

# House dust mite control measures for asthma (Review)

Gøtzsche PC, Johansen HK



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## 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 strategy

PubMed and The Cochrane Library (last searches Nov 2007), reference lists.

### Selection criteria

Randomised trials of mite control measures vs 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. Trial authors were contacted to clarify information.

### Main results

Fifty-four trials (3002 patients) were included. Thirty-six trials assessed physical methods (26 mattress encasings), 10 chemical methods, and 8 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 (1565 patients), the standardised mean difference was 0.00 (95% confidence interval (CI) -0.10 to 0.10). There were no statistically significant differences either in number of patients improved (relative risk 1.01, 95% CI 0.80 to 1.27), asthma symptom scores (standardised mean difference -0.04, 95% CI -0.15 to 0.07), or in medication usage (standardised mean difference -0.06, 95% CI -0.18 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

House dust mite control measures for asthma

The major allergen in house dust comes from mites. Chemical and physical methods of reducing mite allergen levels are intended to reduce asthma symptoms in people who are sensitive to house dust mites. The review did not find an effect of control measures to reduce the exposure to mites or their products.

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House dust mite control measures for asthma (Review)

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## BACKGROUND

Asthma is a chronic inflammatory disorder of the airways. The prevalence has increased and it is now the commonest chronic disease among children. The treatment of asthma is both pharmacological, including immunotherapy (Abramson 1995; Vervloet 1990), 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 (Götsche 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.

## CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

### Types of studies

Randomised trials; we accepted reports in any language. Since some mite control measures are impossible to blind, we accepted non-blinded trials.

### Types of participants

The participants were all diagnosed as having bronchial asthma by a physician. Their mite sensitisation was assessed by skin testing,

bronchial provocation tests or serum assays for specific IgE antibodies.

### Types of intervention

Test: 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

See: Cochrane Airways Group methods used in reviews.

PubMed from 1966 onwards was searched with the terms mite\* AND asthma\*, combined with one or more of the following: random\* OR control\* OR blind\* (last search November 2007). The Cochrane Library was searched with the terms mite\* AND asthma\* (last search November 2007). There was no restriction by language. We also checked the bibliography of each trial report for additional references.

## METHODS OF THE REVIEW

The authors independently selected the trials for inclusion. 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. The adequacy of the allocation concealment was judged according to the Cochrane Collaboration guidelines. When it was not stated at what time of the day the peak flow had been recorded, we assumed it was in the morning. Any ambiguities were resolved by discussion. When necessary we contacted the trial authors for clarification.

**Statistical methods** We calculated 95% confidence intervals (CI) with a fixed effect model. Heterogeneity was tested with the chi-square test and its magnitude was assessed as I square (that gives the amount of between-trial variation in relation to the total variation). If there was heterogeneity ( $P < 0.10$ ), the reasons were explored.

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 continuous data were 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 per cent 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 skew. 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.

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.

## DESCRIPTION OF STUDIES

We included 54 trials (3002 patients) which is an addition of 5 trials since the last update of our review (Gøtzsche 2004). 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 (Charpin 1990; Frederick 1997; Ghazala 2004; Howarth 1992; Jooma 1995; Korsgaard 1983; Manjra 1994; Shapiro 1999; Sooltangos 1992; van der Heide 1997B; van der Heide 1999); 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 Table: Characteristics of included studies). The most frequently reported outcome was PEFR in the morning (1565 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' (Maesen 1977; Zwemer 1973). In three trials, sensitivity was established by specific serum IgE (Luczynska 2003; van der Heide 1999; Woodcock 2003), in two trials by either skin prick testing or IgE (Rijssenbeek 2002; Thiam 1999), and in one trial published only as an abstract, the means of diagnosis was not given (Howarth 1992).

Thirty-six trials used physical methods to reduce exposure to mites, ten used chemical methods, and eight used a combination of chemical and physical methods (see table: Characteristics of included studies). Twenty-six of the trials had used mattress encasings (Burr 1976; Burr 1980B; Carswell 1996; Chen 1996; Cinti 1996; Cloosterman 1999; de Vries 2007; Dharmage 2006; Ehnert 1992; Frederick 1997; Ghazala 2004; Gillies 1987; Halken 2003; Howarth 1992; Jooma 1995; Lee 2003; Luczynska 2003; Marks 1994; Rijssenbeek 2002; Shapiro 1999; Sheikh 2002; Thiam 1999; van den Bemt 2004; van der Heide 1997B; Walshaw 1986; Woodcock 2003). Mite reduction occurred in 17 trials (Carswell 1996; Charpin 1990; Cloosterman 1999; de Vries 2007; Dharmage 2006; Dorward 1988; Fang 2001; Frederick 1997; Halken 2003; Htut 2001; Huss 1992; Rijssenbeek 2002; Shapiro 1999; van den Bemt 2004; Walshaw 1986; Warner 1993; Woodcock 2003), reduction was unsuccessful in 24 and was not measured or reported in the remaining 13 trials.

## METHODOLOGICAL QUALITY

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), 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), coordination 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 (Halken 2003; Gøtzsche 2003), and in another, the intervention frequency differed between the groups (Shapiro 1999). One trial maintained the blinding during data analysis (Sheikh 2002).

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

## RESULTS

We did not find an effect of control measures to reduce the exposure to mites or their products in the 54 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, relative risk 1.01 (95% CI 0.80 to 1.27) (data available for 7 trials).

Asthma symptom scores were very heterogeneous ( $P = 0.0002$  for test of heterogeneity, I-square 62%) (19 trials). The heterogeneity was caused by two small trials of poor quality that were the only ones that reported a significantly positive effect (Thiam 1999; Zwemer 1973). The standardised mean difference for all trials was  $-0.04$  (95% CI  $-0.15$  to  $0.07$ ). After exclusion of the two trials of poor quality, the standardised mean difference was  $-0.00$  (95% CI  $-0.11$  to  $0.11$ ).

Medication usage was very similar in the experimental and control groups (10 trials). The standardised mean difference was  $-0.06$  (95% CI  $-0.18$  to  $0.07$ ). 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 standardised mean difference is  $-0.08$  (95% CI  $-0.20$  to  $0.05$ ).

For FEV1, the standardised mean difference was  $0.11$  (95% CI  $-0.05$  to  $0.28$ ) (14 trials). 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 standardised mean difference is  $0.08$  (95% CI  $-0.08$  to  $0.25$ ).

For peak flow in the morning, the standardised mean difference was  $0.00$  (95% CI  $-0.10$  to  $0.10$ ) (23 trials). For peak flow in the evening, the standardised mean difference was also  $0.00$  (95% CI  $-0.21$  to  $0.21$ ) (12 trials).

For PC 20 was, the standardised mean difference was  $0.05$  (95% CI  $-0.13$  to  $0.22$ ) (13 trials).

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 twelve subjects 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

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 also be 300 L/min, with a 95% confidence interval that ranges from 290 to 310 (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 1339 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).

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 subjects' 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).

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 6 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 6 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.

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 FEV1 and 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 monofaceted 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 to compare these modalities directly in randomised trials (van Schayck 2007).

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 7 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 nonrandomised studies, and the most quoted nonrandomised study had included only 10 patients per group but claimed very positive results (Schmidt 2005). The recently published, very extensive US guidelines for asthma control (US Guidelines 2007) were also misleading. On p. 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 as no outcome data were provided for this group, and one is not relevant as it involved multiple interventions and allergens. What remains are

only five trials and these did not show an effect of mattress encasings.

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.

## 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.

## POTENTIAL CONFLICT OF INTEREST

None.

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\*Indicates the major publication for the study

**TABLES****Characteristics of included studies**

Study	Antonicelli 1991
Methods	Cross-over trial. Randomisation method: not described. Not blind (apart from PD20). Physical.
Participants	N=9 (9 in analyses). Mean age 16 yr (range 10-28). Skin positive to D pter and D far.
Interventions	Test : HEPA-filter (Enviracaire) in bedroom for 8 wks. Control : none. Each period lasted 8 weeks.
Outcomes	Daily symptom score (scale 0-3), 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.
Allocation concealment	B – Unclear

Study	Bahir 1997
Methods	Randomisation method: not described. Double-blind. Chemical.
Participants	N=40 children (30 in analyses), age range 6-17 yr). Skin positive to D pter and/or D far.

**Characteristics of included studies (Continued)**

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.
Allocation concealment	B – Unclear

**Study Burr 1976**

Methods	Cross-over trial. Randomisation method: not described. Not blind. Physical.
Participants	N=32 (32 in analyses). Mean age: 33 yr. 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.
Allocation concealment	B – Unclear

**Study Burr 1980A**

Methods	Randomisation method: not described. Blind assessment. Physical.
Participants	N=55 children (53 in analyses). Age range 5 -14 yr. 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).
Allocation concealment	B – Unclear

**Study Burr 1980B**

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.

### Characteristics of included studies (Continued)

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).
Allocation concealment	B – Unclear

#### Study **Carswell 1996**

Methods	Randomisation method: not described. Double-blind. Combination.
Participants	N=70 children (49 in analyses). Mean age 9.9 yr. Pos 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 wks.
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 four different 2 wk 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).
Allocation concealment	B – Unclear

#### Study **Chang 1996**

Methods	Randomisation method: not described. Not blind. Chemical.
Participants	N=26 (11 children and 15 adults, 26 in analyses). Pos 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).
Allocation concealment	B – Unclear

#### Study **Charpin 1990**

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 yr. Pos 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 vs 2.8 on a 10 cm analogue scale).

## Characteristics of included studies (Continued)

Allocation concealment C – Inadequate

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<b>Study</b>	<b>Chen 1996</b>
Methods	Randomisation method: not described. Double-blind. Physical.
Participants	N=56 (35 in analyses). Age range 5-14 yr). 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.
Allocation concealment	B – Unclear

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<b>Study</b>	<b>Cinti 1996</b>
Methods	Randomisation method: sealed opaque envelopes. Double-blind. Physical.
Participants	N=20 (20 in analyses). Mean age 30 yr (range 10-69). 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.
Allocation concealment	A – Adequate

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<b>Study</b>	<b>Cloosterman 1999</b>
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 16-60). 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.
Notes	Mite antigen reduction achieved (ELISA). Table 2 and figg. 4 and 5 used for data on symptoms and peak flow.
Allocation concealment	C – Inadequate

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<b>Study</b>	<b>Dharmage 2006</b>
Methods	Randomisation method: "permuted blocks of size two", "randomized...by the toss of a coin". Double-blind: "identically-appearing" placebo covers. Physical.

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**Characteristics of included studies (Continued)**

Participants	N=32 (30 in analyses). Mean age 32 yr (SD 6.3). Positive skin test.
Interventions	Test: impermeable mattress, doone and pillow covers. 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.
Allocation concealment	C – Inadequate

**Study Dietemann 1993**

Methods	Randomisation method: not described. Double-blind. Chemical.
Participants	N=26 (23 in analyses). Mean age 35 yr (range 13 to 58). Positive skin test to D pter, RAST pos.
Interventions	Test: solidified benzyl benzoate and tenside agents at the beginning and after 6 months. Control: placebo powder. 1 year.
Outcomes	Asthma symptoms (VAS 0-10), medication score (0-3), FEV1, FVC, FEF25-75, PEFr morning and evening, clinical score (0-4).
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.
Allocation concealment	B – Unclear

**Study Dorward 1988**

Methods	Randomisation method: not described. Blinded assessment. Combination.
Participants	N=21 (18 in analyses). Age range 13-53 yr. Pos 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 0-10), 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.
Allocation concealment	B – Unclear

**Study Ehnert 1992**

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 7-15 yr). Skin pos D pter and D far pos 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 hrs.

**Characteristics of included studies (Continued)**

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 three 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.
Allocation concealment	B – Unclear

**Study Fang 2001**

Methods	Randomisation method: not described. Not blind. Physical.
Participants	N=43 (not clear whether more were randomised). Age 37 (SD 20). Skin pos for D.
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.
Allocation concealment	B – Unclear

**Study Frederick 1997**

Methods	Cross-over. Randomisation method: not described. Single-blind. Physical.
Participants	N=31. Children aged 5-15 yr. Pos 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 vs 282.
Allocation concealment	B – Unclear

**Study Geller-Bernst 1995**

Methods	Randomisation method: not described. Double blind. Combination.
Participants	N=32 (14 in most analyses). Age range 4-12 yr). Pos skin tests only to house dust mites.
Interventions	Test: change of bedsheet 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 (0-3), medication use, FEV1, PEFr, doctor's and patient's opinion of clinical symptoms, serum IgE.
Notes	No reduction in mite allergens. No useful data.

## Characteristics of included studies (Continued)

Allocation concealment B – Unclear

Study	Ghazala 2004
Methods	Randomisation method: not described, “Studienunabhängige Person”. Double blind, no details. Physical.
Participants	N=17 (12 in analyses), crossover trial. Age not stated for asthma patients. Pos skin prick test and pos IgE.
Interventions	Test: covers (VarioProtect) for mattress, washed weekly. Control: cotton covers. Each period lasted 9-11 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.

Allocation concealment B – Unclear

Study	Gillies 1987
Methods	Randomisation method: not described. Not blind. Physical.
Participants	N=26 (25 in analyses). Age range 6-16 yr. Skin pos 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.

Allocation concealment B – Unclear

Study	Halken 2003
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 5-15 yr. Pos 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.

Allocation concealment A – Adequate

Study	Howarth 1992
Methods	Randomisation method: not described. Double blind.

**Characteristics of included studies (Continued)**

	Physical.
Participants	N=35 (number in analyses not reported, some had rhinitis). Age 13-23 yr. Pos 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.
Allocation concealment	D – Not used

<b>Study</b>	<b>Htut 2001</b>
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 18-45 yr. 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.
Notes	Reduction in mite allergens. We combined the two test groups for meta-analysis.
Allocation concealment	C – Inadequate

<b>Study</b>	<b>Huss 1992</b>
Methods	Randomisation method: not described. Not blind. Physical.
Participants	N=52 (52 in analyses). Age range 18-75 yr. 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Jooma 1995</b>
Methods	Randomisation method: open table of random numbers. Not blind. Combination.
Participants	N=60 (not all included in analyses, numbers not stated). Children aged 6-14 yr. Pos skin prick test.
Interventions	Test 1: mattress and pillow covers (Allergy Control Products) + tannic acid to carpets every 8 weeks. Test 2: acaricide (benzylbenzoate + bromopol) applied to carpets and mattresses. Control: none. 6 months.
Outcomes	PC20.

## Characteristics of included studies (Continued)

Notes No reduction in mite allergens. No useable data, no significant changes in PC20.

Allocation concealment C – Inadequate

### Study **Korsgaard 1983**

Methods Randomisation method: not described.  
Not blind.  
Physical.

Participants N=51 (46 in analyses). Median age 30 yr. Pos 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 min 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 vs 460 (P=0.33), evening PEFR 490 for both groups (P=0.82); less symptoms in test group (P=0.02).

Allocation concealment B – Unclear

### Study **Kroidl 1998**

Methods Randomisation method: sealed envelopes with consecutive numbers. Double-blind.  
Chemical.

Participants N=118 (78 in analyses). Age range 8-50 yr. 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 vs 22 patients.

Allocation concealment A – Adequate

### Study **Lee 2003**

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 yr. Positive skin prick test and RAST.

Interventions Test: outer cotton bed covers, boiled 10 min, 3 h 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).

Allocation concealment C – Inadequate

**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Luczynska 2003</b>
Methods	Randomisation method: statistical program generated a list of 1's and 2's 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 18-54. Serum IgE >0.7kU/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 two measures of asthma symptoms should be combined.
Allocation concealment	C – Inadequate

<b>Study</b>	<b>Maesen 1977</b>
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 (15-55 yr) and 5 children (7-14 yr). Pos 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Manjra 1994</b>
Methods	Randomisation method: unclear, "system of random numbers" after matching for 3 factors. Not blind. Chemical.
Participants	N=60 (59 in analyses). Children aged 5-12 yr. Pos 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.
Allocation concealment	B – Unclear

**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Marks 1994</b>
Methods	Randomisation method: not described. Blinded participants. Combination.
Participants	N=39 (35 in analyses). Age range 13-60 yr. All but two 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 (0-10), 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Matthys 1996</b>
Methods	Cross-over trial. Randomisation method: not described. Single-blind (according to thesis). Physical.
Participants	N=14 (10-14 in analyses). Pos 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.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Mitchell 1980</b>
Methods	Cross-over trial. Randomisation method: not described. Not blind. Physical.
Participants	N=10 (10 in analyses). Age range 7-14 yr. Pos skin tes 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 three times a day.
Notes	No assessment of mite reduction. Per cent expected PEFR calculated from Table II. Numbers improved are omitted, since they are unclear.
Allocation concealment	B – Unclear

<b>Study</b>	<b>Popplewell 2000</b>
Methods	Randomisation method: not described. Not blind.

**Characteristics of included studies (Continued)**

	Physical.
Participants	N=60 (51 in analyses). Age: 5-15 yr for 21 children and 22-63 yr 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.
Allocation concealment	B – Unclear

**Study Reiser 1990**

Methods	Randomisation method: not described. Double-blind. Chemical.
Participants	N=51 (46 in analyses). Age range 5-16 yr. Pos skin test to D pter.
Interventions	Test: mattresses sprayed every two weeks for 3 months with natamycin. Control: sprayed with placebo. 3 months.
Outcomes	Asthma symptoms, medication usage, FEV1, PEFR three 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).
Allocation concealment	B – Unclear

**Study Rijssenbeek 2002**

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 11-44 yr. 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.
Allocation concealment	B – Unclear

**Study Sette 1994**

Methods	Randomisation method: not described. Double-blind. Chemical.
Participants	N=24 (24 in analyses). Mean age 13 yr. Skin pos to D pter.
Interventions	Test: treatment of mattresses with benzyl benzoate foam (Acarosan).

**Characteristics of included studies (Continued)**

	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 two exposure periods were used (1 was added to zero values to get a logarithmic value of zero).
Allocation concealment	B – Unclear

**Study Shapiro 1999**

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 6-16 yr. 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.
Allocation concealment	A – Adequate

**Study Sheikh 2002**

Methods	Randomisation method: centralised, using numbers generated from a random numbers table. Double blind, with blinded data analysis. Physical.
Participants	N=47 (43 in analyses). Children, aged 5-14 yr. 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%.
Allocation concealment	A – Adequate

**Study Sooltangos 1992**

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 yr. Pos skin prick test.
Interventions	Test: cleaning and spraying mattresses with acaricide (benzylbenzoate + tannic acid) every 3 months. Control: none. 8 months.
Outcomes	Asthma symptoms, PEFr, FEV1, medication usage.
Notes	Abstract only, authors could not be traced.
Allocation concealment	B – Unclear

**Characteristics of included studies (Continued)**

<b>Study</b>	<b>Thiam 1999</b>
Methods	Randomisation method: not described. Not blind. Physical.
Participants	N=24 (24 in analyses). Children, aged 6-14 yr. 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 (Enviraicare). Control: none. 4 months.
Outcomes	FEV1, PEFR morning and evening, asthma symptoms, exercise bronchoprovocation test.
Notes	No reduction in mite allergens. Sponsored by Honeywell. No data shown for PEFR ("did not improve significantly"). We lumped the two active groups for the meta-analyses. The corresponding author did not answer our letters.
Allocation concealment	B – Unclear
<b>Study</b>	<b>Verrall 1988</b>
Methods	Cross-over trial. Randomisation method: not described. Double-blind. Physical.
Participants	N=16 (13 in analyses). Mean age 14 yr, range 7-27. Pos skin test to D pter.
Interventions	Test: HEPA-filter in the bedroom at night. Control: non-use of HEPA-filter (foam plug). There were four controlled trial phases of 3 weeks each.
Outcomes	Asthma symptoms, medication usage (analyzed for the final 2 wks of each 3 wk period, allowing 1 wk 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).
Allocation concealment	B – Unclear
<b>Study</b>	<b>Walshaw 1986</b>
Methods	Randomisation method: not described. Not blind. Physical.
Participants	N=50 (42 in analyses). Mean age 34 yr. Pos 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.
Allocation concealment	B – Unclear
<b>Study</b>	<b>Warburton 1994</b>
Methods	Cross-over trial. Randomisation method: not described. Double-blind. Physical.

**Characteristics of included studies (Continued)**

Participants	N=13 (12 in analyses). Mean age 46 yr (range 19-64). Pos 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).
Allocation concealment	B – Unclear

**Study Warner 1993**

Methods	Cross-over trial. Randomisation method: not described. Double-blind. Physical.
Participants	N=20 (14 in analyses). Age range 3-11 yr. Pos 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).
Allocation concealment	B – Unclear

**Study Warner 2000**

Methods	Randomisation method: not described. Double blind. Physical.
Participants	N=40, 27 children aged 4-16 yr and 13 adults aged 20-67 yr. 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.
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.
Allocation concealment	B – Unclear

**Study Woodcock 2003**

Methods	Randomisation method: coordination centre, using minimization within each practice (3 factors). Double blind. Physical.
Participants	N=1122, N=732 were mite sensitive (628 of these in analyses). Mean age 36 yr. Mite sensitization: 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.

### Characteristics of included studies (Continued)

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-months data for their power calculation, we used 6-months 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.
Allocation concealment	A – Adequate

#### **Study**                      **Zwemer 1973**

Methods	Cross-over trial. Randomisation method: not described. Double-blind. Physical.
Participants	N=18 (12 in analyses). Age range 6-16 yr. Pos 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.
Allocation concealment	B – Unclear

#### **Study**                      **de Vries 2007**

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 meter). No data for PEFR provided, only P = 0.52 for difference. Funded partly by two drug companies.
Allocation concealment	C – Inadequate

#### **Study**                      **van den Bemt 2004**

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.

**Characteristics of included studies (Continued)**

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.
Allocation concealment	B – Unclear

**Study van der Heide 1997A**

Methods	Randomisation method: not clear whether randomised. Double-blind. Chemical.
Participants	N=59 (40 in analyses). Mean age 31 yr. 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.
Allocation concealment	B – Unclear

**Study van der Heide 1997B**

Methods	Randomisation method: computer using minimization (2 factors). Double-blind. Physical.
Participants	N=30 (for relevant comparison; no information on possibly missing recordings). Age range 18-45 yr. Pos 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.
Allocation concealment	A – Adequate

**Study van der Heide 1999**

Methods	Cross-over. Randomisation method: computer using minimization (2 factors). Double-blind. Physical.
Participants	N=22 (20 in analyses). Mean age 12 years. Pos 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.
Allocation concealment	A – Adequate

PEFR: Peak-expiratory flow rate; FEV1: Forced expiratory volume in 1 second; D pter: Dermatophagoides pteronyssinus; D far: Dermatophagoides farinae

## Characteristics of excluded studies

Study	Reason for exclusion
Bowler 1985	Not an RCT against no treatment, N=12.
Brown 1991	Not an 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.
Elixmann 1988	Not an RCT.
Gallardo 1994	Some patients did not have asthma, but rhinitis (N=17 in whole trial).
Griffin 1989	Only published as abstract, author cannot be traced. Acaricide vs placebo (N=60), FEV1 1.86 in both groups after treatment.
Hannaway 1993	Not relevant comparison: acaricide + encasings versus carpet cleaner + placebo encasings (N=23).
Harving 1994	Not an 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 an RCT.
Krieger 2002	Multifactor intervention trial, 274 children. No clear how many were allergic to mites. Trial to last one year, but only methods paper published, in 2002.
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.
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 an RCT.
Nishioka 2006	Not an RCT.
Olaguibel 1994	No clinical data.
Owen 1990	No clinical data.
Peroni 1994	Not an RCT.
Quek 1994	Not an RCT.

### Characteristics of excluded studies (Continued)

Rebmann 1996	Study of mattresses, not patients.
Reisman 1990	Only 11 of the 32 patients had asthma (results were quite similar in the two groups).
Sarsfield 1974	Not an RCT.
Scherr 1977	No information on mite sensitisation. Aimed more generally at filtering 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 an 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.
de Blay 2003	No clinical data.

RCT: randomised clinical trial.

## ANALYSES

### Comparison 01. House dust mite reduction versus control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Numbers improved	7	338	Relative Risk (Fixed) 95% CI	1.01 [0.80, 1.27]
02 Asthma symptoms score	19	1385	Standardised Mean Difference (Fixed) 95% CI	-0.04 [-0.15, 0.07]
03 Medication usage	10	1015	Standardised Mean Difference (Fixed) 95% CI	-0.06 [-0.18, 0.07]
04 FEV1 (Forced expiratory volume in one second)	14	575	Standardised Mean Difference (Fixed) 95% CI	0.11 [-0.05, 0.28]
05 PEFr morning (Peak Expiratory Flow Rate)	23	1565	Standardised Mean Difference (Fixed) 95% CI	0.00 [-0.10, 0.10]
06 PEFr evening (Peak Expiratory Flow Rate)	12	367	Standardised Mean Difference (Fixed) 95% CI	-0.00 [-0.21, 0.21]
07 PC20 (Provocative concentration for 20% fall in FEV1)	14	493	Standardised Mean Difference (Fixed) 95% CI	0.05 [-0.13, 0.22]

## 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

## COVER SHEET

<b>Title</b>	House dust mite control measures for asthma
<b>Authors</b>	Gøtzsche PC, Johansen HK
<b>Contribution of author(s)</b>	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).
<b>Issue protocol first published</b>	1996/1
<b>Review first published</b>	1998/3
<b>Date of most recent amendment</b>	19 December 2007
<b>Date of most recent SUBSTANTIVE amendment</b>	19 December 2007
<b>What's New</b>	Five new included studies added (de Vries 2007; Dharmage 2006; Fang 2001; Ghazala 2004; van den Bemt 2004), one new excluded study added (Shedd). The conclusions of the review have not altered.
<b>Date new studies sought but none found</b>	Information not supplied by author
<b>Date new studies found but not yet included/excluded</b>	Information not supplied by author
<b>Date new studies found and included/excluded</b>	31 May 2007
<b>Date authors' conclusions section amended</b>	Information not supplied by author
<b>Contact address</b>	Dr Peter Gøtzsche Director The Nordic Cochrane Centre Rigshospitalet, Dept. 3343 Blegdamsvej 9 Copenhagen Ø 2100 DENMARK E-mail: pcg@cochrane.dk Tel: +45 35 45 71 12 Fax: +45 35 45 70 07
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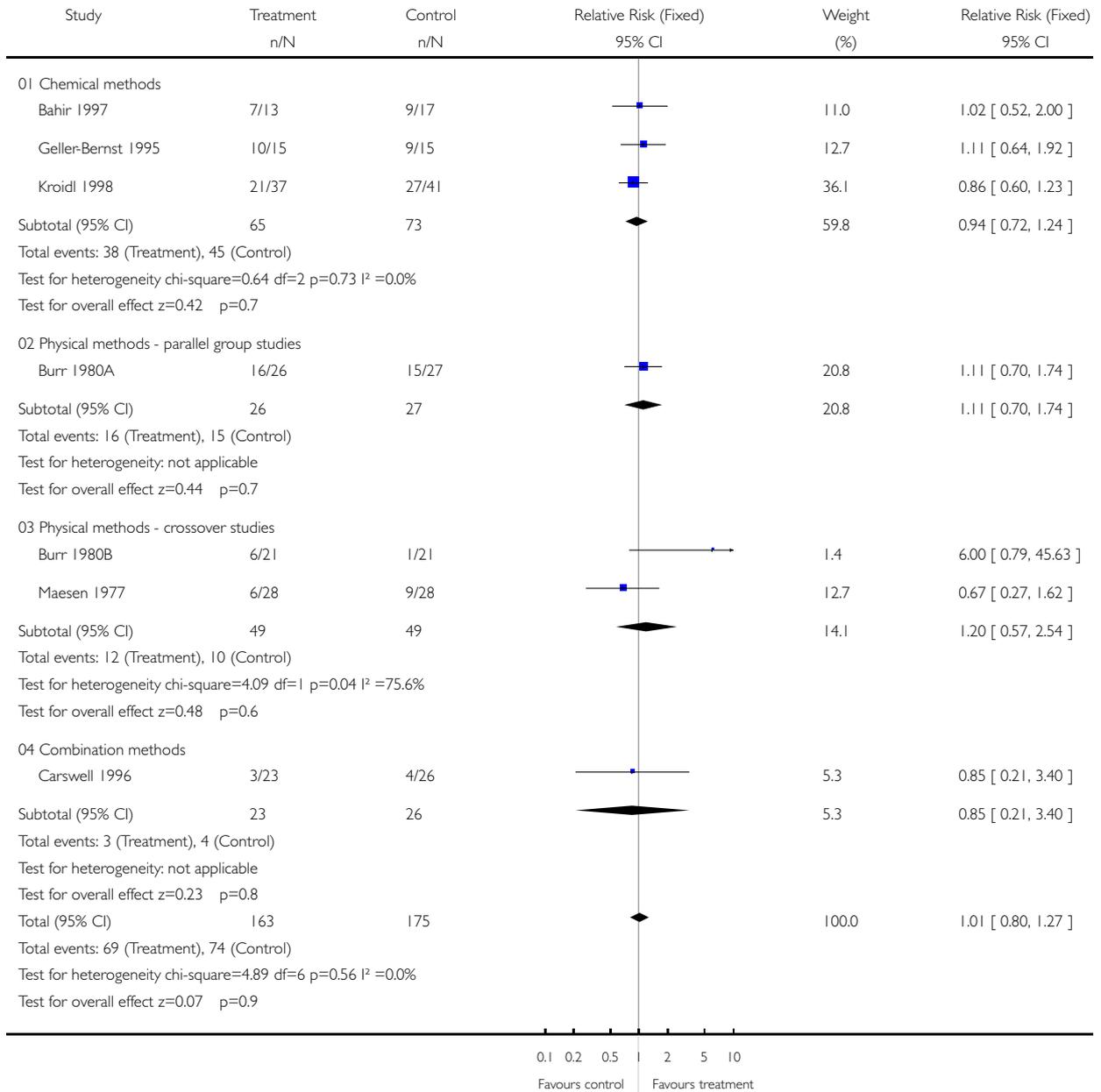
## GRAPHS AND OTHER TABLES

### Analysis 01.01. Comparison 01 House dust mite reduction versus control, Outcome 01 Numbers improved

Review: House dust mite control measures for asthma

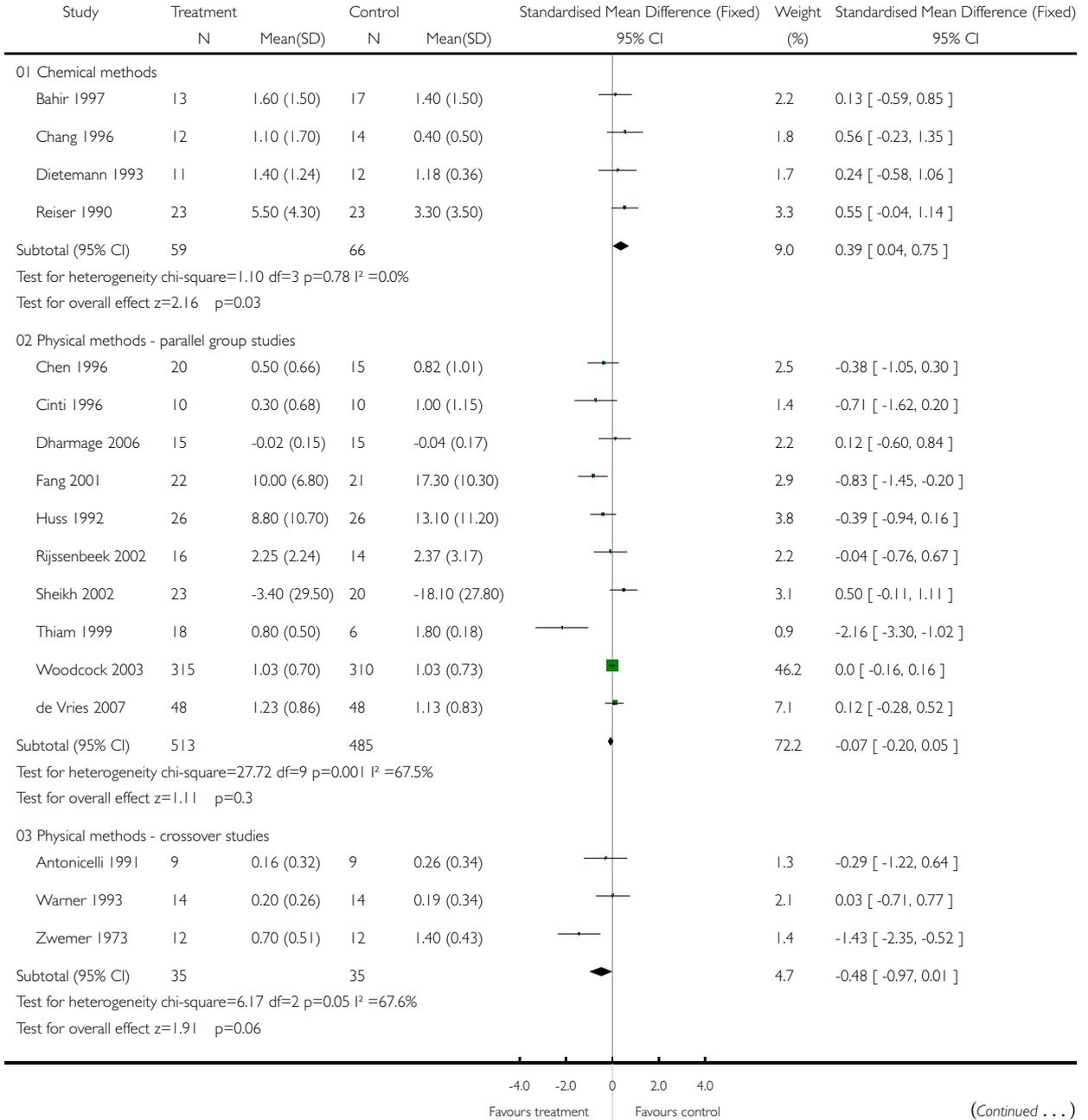
Comparison: 01 House dust mite reduction versus control

Outcome: 01 Numbers improved



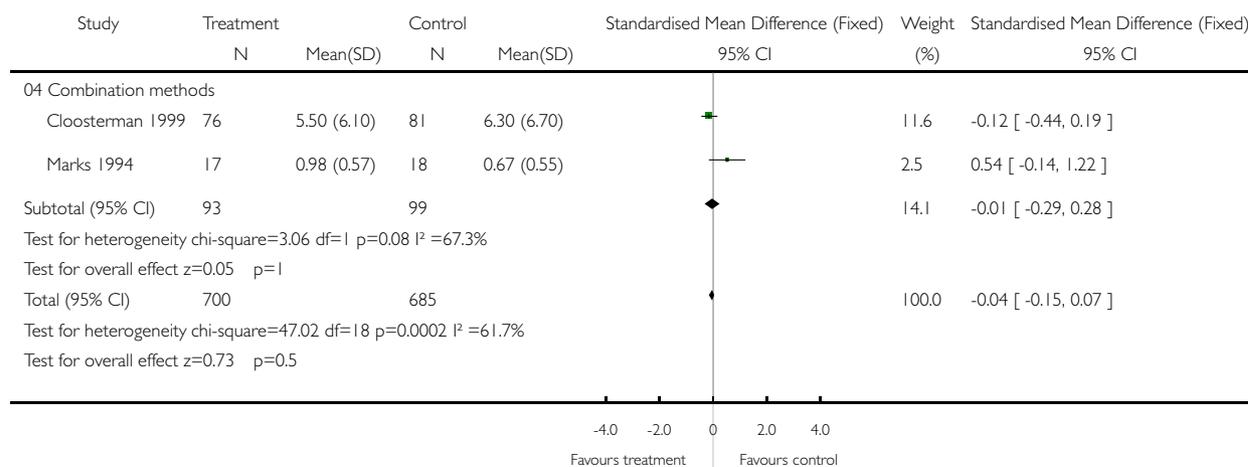
**Analysis 01.02. Comparison 01 House dust mite reduction versus control, Outcome 02 Asthma symptoms score**

Review: House dust mite control measures for asthma  
 Comparison: 01 House dust mite reduction versus control  
 Outcome: 02 Asthma symptoms score



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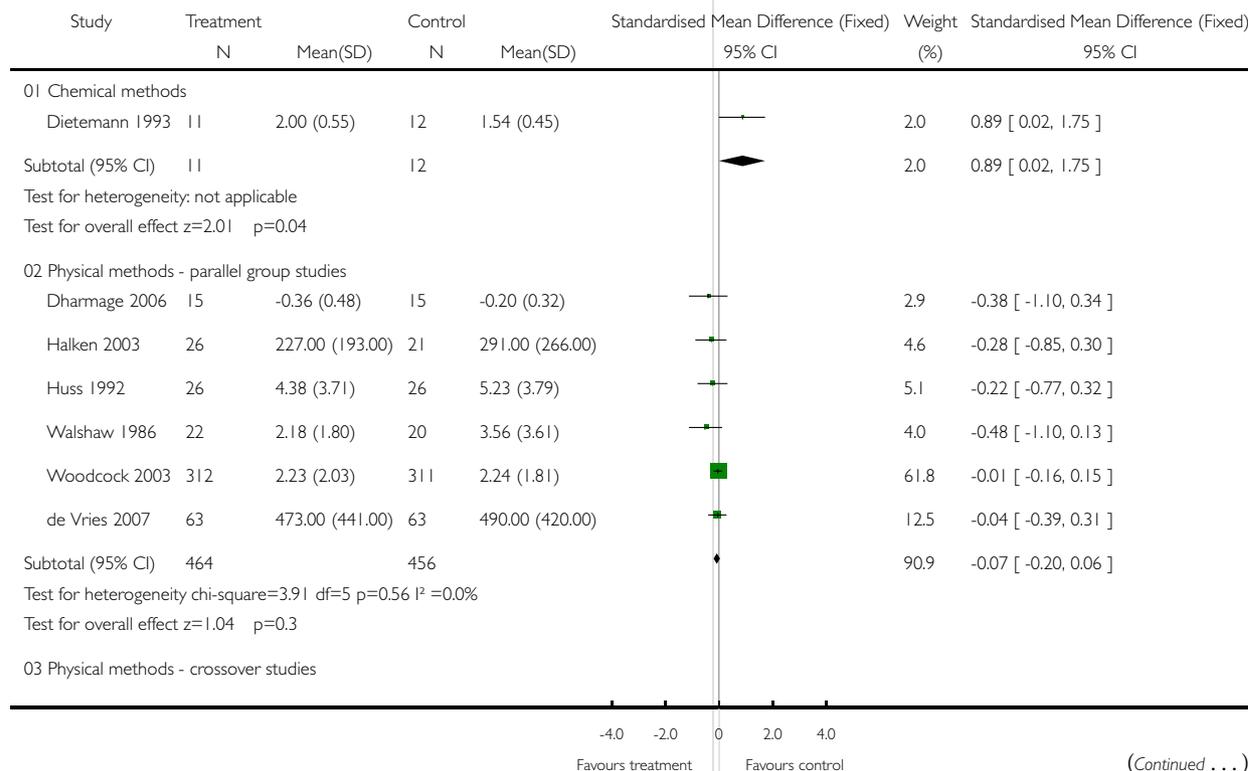


### Analysis 01.03. Comparison 01 House dust mite reduction versus control, Outcome 03 Medication usage

Review: House dust mite control measures for asthma

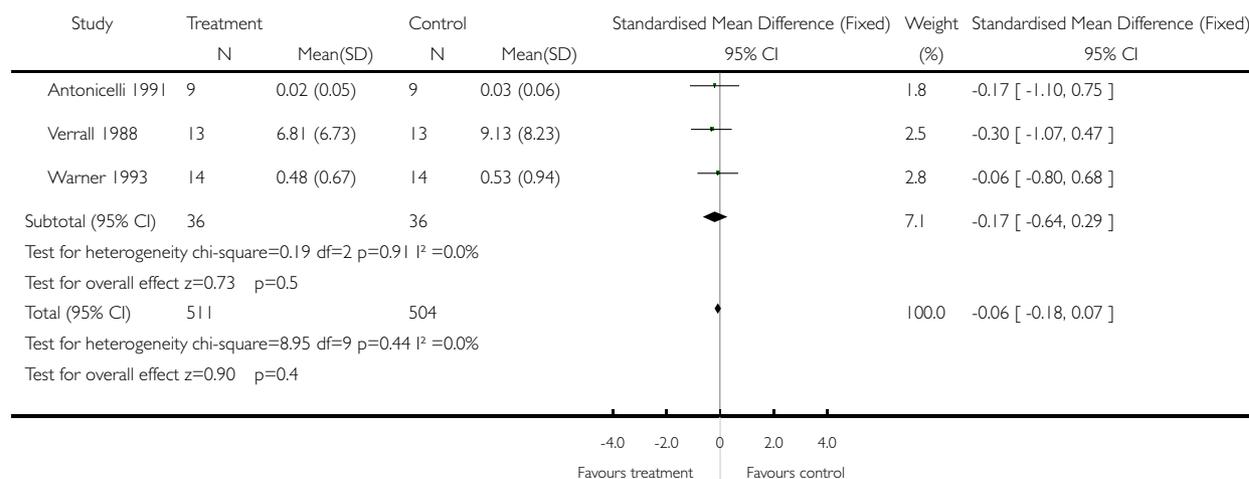
Comparison: 01 House dust mite reduction versus control

Outcome: 03 Medication usage



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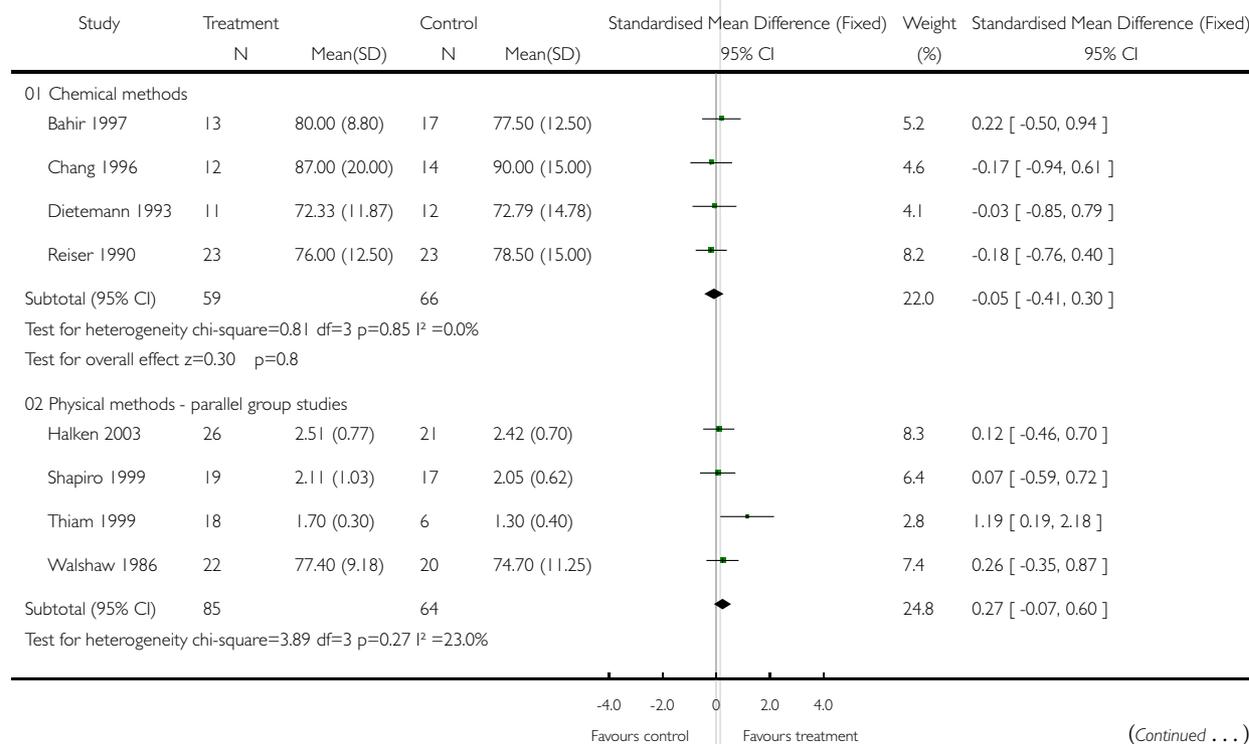


### Analysis 01.04. Comparison 01 House dust mite reduction versus control, Outcome 04 FEV1 (Forced expiratory volume in one second)

Review: House dust mite control measures for asthma

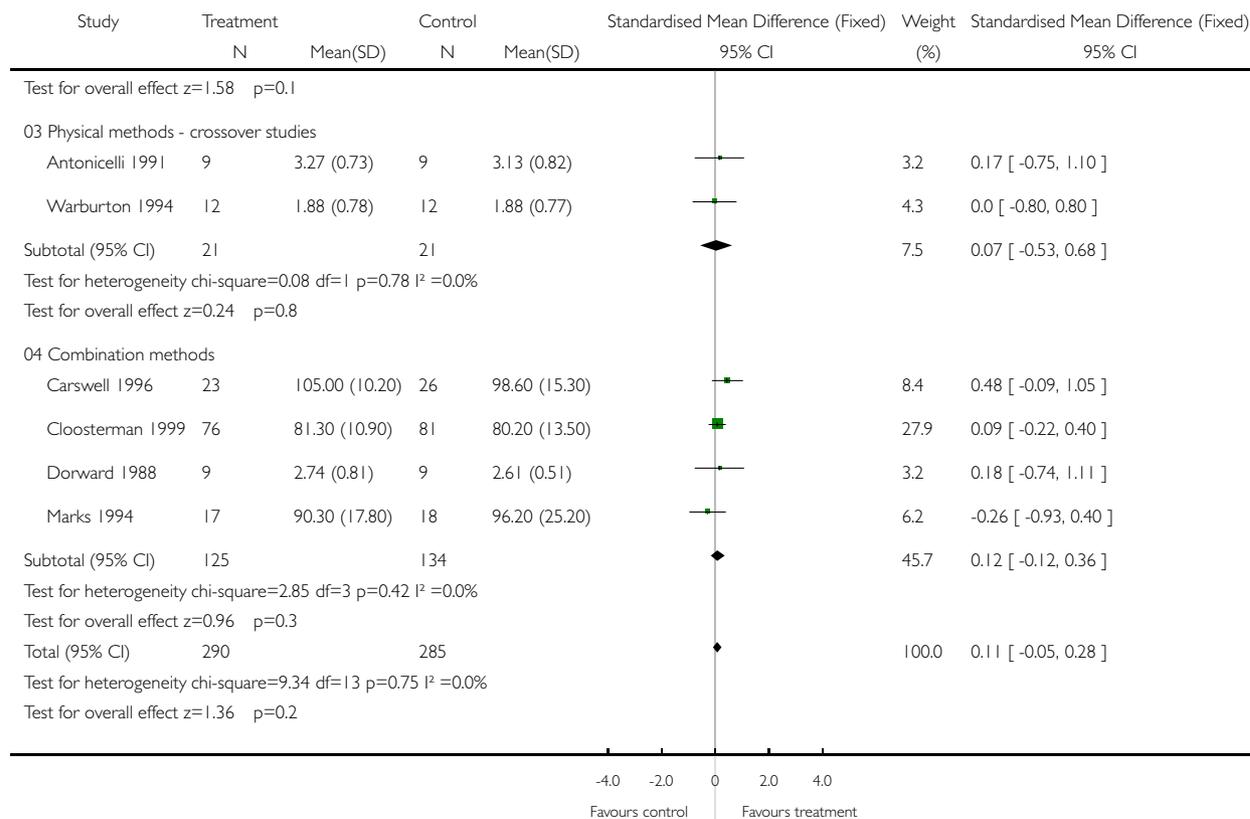
Comparison: 01 House dust mite reduction versus control

Outcome: 04 FEV1 (Forced expiratory volume in one second)



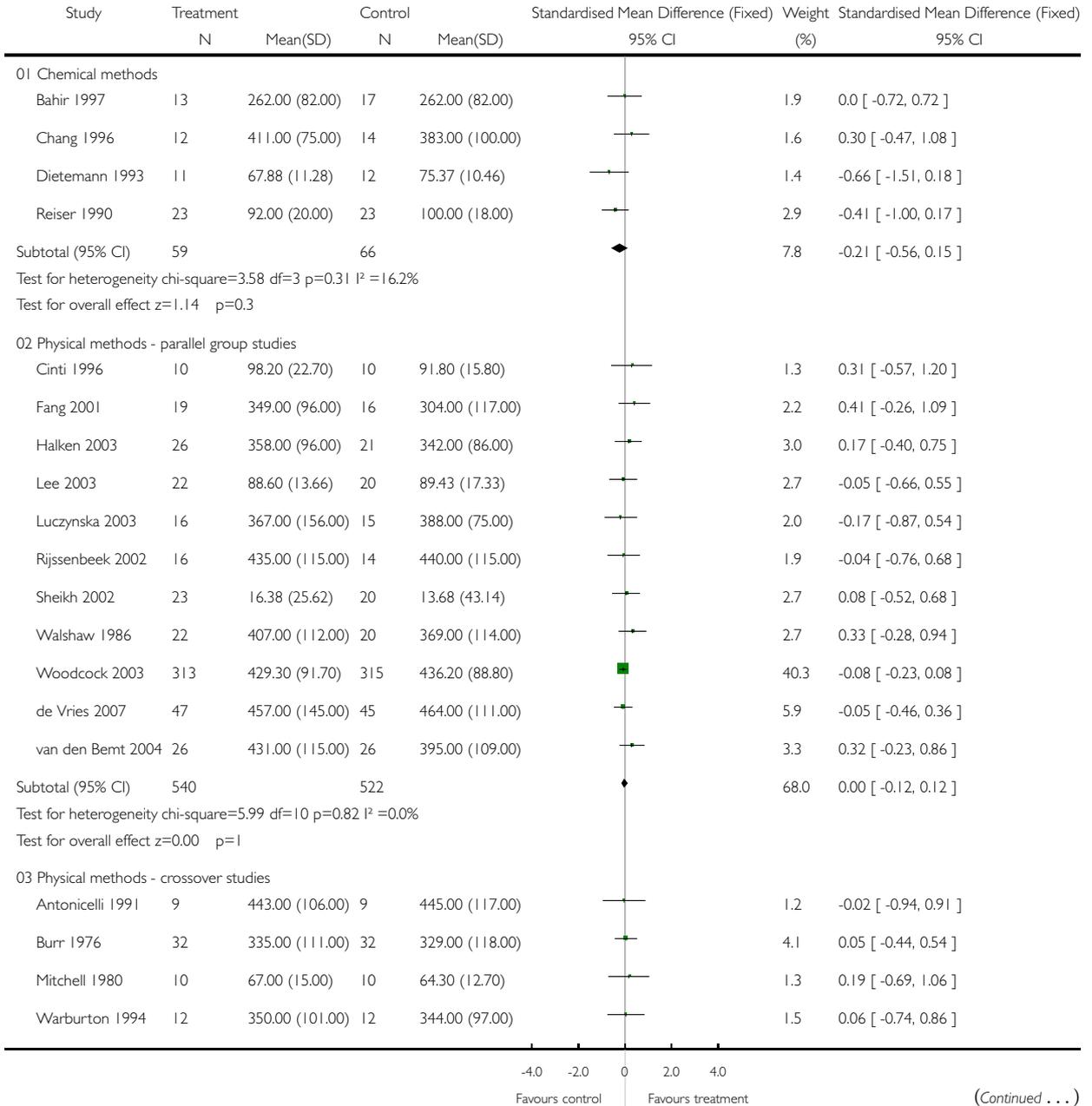
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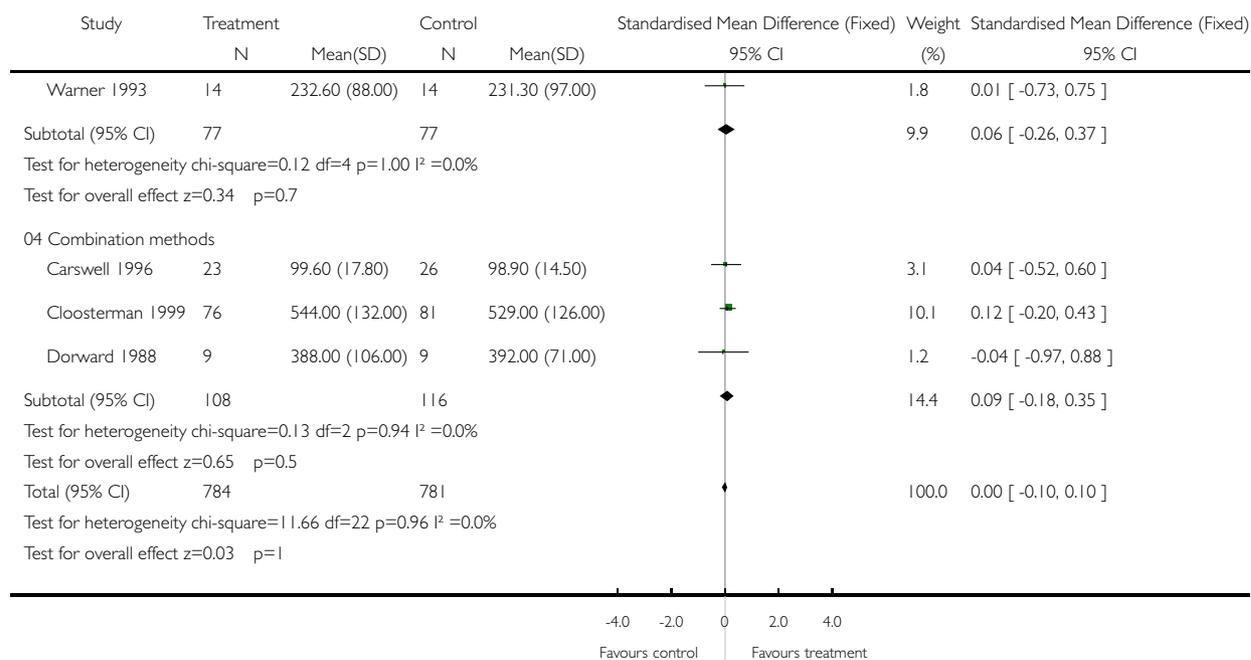


**Analysis 01.05. Comparison 01 House dust mite reduction versus control, Outcome 05 PEFR morning (Peak Expiratory Flow Rate)**

Review: House dust mite control measures for asthma  
 Comparison: 01 House dust mite reduction versus control  
 Outcome: 05 PEFR morning (Peak Expiratory Flow Rate)



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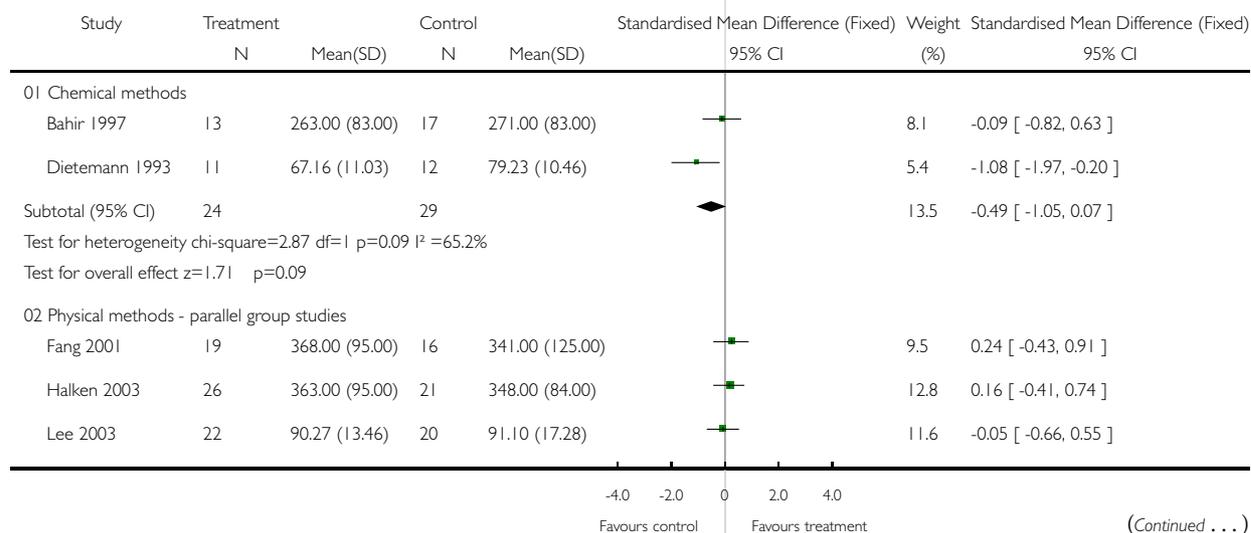


### Analysis 01.06. Comparison 01 House dust mite reduction versus control, Outcome 06 PEFR evening (Peak Expiratory Flow Rate)

Review: House dust mite control measures for asthma

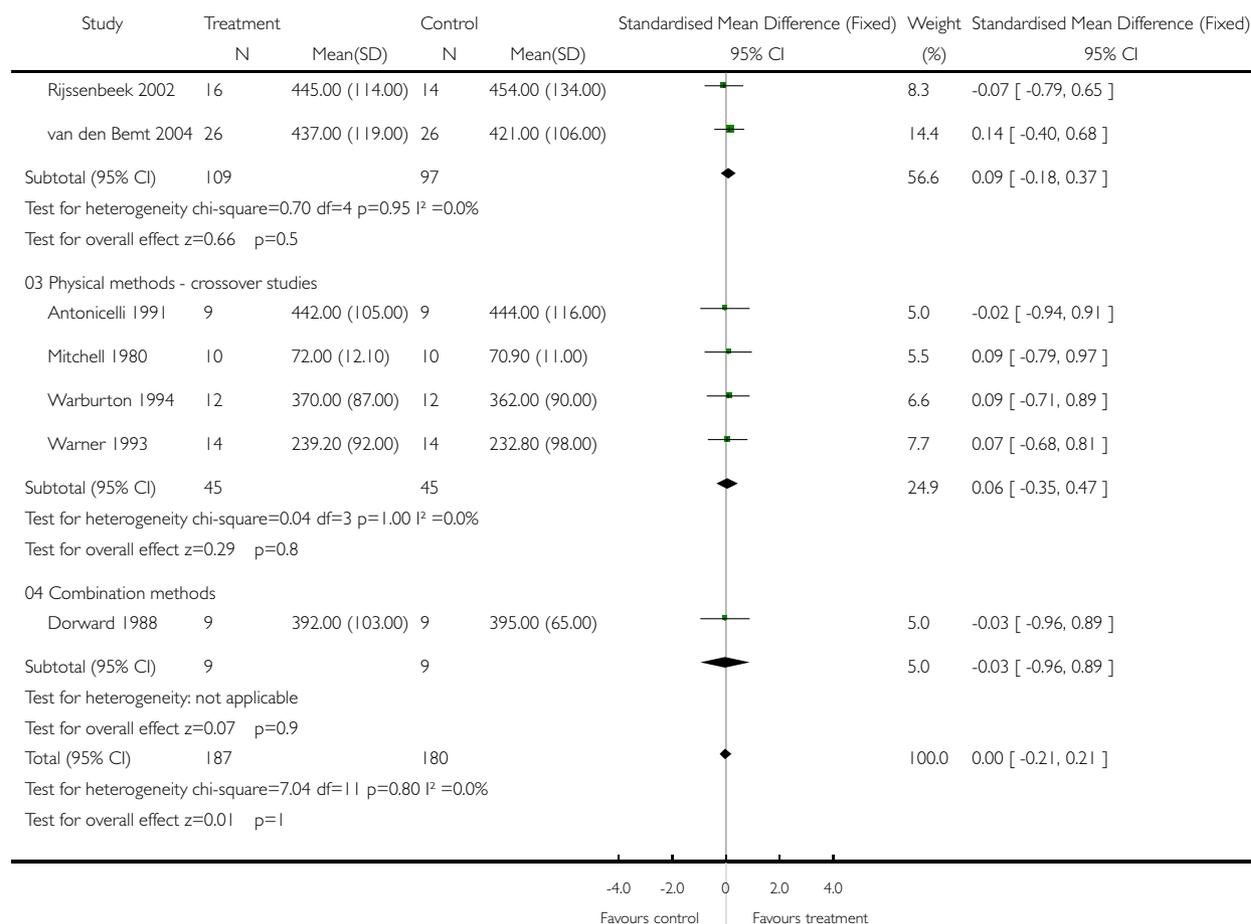
Comparison: 01 House dust mite reduction versus control

Outcome: 06 PEFR evening (Peak Expiratory Flow Rate)



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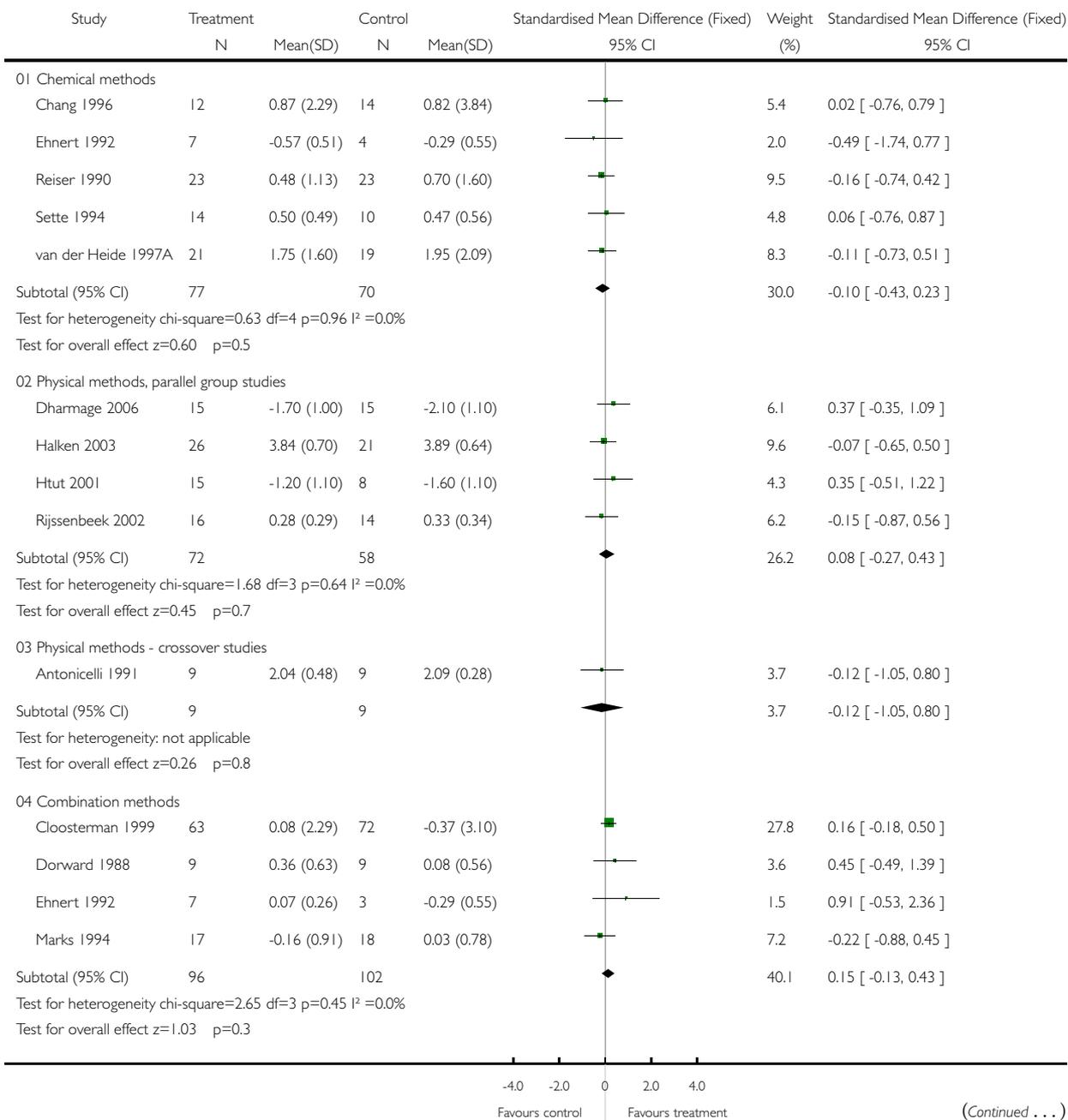


**Analysis 01.07. Comparison 01 House dust mite reduction versus control, Outcome 07 PC20 (Provocative concentration for 20% fall in FEV1)**

Review: House dust mite control measures for asthma

Comparison: 01 House dust mite reduction versus control

Outcome: 07 PC20 (Provocative concentration for 20% fall in FEV1)



(... Continued)

