Dorward 1988	388	106	9	392	71	9	1.1%	-0.04 [-0.97 , 0.88]
Subtotal (95% CI)			**108**			**116**	**13.5%**	**0.09 [-0.18 , 0.35]**
Heterogeneity: Chi² = 0.13, df = 2 (P = 0.94); I² = 0%								
Test for overall effect: Z = 0.65 (P = 0.52)								
Total (95% CI)			**837**			**828**	**100.0%**	**0.01 [-0.08 , 0.11]**
Heterogeneity: Chi² = 12.61, df = 23 (P = 0.96); I² = 0%								
Test for overall effect: Z = 0.28 (P = 0.78)								
Test for subgroup differences: Chi² = 1.85, df = 3 (P = 0.60), I² = 0%								

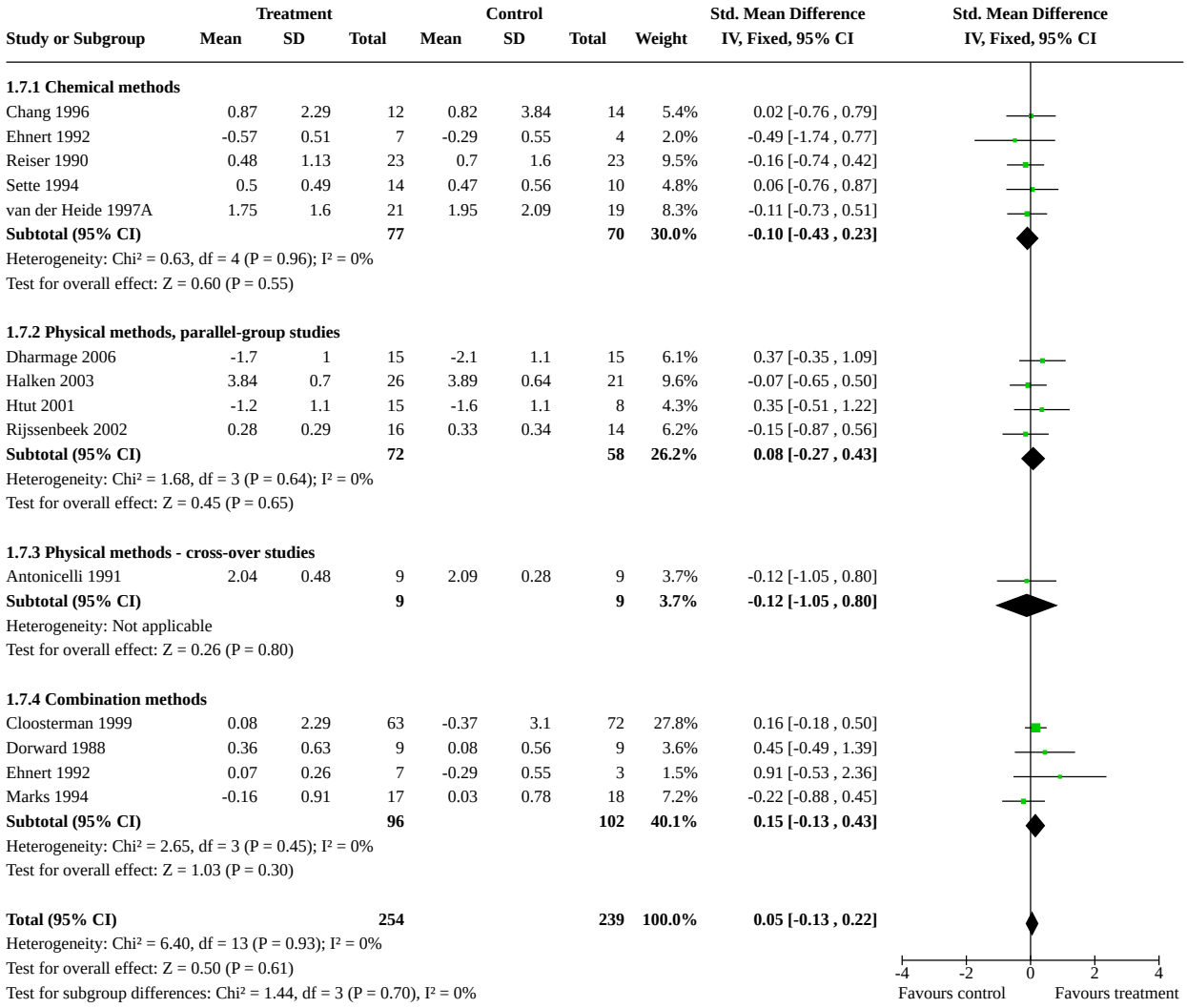


Analysis 1.6. Comparison 1: House dust mite reduction versus control, Outcome 6: PEFR evening (Peak Expiratory Flow Rate)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.6.1 Chemical methods								
Bahir 1997	263	83	13	271	83	17	6.4%	-0.09 [-0.82 , 0.63]
Dietemann 1993	67.16	11.03	11	79.23	10.46	12	4.2%	-1.08 [-1.97 , -0.20]
Subtotal (95% CI)			**24**			**29**	**10.6%**	**-0.49 [-1.05 , 0.07]**
Heterogeneity: Chi² = 2.87, df = 1 (P = 0.09); I² = 65%								
Test for overall effect: Z = 1.71 (P = 0.09)								
1.6.2 Physical methods - parallel-group studies								
Fang 2001	368	95	19	341	125	16	7.5%	0.24 [-0.43 , 0.91]
Halken 2003	363	95	26	348	84	21	10.1%	0.16 [-0.41 , 0.74]
Lee 2003	90.27	13.46	22	91.1	17.28	20	9.1%	-0.05 [-0.66 , 0.55]
Rijssenbeek 2002	445	114	16	454	134	14	6.5%	-0.07 [-0.79 , 0.65]
van den Bemt 2004	437	119	26	421	106	26	11.3%	0.14 [-0.40 , 0.68]
Wright 2009	436.1	124.7	53	405.9	93.4	47	21.5%	0.27 [-0.12 , 0.66]
Subtotal (95% CI)			**162**			**144**	**65.9%**	**0.15 [-0.08 , 0.37]**
Heterogeneity: Chi² = 1.22, df = 5 (P = 0.94); I² = 0%								
Test for overall effect: Z = 1.30 (P = 0.19)								
1.6.3 Physical methods - cross-over studies								
Antonicelli 1991	442	105	9	444	116	9	3.9%	-0.02 [-0.94 , 0.91]
Mitchell 1980	72	12.1	10	70.9	11	10	4.3%	0.09 [-0.79 , 0.97]
Warburton 1994	370	87	12	362	90	12	5.2%	0.09 [-0.71 , 0.89]
Warner 1993	239.2	92	14	232.8	98	14	6.1%	0.07 [-0.68 , 0.81]
Subtotal (95% CI)			**45**			**45**	**19.6%**	**0.06 [-0.35 , 0.47]**
Heterogeneity: Chi² = 0.04, df = 3 (P = 1.00); I² = 0%								
Test for overall effect: Z = 0.29 (P = 0.77)								
1.6.4 Combination methods								
Dorward 1988	392	103	9	395	65	9	3.9%	-0.03 [-0.96 , 0.89]
Subtotal (95% CI)			**9**			**9**	**3.9%**	**-0.03 [-0.96 , 0.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.07 (P = 0.94)								
Total (95% CI)			**240**			**227**	**100.0%**	**0.06 [-0.13 , 0.24]**
Heterogeneity: Chi² = 8.46, df = 12 (P = 0.75); I² = 0%								
Test for overall effect: Z = 0.61 (P = 0.54)								
Test for subgroup differences: Chi² = 4.33, df = 3 (P = 0.23), I² = 30.7%								



Analysis 1.7. Comparison 1: House dust mite reduction versus control, Outcome 7: PC20 (provocative concentration for 20% fall in FEV1)



Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.7.1 Chemical methods								
Chang 1996	0.87	2.29	12	0.82	3.84	14	5.4%	0.02 [-0.76 , 0.79]
Ehnert 1992	-0.57	0.51	7	-0.29	0.55	4	2.0%	-0.49 [-1.74 , 0.77]
Reiser 1990	0.48	1.13	23	0.7	1.6	23	9.5%	-0.16 [-0.74 , 0.42]
Sette 1994	0.5	0.49	14	0.47	0.56	10	4.8%	0.06 [-0.76 , 0.87]
van der Heide 1997A	1.75	1.6	21	1.95	2.09	19	8.3%	-0.11 [-0.73 , 0.51]
Subtotal (95% CI)			**77**			**70**	**30.0%**	**-0.10 [-0.43 , 0.23]**
Heterogeneity: Chi² = 0.63, df = 4 (P = 0.96); I² = 0%								
Test for overall effect: Z = 0.60 (P = 0.55)								
1.7.2 Physical methods, parallel-group studies								
Dharmage 2006	-1.7	1	15	-2.1	1.1	15	6.1%	0.37 [-0.35 , 1.09]
Halken 2003	3.84	0.7	26	3.89	0.64	21	9.6%	-0.07 [-0.65 , 0.50]
Htut 2001	-1.2	1.1	15	-1.6	1.1	8	4.3%	0.35 [-0.51 , 1.22]
Rijssenbeek 2002	0.28	0.29	16	0.33	0.34	14	6.2%	-0.15 [-0.87 , 0.56]
Subtotal (95% CI)			**72**			**58**	**26.2%**	**0.08 [-0.27 , 0.43]**
Heterogeneity: Chi² = 1.68, df = 3 (P = 0.64); I² = 0%								
Test for overall effect: Z = 0.45 (P = 0.65)								
1.7.3 Physical methods - cross-over studies								
Antonicelli 1991	2.04	0.48	9	2.09	0.28	9	3.7%	-0.12 [-1.05 , 0.80]
Subtotal (95% CI)			**9**			**9**	**3.7%**	**-0.12 [-1.05 , 0.80]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.26 (P = 0.80)								
1.7.4 Combination methods								
Cloosterman 1999	0.08	2.29	63	-0.37	3.1	72	27.8%	0.16 [-0.18 , 0.50]
Dorward 1988	0.36	0.63	9	0.08	0.56	9	3.6%	0.45 [-0.49 , 1.39]
Ehnert 1992	0.07	0.26	7	-0.29	0.55	3	1.5%	0.91 [-0.53 , 2.36]
Marks 1994	-0.16	0.91	17	0.03	0.78	18	7.2%	-0.22 [-0.88 , 0.45]
Subtotal (95% CI)			**96**			**102**	**40.1%**	**0.15 [-0.13 , 0.43]**
Heterogeneity: Chi² = 2.65, df = 3 (P = 0.45); I² = 0%								
Test for overall effect: Z = 1.03 (P = 0.30)								
Total (95% CI)			**254**			**239**	**100.0%**	**0.05 [-0.13 , 0.22]**
Heterogeneity: Chi² = 6.40, df = 13 (P = 0.93); I² = 0%								
Test for overall effect: Z = 0.50 (P = 0.61)								
Test for subgroup differences: Chi² = 1.44, df = 3 (P = 0.70), I² = 0%								

APPENDICES

Appendix 1. Sources and search methods for the Cochrane Airways Group Specialised Register (CAGR)

Electronic searches: core databases

Database	Frequency of search
MEDLINE (Ovid)	Weekly
EMBASE (Ovid)	Weekly
CENTRAL (*T he Cochrane Library*)	Quarterly (4 issues per year)
PSYCINFO (Ovid)	Monthly

(Continued)

CINAHL (EBSCO)	Monthly
AMED (EBSCO)	Monthly

Handsearches: core respiratory conference abstracts

Conference	Years searched
American Academy of Allergy, Asthma and Immunology (AAAAI)	2001 onwards
American Thoracic Society (ATS)	2001 onwards
Asia Pacific Society of Respirology (APSR)	2004 onwards
British Thoracic Society Winter Meeting (BTS)	2000 onwards
Chest Meeting	2003 onwards
European Respiratory Society (ERS)	1992, 1994, 2000 onwards
International Primary Care Respiratory Group Congress (IPCRG)	2002 onwards
Thoracic Society of Australia and New Zealand (TSANZ)	1999 onwards

Condition search

1. exp Asthma/
2. asthma$.mp.
3. (antiasthma$ or anti-asthma$).mp.
4. Respiratory Sounds/
5. wheez$.mp.
6. Bronchial Spasm/
7. bronchospas$.mp.
8. (bronch$ adj3 spasm$).mp.
9. bronchoconstrict$.mp.
10. exp Bronchoconstriction/
11. (bronch$ adj3 constrict$).mp.
12. Bronchial Hyperreactivity/
13. Respiratory Hypersensitivity/
14. ((bronchial$ or respiratory or airway$ or lung$) adj3 (hypersensitiv$ or hyperreactiv$ or allerg$ or insufficiency)).mp.

15. ((dust or mite$) adj3 (allerg$ or hypersensitiv$)).mp.

16. or/1-15

17. exp Aspergillosis, Allergic Bronchopulmonary/

18. lung diseases, fungal/

19. aspergillosis/

20. 18 and 19

21. (bronchopulmonar$ adj3 aspergillosis).mp.

22. 17 or 20 or 21

23. 16 or 22

24. Lung Diseases, Obstructive/

25. exp Pulmonary Disease, Chronic Obstructive/

26. emphysema$.mp.

27. (chronic$ adj3 bronchiti$).mp.

28. (obstruct$ adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).mp.

29. COPD.mp.

30. COAD.mp.

31. COBD.mp.

32. AECB.mp.

33. or/24-32

34. exp Bronchiectasis/

35. bronchiect$.mp.

36. bronchoect$.mp.

37. kartagener$.mp.

38. (ciliary adj3 dyskinesia).mp.

39. (bronchial$ adj3 dilat$).mp.

40. or/34-39

41. exp Sleep Apnea Syndromes/

42. (sleep$ adj3 (apnea$ or apnoea$)).mp.

43. (hypopnea$ or hypopnoea$).mp.

44. OSA.mp.

45. SHS.mp.

46. OSAHS.mp.

47. or/41-46

48. Lung Diseases, Interstitial/

49. Pulmonary Fibrosis/

50. Sarcoidosis, Pulmonary/

51. (interstitial$ adj3 (lung$ or disease$ or pneumon$)).mp.

52. ((pulmonary$ or lung$ or alveoli$) adj3 (fibros$ or fibrot$)).mp.

53. ((pulmonary$ or lung$) adj3 (sarcoid$ or granulom$)).mp.

54. or/48-53

55. 23 or 33 or 40 or 47 or 54

Filter to identify RCTs

1. exp "clinical trial [publication type]"/

2. (randomized or randomised).ab,ti.

3. placebo.ab,ti.

4. dt.fs.

5. randomly.ab,ti.

6. trial.ab,ti.

7. groups.ab,ti.

8. or/1-7

9. Animals/

10. Humans/

11. 9 not (9 and 10)

12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases

WHAT'S NEW

Date	Event	Description
14 July 2021	Amended	Editorial note added.

HISTORY

Protocol first published: Issue 1, 1996
Review first published: Issue 3, 1998

Date	Event	Description
12 July 2011	New search has been performed	One new trial added (Wright 2009). No changes to conclusions made. Minor copy edits made.
28 July 2008	Amended	Converted to new review format.
19 December 2007	New citation required and conclusions have changed	Five new included studies added (de Vries 2007; Dharmage 2006; Fang 2001; Ghazala 2004; van den Bemt 2004), one new exclud-

Date	Event	Description
		ed study added (Shedd 2007). The conclusions of the review have not altered substantially.

CONTRIBUTIONS OF AUTHORS

PCG and HKJ selected the trials for inclusion in the update of the review. Trials were reviewed by the authors, outcome data were extracted primarily by PCG (but checked by HKJ). Guarantors: both authors for the text, PCG for the statistical calculations.

(Cecilia Hammarquist and Michael Burr selected trials for inclusion for the first version of the review, Lasse Schmidt for the third version. The first manuscript was drafted by CH for *The Cochrane Library* and by PCG for the *British Medical Journal*).

DECLARATIONS OF INTEREST

None.

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- Nordic Council of Ministers, Denmark
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INDEX TERMS

Medical Subject Headings (MeSH)

Allergens [*immunology]; Asthma [immunology] [*prevention & control]; Dust; *Environment, Controlled; *Insecticides; Mites [*immunology]; Randomized Controlled Trials as Topic

MeSH check words

Animals; Humans