



Impermeable dust mite covers in the primary and tertiary prevention of allergic disease: a meta-analysis

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ABSTRACT

Background: Up to 40% of the world's population has been diagnosed with an allergic disease. The most prevalent allergy is to house dust mites. Impermeable mattress covers are often the first treatment in the prevention and decrease of symptoms of allergic disease.

Objective: To perform a meta-analysis evaluating the effectiveness of impermeable mattress covers in the primary prevention of allergic disease and as a single intervention in the tertiary prevention of allergic disease symptoms.

Methods: MEDLINE, Embase, Web of Science, and CINAHL were systematically searched for relevant publications. Seven primary prevention trials ($n = 3,461$) and 17 tertiary prevention trials ($n = 1,671$) met the inclusion criteria and were included in the review. All article reviews and abstractions were performed in duplicate.

Results: No significant pooled relative risks were found for the prevention of allergic disease. The pooled relative risks were 0.97 (95% confidence interval [CI] 0.62–1.51) for house dust mite sensitization, 0.92 (95% CI 0.81–1.05) for wheeze, 0.85 (95% CI 0.70–1.02) for asthma, 1.03 (95% CI 0.90–1.19) for allergic rhinitis, and 1.05 (95% CI 0.84–1.32) for allergic dermatitis. Likewise, no significant pooled standardized mean differences were found in the tertiary prevention of symptoms. The pooled standardized mean differences were -0.03 (95% CI -0.15 to 0.09) for peak flow, -0.06 (95% CI -0.32 to 0.20) for asthma symptom score, and -0.39 (95% CI -0.88 to 0.11) for nasal symptom score. A significant effect was seen in the decrease of house mite dust level in the mattress (-0.79 , 95% CI -0.98 to -0.60).

Conclusion: No evidence was found to support the use of impermeable mattress covers in the primary prevention of allergic disease or in the tertiary prevention of allergic disease symptoms.

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Introduction

The prevalence of allergic disease continues to increase worldwide, with as many as 40% of the population diagnosed with an allergic disease or with allergic sensitization in 2011 to 2012. The World Health Organization has reported that allergic rhinitis affects 10% to 30% of the population, allergic dermatitis affects 15% to 30% of children and 2% to 10% of adults, and asthma prevalence ranges from 4% to 32%.¹ These allergic diseases represent a significant public health burden. The most prevalent allergic sensitization is to house dust mites (HDMs), with prevalence estimates ranging from 18% to 30%.² In the clinical management of allergic disease, one of the first lines of treatment is to advise dust mite–avoidance procedures, the most common of which are impermeable mattress and pillow covers.

Multiple randomized controlled trials have investigated the effectiveness of impermeable mattress covers as a single intervention on dust mite exposure levels, on their effectiveness in preventing allergic disease, and in the decrease of allergic symptoms, with inconsistent results. The use of impermeable mattress covers is currently recommended by multiple national and international organizations (including the Centers for Disease Control and Prevention; the American Lung Association; the National Heart, Lung, and Blood Institute; and the World Health Organization; among others) in the prevention and treatment of allergic diseases, particularly in those with dust mite allergies.^{3–6} However, the Global Initiative for Asthma, the British Thoracic Society guidelines, and an expert panel review of housing interventions have noted that there is insufficient evidence to recommend HDM control measures in the prevention of morbidity.^{7–9} This discordance among these prominent organizations highlights the need to evaluate the effectiveness of impermeable dust mite covers in the prevention and management of allergic disease.

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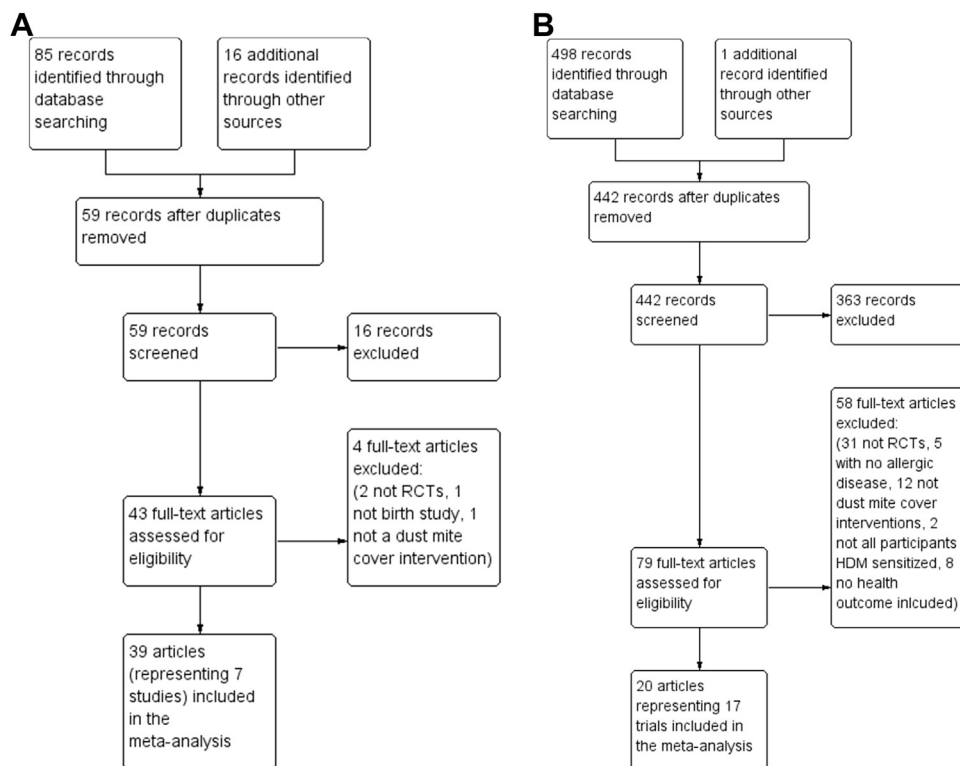


Figure 1. (A) Selection of primary prevention articles. (B) Selection of tertiary prevention articles. HDM, house dust mite; RCTs, randomized controlled trials.

There have been several reviews examining the effects of multiple measures to decrease dust mite exposure for the tertiary prevention of allergic disease symptoms,^{10–12} but none have examined the effects of mattress covers as a single intervention despite this being the recommendation by physicians and prominent health organizations. In addition, a previous review article discussed the environmental interventions used in the primary prevention of allergic disease in 7 birth cohort studies in which impermeable dust mite covers were the main, or only, environmental intervention¹³; however, no meta-analysis has addressed their effectiveness. The purpose of this meta-analysis was to evaluate the effectiveness of impermeable mattress casings as the main intervention in the *primary prevention* of allergic disease and as a single intervention in the *tertiary prevention* of symptoms in those diagnosed with allergic disease.

Methods

Data Sources and Searches

The MEDLINE online database (January 1, 1966 through July 16, 2013), EMBASE, Web of Science, CINAHL, and Cochrane Database of Systematic Reviews were systematically searched for relevant randomized controlled trials (the search was last updated on August 13, 2013). For the primary prevention aim, the following MEDLINE terms were searched: “(asthma OR atopy or sensitization or rhinitis or wheeze) and (birth or birth cohort or infant or pregnancy) and (impermeable or mattress or cover).” For the tertiary prevention aim, the following MEDLINE terms were searched: “(asthma or allergic rhinitis or allergic dermatitis or eczema or atopy or sensitization) and (mattress or impermeable or cover).” Searches were limited to studies classified as randomized controlled trials; there were no language restrictions. In addition to database searches, manual reference searches were conducted on all selected publications and from relevant review articles. **Figure 1** shows an outline of the literature search process.

Study Selection and Data Extraction

The inclusion criteria for the primary prevention aim were as follows: (1) randomized controlled trial; (2) infants at risk of developing allergic disease, defined as at least 1 parent diagnosed with HDM sensitization, asthma, rhinitis, or other allergic condition; (3) impermeable dust mite covers as the primary intervention; (4) controls received placebo covers or no intervention (other than education or standard care); and (5) information on the development of HDM sensitization or development of allergic disease (asthma, allergic rhinitis, or allergic dermatitis) during the follow-up period. Studies were excluded if the treatment allocation was not random, if the intervention was not applied at the time of birth, if there were differences between the control and intervention groups other than the intervention, or if the variance of the outcome could not be calculated. Seven individual trials were identified that met these criteria, with multiple publications each. Trial characteristics are listed in **Table 1**.^{14–48} Outcome data for the primary prevention aim were reported at multiple time points for each trial. If a study published multiple results within an age range, results from the older age were used in the analysis. The age ranges included for each outcome were 2 to 4 years for HDM sensitization, 0 to 3 years for wheeze, 2 to 4 years for allergic dermatitis, 5 to 8 years for asthma, and 5 to 8 years for allergic rhinitis. Multiple definitions of wheeze were used across studies and within studies. Where possible, wheeze was defined as recurrent wheeze occurring at least 3 times within the first 3 years of life. HDM sensitization was confirmed by a skin prick test (SPT; wheal size ≥ 2 or ≥ 3 mm, depending on trial definition) or by radioallergosorbent test IgE analysis (≥ 0.35 kU/L).

The inclusion criteria for the tertiary prevention aim were as follows: (1) randomized controlled trial; (2) patients with diagnosed allergic disease (asthma, allergic rhinitis, or allergic dermatitis) who were sensitized to dust mites; (3) impermeable dust mite mattress covers (could include other covers such as pillow or duvet

Table 1

Study characteristics of studies included in the primary prevention of allergic disease analysis

Study/location	N; randomization; blinding	Interventions	Outcomes available by age	Outcomes included in analysis
Isle of Wight/UK ^{14,21–24} ; begun in 1990; 1-y intervention	active 58, control 62; randomization method not specified; double blinded; LTF 0%	active: mattress cover, dietary intervention, Acarosan treatment on carpets and furniture; control: nothing	1 y: HDM sensitization, asthma, AD, rhinitis, spirometry, BHR, wheeze, nocturnal cough, IgE, SPT, total allergy 2 y: HDM sensitization, AR, AD, SPT, asthma, food allergy, total allergy 4 y: total allergy, asthma, AD, AR, food intolerance, SPT, HDM sensitization, wheeze 8 y: wheeze, nocturnal cough, BHR, SPT, IgE, HDM sensitization, FEV ₁ , peak flow 17 y: AD, asthma	HDM sensitization at 4 y old; asthma at 8 y old; AR at 8 y old; AD at 2 y old; wheeze at 4 y old
PIAMA/Netherlands ^{15,25–30} ; begun in 1996; 8-y intervention	active 416, control 394; simple randomization; double blinded; LTF 25% at 4 y, 35% at 8 y	active: mattress cover for infants' and parents' beds; control: placebo mattress cover	1 y: wheeze, nocturnal cough, respiratory symptoms, AD, IgE, HDM sensitization, HDM exposure 2 y: wheeze, nocturnal cough, respiratory symptoms, AD 4 y: HDM sensitization, wheeze, nocturnal cough, AD, AR, IgE 8 y: asthma, wheeze, hay fever, AR, AD, BHR, allergic sensitization, HDM sensitization, HDM exposure	HDM sensitization at 4 y old; asthma at 8 y old; AR at 8 y old; AD at 2 y old; wheeze at 2 y old
SPACE/Austria, Germany, UK, Greece, Lithuania ^{16,31} ; begun in 1997; 2-y intervention	active 347, control 349; block randomization; single blinded; LTF 6% at 2 y	active: mattress cover, dietary; control: nothing	1 y: HDM sensitization, SPT, wheezy bronchitis, AD, food allergy, wheeze, food intolerance, nocturnal cough, wheeze, asthma, AR 2 y: HDM sensitization, nocturnal cough, wheeze, asthma, AD, AR	HDM sensitization at 2 y old; AD at 2 y old; wheeze at 2 y old
PREVASC/Netherlands ^{19,32} ; begun in 1997; 2-y intervention	active 242, control 234; cluster randomization by ZIP code and GP practice; open; LTF 7% at 2 y	active: mattress, pillow and duvet covers for parents' and infants' beds, smoking cessation, dietary intervention, daily cleaning of floors, bedding hot wash, carpet removal; control: usual care	2 y: HDM sensitization, total and specific IgE, wheeze, nocturnal cough, asthma, AD, HDM exposure	HDM sensitization at 2 y old; AD at 2 y old; wheeze at 2 y old
MAAS/UK ^{18,33–38} ; begun in 1997; duration of intervention not clear	active 133; control 123; randomization method not specified; open; LTF 7% at 3 y	active: mattress covers for infants' and parents' beds; control: nothing	1 y: HDM sensitization, wheeze, cough, asthma, AD, food/medicine allergies, HDM exposure, SPT 3 y: wheeze, cough, asthma, AR, AD, HDM exposure, SPT, specific IgE	HDM sensitization at 3 y old; asthma at 3 y old; AR at 3 y old; AD at 3 y old; wheeze at 3 y old
CAPS/Australia ^{17,39–44} ; begun in 1998; 5-y intervention	active 276, control 278, simple randomization; single blinded; LTF 7% at 5 y	active: mattress covers, acaricide detergent for sheets/bedding, avoid soft toys and sheepskin; control: standard care	1 y: HDM sensitization, wheeze, cough, eczema, HDM exposure, SPT, medication use 2 y: HDM sensitization, HDM exposure 3 y: asthma, cough, wheeze, AD, HDM sensitization, atopy 5 y: HDM exposure, asthma, wheeze, cough, rhinitis, AD, SPT, HDM sensitization, spirometry 7 y: HDM exposure	HDM sensitization at 3 y old; asthma at 5 y old; AR at 5 y old; AD at 3 y old; wheeze at 3 y old
CAPPS/Canada ^{20,45–48} ; begun in 1994; 1-y intervention	active 281; control 268; randomization method not specified; blinding not specified; LTF 12% at 7 y	active: mattress and box spring covers for infants' and parents' beds, Acarosan-treated carpets/furniture, pet avoidance, smoke free, breastfeeding, delay of solid foods, avoid daycare centers; control: usual care	1 y: HDM exposure, asthma, AR, SPT, wheeze, cough	asthma at 7 y old; AR at 7 y old; wheeze at 2 y old

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Table 1 (continued)

Study/location	N; randomization; blinding	Interventions	Outcomes available by age	Outcomes included in analysis
			2 y: HDM exposure, asthma, atopy, wheeze, cough 7 y: wheeze, cough, medication usage, asthma, AR, AD, BHR, atopy, HDM exposure	

Abbreviations: AD, allergic dermatitis/eczema; AR, allergic rhinitis; BHR, bronchial hyper-responsiveness; CAPPS, Canadian Asthma Primary Prevention Study; CAPS, Childhood Asthma Prevention Study; FEV₁, force expiration volume in 1 second; GP, general practitioner; HDM, house dust mite; IgE, immunoglobulin E; LTF, loss to follow-up; MAAS, Manchester Asthma and Allergy Study; PIAMA, Prevention and Incidence of Asthma and Mite Allergy Study; PREVASC, Primary Prevention of Asthma in Children Study; SPACE, Study on the Prevention of Allergy in Children in Europe; SPT, skin prick test; UK, United Kingdom.

covers) as the primary intervention; (4) controls received placebo covers or no intervention (other than education or standard care); and (5) outcomes included at least 1 of the following: asthma symptom score, peak flow, quality of life, bronchial hyper-responsiveness, medication use, nasal symptom score, or dermatitis score. Studies were excluded if treatment allocation was not random, if there was a difference between the intervention and control groups other than the impermeable dust mite mattress covers, if outcomes were not reported by intervention status, if the variance of the outcomes could not be calculated, or if the intervention was shorter than 1 week. If study results were published more than once, then the most recent or most complete article was included in the analysis. Twenty articles representing 17 trials were identified for inclusion. Study characteristics and outcomes are listed in Table 2.^{49–69} Each outcome was analyzed separately for each allergic condition, with the exception of dust mite levels in the mattress, which were combined across the 3 allergic diseases.

Data for each outcome were abstracted from published articles. Attempts were made to contact the primary investigators to obtain relevant data that were not published. All selected publications were reviewed independently by 2 authors who made decisions on inclusion based on the criteria outlined earlier. Discrepancies were resolved by consensus and, when necessary, with the aid of a third author until a mutual agreement was reached.

For each aim, 2 authors independently abstracted data from selected articles using standardized data collection forms. For aim 1, data were collected on article title, journal, primary author's name, year, country, blinding status, length of follow-up, type of comparison group, "at-risk" definition, sample size, and outcome results. For aim 2, data were collected on article title, journal, primary author's name, year, country of origin, study design, blinding, length of follow-up, type of comparison group, age of population, type of allergic disease and HDM sensitivity assessment, characteristics of the study population (sample size, age, and sex), and outcome results. Any disagreements were resolved by consensus.

Statistical Methods

For each analysis, the total effect and 95% confidence intervals (CIs) using fixed-effects and random-effects models were calculated. The magnitude of between-trial heterogeneity was assessed across studies using the I^2 statistic for each outcome. Because of differences among studies in the number of subjects, duration of intervention, and other unmeasured factors that could lead to heterogeneity, only results from the random-effects models are presented. All analyses were conducted with RevMan 5.2 (<http://ims.cochrane.org/revman>) and STATA 11 (StataCorp LP, College Station, Texas).

For the primary prevention aim, analyses were conducted for the following outcomes: HDM sensitization, eczema, wheeze, rhinitis, and asthma. Each outcome was analyzed in a separate analysis. Relative risks (RRs) and 95% CIs were calculated for each outcome and then pooled for analysis using the Mantel-Haenszel method. The total number of participants randomized at birth

was used in calculating the RRs. To make the results as comparable as possible, clinically relevant age ranges were identified for each outcome.

For the tertiary prevention aim, analyses were conducted for the following outcomes: peak flow, asthma symptom score, nasal symptom score, and HDM level in the mattress. For all continuous outcomes, the standardized mean difference (SMD) was calculated using the inverse variance weighting method. The SMD allows the combination of data presented on different scales. The SMD was calculated by taking the difference in effect size (treatment minus placebo) divided by the pooled SD of these measurements. For example, trials used different asthma symptom scores and scale ranges, but all scales measured similar symptoms, which allowed them to be combined. All HDM-level data were presented as geometric means. Studies that presented data as nanograms per gram were converted to micrograms per gram. Geometric means and their 95% CIs were transformed to normalize the distribution before analysis.

Sensitivity analyses were conducted by excluding each study (within each outcome) in turn, removing studies with less than 20% loss to follow-up (or with no loss to follow-up data available), studies with an intervention shorter than 6 months, trials older than 20 years, and studies with fewer than 15 participants in each arm. In addition, for birth trials, a sensitivity analysis was conducted for HDM sensitization by looking at studies using SPT vs IgE. Potential publication bias was assessed by visual inspection of funnel plots of the SE against the SMD or RR for each study.

Results

Study Characteristics

Trials included in the analysis are presented in Figure 1. For the primary prevention aim, 85 articles were identified through the database search. After removing duplicates, 59 titles and abstracts were reviewed and 43 articles were identified for full-text review. After a full-text review and manual search of all articles and trials meeting the inclusion criteria, 7 individual trials, with 39 publications, were included in the meta-analysis. For the tertiary prevention aim, 498 articles were identified through database searching, and 1 was identified after a manual search. After duplicates were removed, 442 titles and abstracts were reviewed. Seventy-nine articles were identified for full-text review, of which 20 (representing 17 trials) were deemed eligible for inclusion.

The characteristics of the 7 trials included in the primary prevention aim are listed in Table 1. Two trials were double blinded,^{14,15} 2 were single blinded,^{16,17} 2 were open,^{18,19} and in 1 article blinding was not specified.²⁰ Trial start dates ranged from 1990 to 1998, and trial duration ranged from 1 to 8 years. In total, 3,461 participants were included, with losses to follow-up ranging from 0% to 12%.

Characteristics of the 17 trials included in the tertiary prevention aim are listed in Table 2. Fifteen trials were parallel, and 2 had a crossover design.^{49,50} In 4 trials, participants were blinded to the intervention. The type of blinding was not mentioned in 1 trial,⁵¹ and 2 of the trials were open.⁵² Publication dates ranged from

Table 2

Study characteristics of studies included in the tertiary prevention of allergic disease symptoms analysis

Study/location/design/ duration	Allergic disease	Participants; ages; randomization; blinding	Interventions	Outcomes with reported data	Outcome results
Brehler 2006 ⁵³ /Germany/ parallel/12 mo	allergic rhinitis	intervention 10, control 11; age range 24–65 y; randomization not specified; double blinded; LTF 34%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	nasal eye lung skin symptoms antiallergic drug use symptom load peak flow	NS SWI SWI NS NS SWI NS
Burr et al 1976 ⁴⁹ /UK/ crossover/6 wk per arm	asthma	intervention 15, control 17; mean age 32.8 y men, 32.6 y women; simple randomization; single blinded; LTF not reported	intervention: mattress covers, vacuuming of mattress, pillows, and bed, washing sheets and blankets; control: placebo procedure including upholstery and carpet vacuumed in living room	peak flow	NS
Cinti et al 1996 ⁵⁴ /Italy/ parallel/12 wk	asthma	intervention 10, control 10; age range 13–69 y; simple randomization; double blinded; LTF 0%	intervention: mattress and pillow covers; control: placebo mattress and pillow covers	eosinophil cationic protein asthma symptom score medication use	SWI NS NS
de Vries et al 2007, ⁵⁵ van den Bemt et al 2007 ⁵⁶ / Netherlands/parallel/ 24 mo	asthma	intervention 63, control 63; age range 16–60 y; simple randomization; double blinded; LTF 17%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	asthma symptom score HDM exposure QoL peak flow dose–response slope	NS SI NS NS NS
Dharmage et al 2006 ⁵⁷ / Australia/parallel/6 mo	asthma	intervention 16, control 16; average age 33.2 ± 7.2 y (control), 29.8 ± 5.3 y (intervention); stratified by bedroom floor covering and then by block; double blinded; LTF 6%	intervention: mattress, pillow, duvet covers, routine care; control: placebo mattress, pillow, duvet covers, routine care	PD ₂₀ peak flow asthma symptom score medication use HDM exposure QoL PC ₂₀	NS NS NS NS SI NS NS
Frederick et al 1997 ⁵⁰ /UK/ crossover/6 mo	asthma	N = 31; age range 5–15 y; randomization by order of recruitment; single blinded; LTF not reported	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	FEV ₁ peak flow asthma symptom score medication use HDM exposure eosinophil cationic protein asthma symptom score	NS NS NS NS SI NS NS
Ghazala 2004 ⁵⁸ / Switzerland/crossover/ 12 wk	asthma	intervention 10, control 10; average age 29.8 y; block randomization?; double blinded; LTF 13%	intervention: mattress covers; control: placebo mattress covers	rhinitis symptom score HDM exposure eosinophil cationic protein medication use	SWI, SWC SI SI SI
Halken et al 2003 ⁵⁹ / Denmark/parallel/12 mo	asthma	intervention 30, control 30; age range 6–15 y; block randomization; double blinded; LTF 17%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers, routine care		
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Table 2 (continued)

Study/location/design/duration	Allergic disease	Participants; ages; randomization; blinding	Interventions	Outcomes with reported data	Outcome results
Incorvaia et al 2008 ⁶⁰ /Italy/factorial/6 mo ^a	allergic rhinitis	N = 29; age not specified; randomization not specified; double blinded; LTF 14%	intervention: mattress cover; control: placebo mattress cover	HDM exposure	SI
				PC ₂₀	NS
Luczynska et al 2003 ⁶¹ /UK/parallel/12 mo	asthma	intervention 30, control 25; age range 15–54 y; randomization not specified; single blinded; LTF 44%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	asthma symptom score	NS
				FEV ₁	NS
Moon and Choi 1999 ⁵¹ /Korea/parallel/1 mo	allergic rhinitis	intervention 15, control 14; age range 6–31 y; simple randomization; blinding not specified; LTF not reported	intervention: mattress covers; control: standard care	peak flow	NS
				days with chest tightness	NS
Rijssenbeek-Nouwens et al 2002 ^{62,63} /Netherlands/parallel/12 mo	asthma, allergic rhinitis	intervention 16, control 14; age range 11–51 y; randomization not specified; double blinded; LTF 21%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	HDM exposure	SI
				nasal symptom severity score	SI
Sheikh et al 2002 ⁶⁴ /UK/parallel/6 mo	asthma, allergic rhinitis	intervention 26, control 21; age range 5–14 y; simple randomization; triple blinded; LTF 8%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	asthma symptom score	NS
				nasal symptom score	NS
Terreehorst et al 2003, ⁶⁵ Oosting et al 2002 ⁶⁶ /Netherlands/parallel/12 mo	allergic rhinitis	intervention 114, control 118; age range 8–50 y; block randomization; double blinded; LTF 17%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	peak flow	NS
				PC ₂₀	NS
Thiam et al 1999 ⁵² /Singapore/parallel/4 mo	asthma	intervention 6, control 6; age range 6–14 y; randomization not specified; open; LTF 0%	intervention: mattress, pillow, bolster covers; control: education/standard care	total blood eosinophils	NS
				HDM exposure	NS
	allergic dermatitis	intervention 38, control 35; AD LTF 10.5%		nasal allergen provocation test	NS
				daily symptom score	NS
				HDM exposure	SI
				HDM exposure	SI
				LSS severity scores	NS
				LSS extent	NS
				VAS score for itching	NS
				VAS score for sleeplessness	NS
				IDT	NS
				APT	NS
				total IgE	NS
				specific IgE	NS
				total blood eosinophils	NS
				HDM exposure	NS

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Table 2 (continued)

Study/location/design/duration	Allergic disease	Participants; ages; randomization; blinding	Interventions	Outcomes with reported data	Outcome results
van den Bemt et al 2004 ⁶⁷ / Netherlands/parallel/ 9 wk	asthma	intervention 26, control 26; age range 12–60 y; randomization not specified; double blinded; LTF 2%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	asthma symptom score peak flow FEV ₁ HDM exposure	SI SWI SI SI
van der Heide et al 1997 ⁶⁸ / Netherlands/parallel/ 12 mo	asthma	intervention 19, control 19; average age 32.3 ± 8.8 y (intervention), 30.1 ± 7.2 y (control); randomization not specified; double blinded; LTF not reported	intervention: mattress, pillow covers; control: placebo detergent	peak flow HDM exposure	SI SI
Woodcock et al 2003 ⁶⁹ /UK/ parallel/6 mo	asthma	intervention 366, control 366; age range 24–65 y; simple stratification; double blinded; LTF 14%	intervention: mattress, pillow, duvet covers; control: placebo mattress, pillow, duvet covers	PC ₂₀ peak flow	NS NS
				medication use asthma symptom score days of work missed exacerbations QoL	NS NS NS NS NS NS

Abbreviations: APT, atopic patch test; FEV₁, forced expiration volume in 1 second; GP, general practitioner; HDM, house dust mite; ICS, inhaled corticosteroids; IDT, intra-dermal test; IgE, immunoglobulin E; LSS, Leicester sign score; LTF, loss to follow-up; NS, no significant difference between groups in outcome; PC₂₀, provocation concentration that caused a decrease in forced expiration volume in 1 second of 20%; PD₂₀, provocation dose that caused a decrease in forced expiration volume in 1 second of 20%; PEF, peak expiratory flow; QoL, quality of life; SC, significant difference between groups in outcome, favoring control; SI, significant difference between groups in outcome, favoring intervention; SWI, significant improvement within control group; SWI, significant improvement within intervention group; UK, United Kingdom; VAS, visual analog scale. ^aStudy included 4 arms (intervention bed covers plus placebo acaricide, placebo covers plus intervention acaricide, intervention plus intervention, placebo plus placebo). Only intervention covers plus placebo spray and placebo plus placebo are included in the review. Article does not break out the number of patients per group.

1976 to 2007, trial duration ranged from 1 month to 2 years, and 1,671 participants 5 to 65 years old were included. Each trial reported multiple outcomes, and loss to follow-up, when reported, ranged from 0% to 44%.

Primary Prevention of Allergic Disease and HDM Sensitization

None of the pooled RRs for development of any of the 5 outcomes analyzed were significant (Fig 2). The pooled RRs were 0.97 (95% CI 0.62–1.51) for HDM sensitization, 0.92 (95% CI 0.81–1.05) for wheeze, 0.85 (95% CI 0.70–1.02) for asthma, 1.03 (95% CI 0.90–1.19) for allergic rhinitis, and 1.05 (95% CI 0.84–1.32) for allergic dermatitis. There was significant heterogeneity in the HDM sensitization analysis ($I^2 = 67\%$, $P = .01$). Therefore a sensitivity analysis was conducted by separating the sensitization result obtained by SPT and the results obtained by IgE analysis (results not shown). One study combined SPT and IgE results and was not included in the sensitivity analysis. Studies that used SPT to determine sensitization had an RR of 0.75 (95% CI 0.29–1.91, $I^2 = 84\%$, $P = .002$), whereas studies that assessed HDM sensitization by IgE analysis had an RR of 1.22 (95% CI 0.78–1.90, $I^2 = 0\%$, $P = .94$). No other results changed after performing sensitivity analysis. No differences were seen when analyses were limited to those studies that had dust mite covers as the only environmental intervention, except in HDM sensitization, which somewhat favored the controls with an RR of 1.34 (95% CI 0.95–1.94). Loss to follow-up in birth trials was examined and considered randomly distributed between intervention and control groups for all trials. A visual inspection of the funnel plots for publication bias indicated a slight bias in favor of the intervention in smaller studies when considering wheeze as the outcome.

Tertiary Prevention of Allergic Disease Symptoms

No significant effect of dust mite covers was found on any outcome except HDM level in the mattress. Figure 3 shows the results by outcome. The pooled SMDs were -0.03 (95% CI -0.15 to 0.09) for peak flow and -0.06 (95% CI -0.32 to 0.20) for asthma symptom score. Nasal symptom score showed a small but nonsignificant effect (SMD -0.39 , 95% CI -0.88 to 0.11). A large and significant effect was seen in the decrease of HDM level in the mattress (SMD -0.79 , 95% CI -0.98 to -0.60). The magnitude of all SMDs was interpreted using the guidelines suggested by Cohen⁷⁰; an SMD of 0.2 was considered a small effect, an SMD of 0.5 a medium effect, and an SMD of 0.8 a large effect.

In sensitivity analyses, the overall SMD did not change for peak flow, asthma symptom score, or HDM level in the mattress, and significant heterogeneity was not detected. Nasal symptom score demonstrated significant heterogeneity ($I^2 = 69\%$, $P = .01$). In the sensitivity analysis (results not shown), when trials shorter than 6 months were removed, the SMD was 0.27 (95% CI -0.79 to 0.24); when trials with less than 80% completions were removed, the SMD was 0.03 (95% CI -0.24 , 0.30). When trials with fewer than 15 participants per arm at baseline were removed, the SMD was 0.03 (95% CI -0.21 to 0.27). These results indicate a shift toward null results as lower-quality studies were removed. Visual inspection of the funnel plots indicated a slight risk for publication bias for asthma symptom score and for nasal symptom score results that indicated studies with null results or results favoring controls may be missing (results not shown).

Discussion

This meta-analysis found no evidence in support of impermeable dust mite covers in the primary prevention of allergic disease

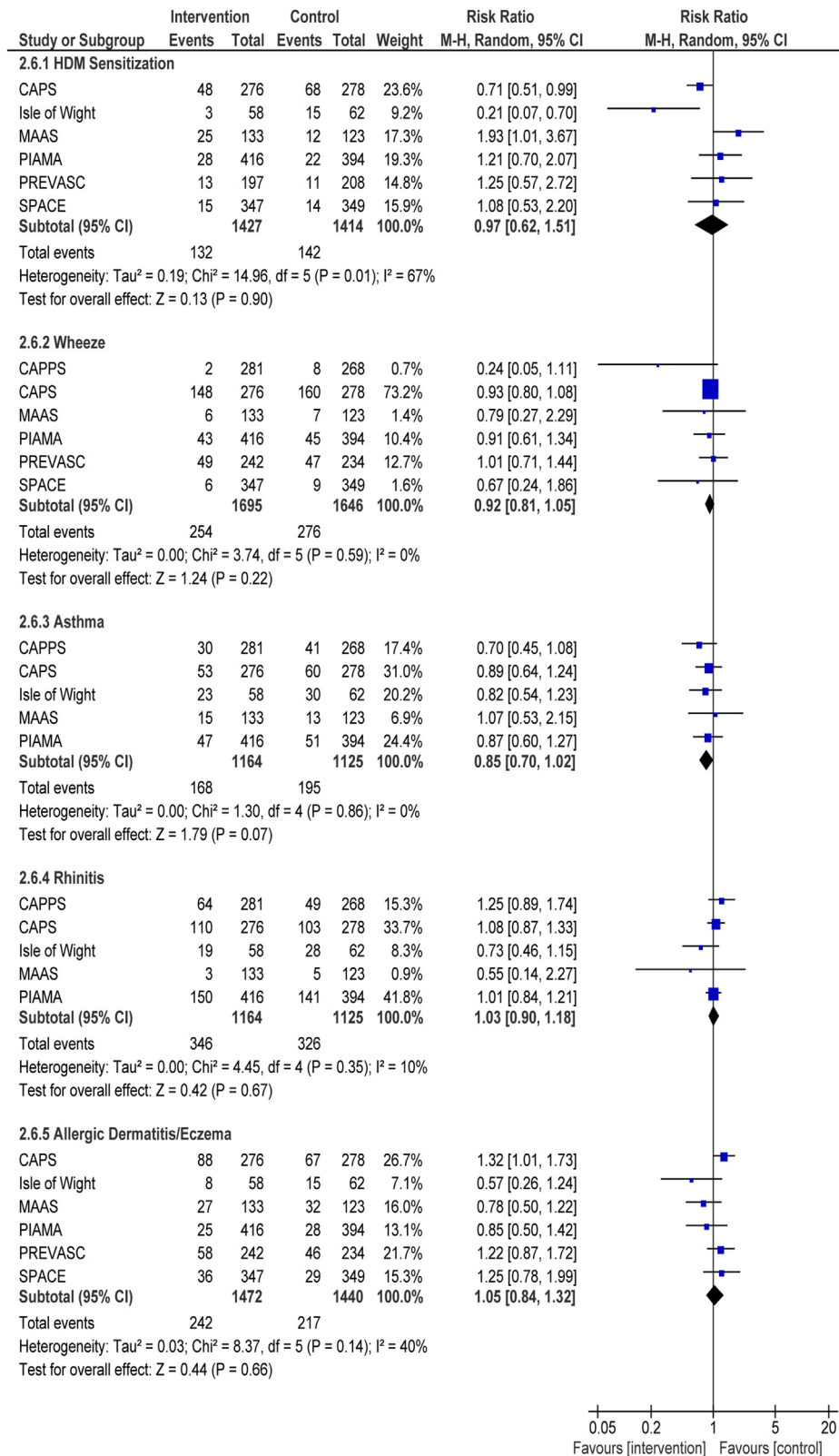
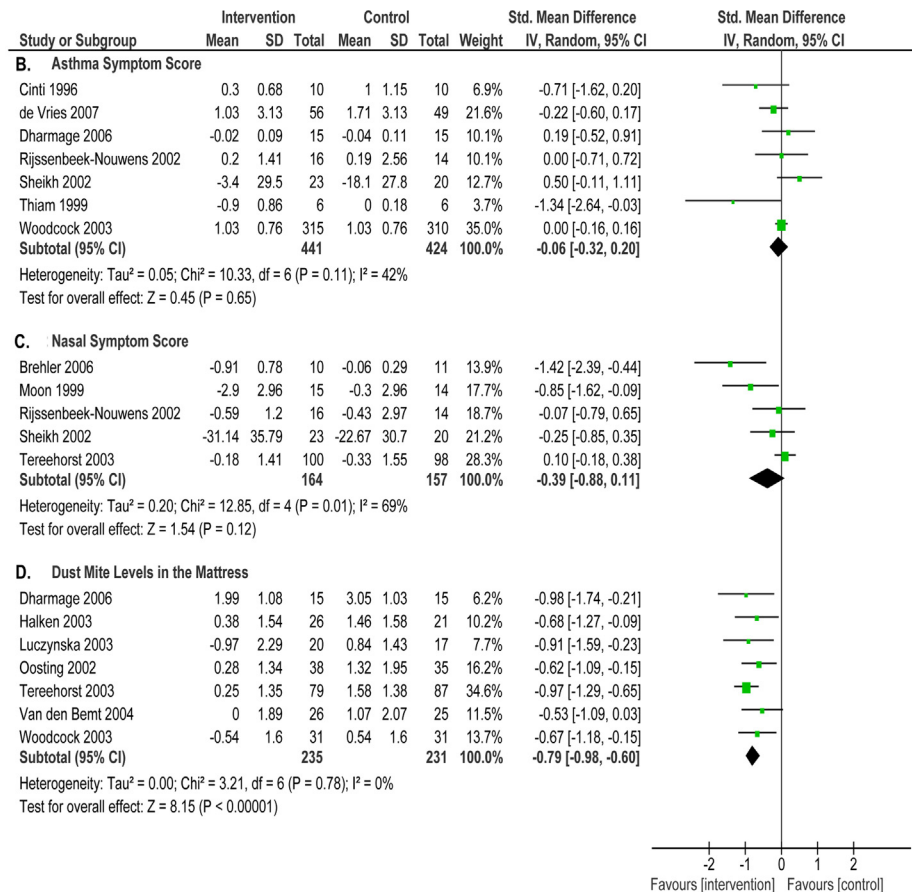
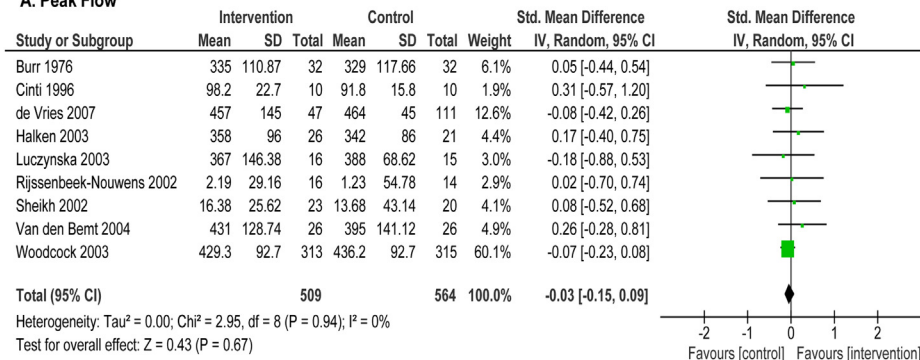


Figure 2. Meta-analysis of primary prevention of allergic disease. CAPPS, Canadian Asthma Primary Prevention Study; CAPS, Childhood Asthma Prevention Study; CI, confidence interval; HDM, house dust mite; M-H, Mantel-Haenszel; MAAS, Manchester Asthma and Allergy Study; PIAMA, Prevention and Incidence of Asthma and Mite Allergy Study; PREVASC, Primary Prevention of Asthma in Children Study; SPACE, Study on the Prevention of Allergy in Children in Europe.

or in the tertiary prevention of respiratory symptoms in those diagnosed with allergic disease. Only nasal symptom scores in the tertiary prevention trials showed evidence of a trend toward a

beneficial effect, although it was nonsignificant. The trend in nasal symptom score was attenuated when lower-quality studies were removed. Despite a significant decrease in HDM level in the

A. Peak Flow**Figure 3.** Meta-analysis of tertiary prevention of allergic disease symptoms and dust mite levels in the mattress.

mattress, a lack of improvement in health effects supports the authors' hypothesis that dust mite covers are not effective in preventing allergic disease or in decreasing symptoms.

There are several limitations to this systematic review and analysis. The first is the relatively small number of studies included for each outcome. Although 17 individual trials in the tertiary prevention aim were identified, there were a wide range of outcomes reported across the trials, making the combination of data difficult. Standardizing outcomes in asthma and allergic disease research will make future research more comparable.⁷¹ In addition, many studies did not report data for nonsignificant outcomes. This is a well-known limitation of meta-analyses, although the inclusion of these data would have reinforced the study findings. Initially an analysis of allergic dermatitis symptoms score was planned; however, only 1 allergic dermatitis trial met the inclusion criteria,

which precluded a pooled analysis, although this study found no significant clinical differences between active and placebo groups.⁶⁶ Only 2 of the 7 trials included in the primary prevention aim had a dust mite cover mono-intervention; others included a dietary intervention or some additional dust mite interventions, such as a chemical intervention. These trials were included in this analysis owing to the small number of mono-intervention trials available; however, a sensitivity analysis of only the mono-interventions was consistent with the results of the main analyses. The only difference noted was in the development of HDM sensitization, which favored the control group (although not significantly) in the sensitivity analysis.

The results of this meta-analysis are consistent with previous reviews of multifaceted HDM avoidance studies. As the most recommended environmental intervention in allergic disease

treatment, it is important to know the effects of impermeable dust mite covers as a single intervention. A systematic review by Gotzsche and Johansen¹⁰ published in 2008 evaluated the effects of multiple dust mite control measures on asthma outcomes. They found no significant effects of chemical, physical, or a combination of dust mite measures in the prevention of asthma symptoms. A similar review by MacDonald et al⁷² in 2007 found no sufficient evidence to suggest implementing dust mite avoidance measures. A review by Recer¹² published in 2004 assessing dust mite cover studies and the effects on the outcomes of exposure levels and bronchial hyper-responsiveness also failed to find a significant clinical benefit. In 2012, Nurmatov et al¹¹ reviewed 9 trials of HDM avoidance measures for patients with allergic rhinitis, of which 5 studies included HDM covers as a single intervention. They concluded that there was “reasonably strong evidence that isolated use of HDM impermeable bedding is unlikely to prove effective.” A previous review of the 7 primary prevention trials found a decrease in HDM exposure but found mixed results in the prevention of allergic disease.¹³ This study was not a systematic review and did not conduct a meta-analysis. The present review and analysis was better able to compare the effects of these trials by identifying clinically relevant age ranges for the development of disease.

The present findings, which are largely consistent with those of previous review articles, indicate that impermeable dust mite covers are effective in decreasing exposure levels to dust mites but are not effective in the decrease of symptoms or in the prevention of allergic disease. The reason for this finding is unknown. Although HDM levels in the mattress are lower, the levels might not be low enough to alleviate symptoms or prevent disease, because it has been observed that repeated exposure to low, subclinical doses of allergen can lead to bronchial inflammation and responsiveness.^{73,74} In addition, the mattress may not be the primary location of HDM exposure^{75–77} or HDMs may not be a driving factor in the development and morbidity of allergic disease. The authors' recent analysis of National Health and Nutrition Examination Survey data identified HDM-specific IgE as more relevant to adult asthma than to childhood asthma.⁷⁸

In recent years, a call has gone up from the scientific community advocating the discontinued use of dust mite covers and the removal of dust mite cover use from the recommended clinical guidelines in the prevention and management of allergic disease.^{9,79–81} Although some international guidelines currently express uncertainty on the effectiveness of HDM covers and other avoidance measures,^{7,8} the vast majority of US and international guidelines still recommend their use. Although there have been detractors of the evidence presented in previous reviews,^{82,83} the present study adds weight to the evidence against dust mite covers. It is interesting to note that no trials studying a dust mite cover intervention have been published since 2007, indicating that the scientific community has become aware of the lack of benefit of these covers. The authors agree with the conclusions of Tovey and Ferro⁷⁹ (2012) that despite the presence of several high-quality and adequately powered trials, the evidence for a beneficial effect of HDM covers on prevention or on the symptoms of allergic disease has not been seen, and that there is no value in repeating these failed approaches. In recent years, newer, multifaceted interventions have been tested that target multiple allergens in the home, such as cockroaches and mice, which have been shown to be triggers of allergic disease, in addition to dust mites. Although some of these have had moderate success, whether impermeable dust mite covers are beneficial in preventing disease or symptoms in these interventions is unknown. A review of these interventions is outside the scope of this meta-analysis.

Clinical guidelines recommending the use of impermeable dust mite covers should be reviewed, and evidence-based

recommendations should be encouraged. The evidence does not support the effectiveness of HDM covers in the decrease of symptoms or in the prevention of allergic disease, and at least 1 expert panel has concluded they are not effective in preventing allergic disease or symptoms.⁹ Dust mite covers for mattresses and pillows can cost up to \$100 each. This cost is an extra burden on patients with asthma and their families, particular in those with a low income.^{84–86} The economic burden of asthma on these families is already high, and it is the patients and families who pay for recommended interventions. Recommendations and guidelines should be changed to reflect the scientific literature on the most effective measures.

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