Associations between environmental exposures and asthma control and exacerbations in young children – a systematic review

On line supplement
Table I Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Definition of asthma used</th>
<th>Outcome reported</th>
<th>Design</th>
<th>Study population</th>
<th>Objectives</th>
<th>Programme content</th>
<th>Outcome</th>
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<tbody>
<tr>
<td><strong>Environmental Tobacco Smoke</strong></td>
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<tr>
<td>Health effects of indoor nitrogen dioxide and passive smoking on urban asthmatic children (2007) † USA</td>
<td>Physician diagnosed asthma and symptoms in the previous year</td>
<td>Symptom score Peak expiratory flow</td>
<td>Longitudinal study</td>
<td>1449 children presenting to emergency departments or attending clinics aged 4-9 years</td>
<td>Relate outcomes to exposures to ETS and indoor NO₂</td>
<td>Urinary cotinine concentrations and indoor NO₂ concentrations (measured over a week in 663 houses) were measured at enrolment and 3, 6 and 9 months afterwards peak flow and symptoms were recorded (the latter over telephone)</td>
<td>Higher NO₂ (&gt;53ppb) was linked to increased symptoms among non-atopic children (RR 1.8 [1.1, 2.8]). Exposure to ETS (cotinine/ creatinine &gt;30ng/mg) and higher NO₂ were both associated with reduced peak flow (&lt;80% predicted) during the winter months – RR 1.2 [1.0,1.5] and 1.5 [1.1, 2.0] respectively.</td>
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<tr>
<td>Environmental tobacco smoke and its effect on the symptoms and medication in children with asthma . (2009) ‡ Japan <em>POOR STUDY DESIGN</em></td>
<td>Physician diagnosed asthma</td>
<td>Level of preventor medication needed</td>
<td>Cross sectional study</td>
<td>282 asthmatic children 0-17 years of age (mean age 6.9 years)</td>
<td>To investigate the influence of second hand smoke on the symptoms of asthmatic children and its effect on the efficacy of their medication.</td>
<td>Information was gathered from parents and carers of the children on smoke exposure and medication. Data were also gathered for asthmatic symptoms and use of anti asthmatic drugs.</td>
<td>There was no significant difference for severity of asthmatic symptoms between the no/ mild ETS exposure groups compared with heavy ETS exposure group. Prevalence of anti asthma drug use of leukotriene receptor antagonists was significantly higher among the high ETS exposure group compared to the other group (p=0.002).</td>
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<tr>
<td>Environmental tobacco smoke exposure and nocturnal symptoms among inner-city children with asthma (2002)</td>
<td>At least one of the following: (i) physician diagnosed asthma (ii) symptoms suggestive of asthma (iii) ED presentation with asthma</td>
<td>Symptom diary</td>
<td>Cross sectional study</td>
<td>School children with asthma (n=590)</td>
<td>To examine the relationship among ETS exposure, select asthma symptoms and consequences among inner-city children with asthma.</td>
<td>Data were gathered from parents or carers on home ETS exposure, information on limited physical activity as a result of asthma related symptoms and number of school days missed.</td>
<td>Exposure to high levels of ETS was associated with a significant increase in the nocturnal symptoms in children (OR 2.83, 95% CI 1.22-6.55).</td>
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<tr>
<td>Association between exposure to environmental tobacco smoke and exacerbations of asthma in children (1993)</td>
<td>Children with asthma</td>
<td>Exacerbation</td>
<td>Cross sectional study</td>
<td>Asthmatic children (n=199)</td>
<td>To study the association between exposure to ETS and asthma exacerbations in children.</td>
<td>Data were collected in the form of urinary cotinine levels and pulmonary function tests were carried out. Data were gathered on exposure to ETS and episodes of acute exacerbations.</td>
<td>There was a significantly increased risk for acute exacerbations of asthma following exposure to ETS and this was dose dependent (RR 1.8, 95% CI 1.4-2.2-for reported exposure and RR 1.7, 95% CI 1.4-2.1- for exposure indicated cotinine levels). Forced expiratory volume in one second (FEV$_1$) decreased with increases in both measures of exposure.</td>
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**Air quality**

**Ozone**

<table>
<thead>
<tr>
<th>Acute respiratory</th>
<th>Persistent</th>
<th>Asthma</th>
<th>Longitudin</th>
<th>861 children from</th>
<th>To relate outdoor air</th>
<th>After recruitment,</th>
<th>Air pollutant</th>
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**Programme content**

**Outcome**
<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td>health effects of air pollution on children with asthma in US inner cities (2008)  5 USA</td>
<td>asthma and positive skin prick test</td>
<td>symptoms, school days missed, peak flow and FEV1</td>
<td>al study</td>
<td>inner cities aged 5-12 years (mean age 7.7 years)</td>
<td>quality (NO2, SO2, PM2.5, CO and O3) to symptoms and lung function over 2 years</td>
<td>symptoms were captured by 2-monthly telephone calls. Children completed spirometry each 6 months. Increases in routinely acquired air quality data (from the 10th to 90th centile) were related to symptoms and spirometry.</td>
<td>concentrations were within recommended limits. In single pollutant models, NO2, SO2 and PM2.5 (but not CO or O3) were related to outcomes. In a 3-pollutant model, increased NO2 was associated with increased cough and wheeze (OR 1.2 [95% CI 1.0, 1.5] and reduced %FEV1 (mean reduction 1.1% [95% CI 0.4, 1.8]). Increased PM2.5 exposures were linked to reduced FEV1 (mean reduction 0.7% [95% CI 0.1, 1.3])</td>
</tr>
<tr>
<td>he effect of air pollution on inner-city children with asthma (2002)  6 USA</td>
<td>Physician-diagnosed asthma and/or asthma symptoms in the previous year</td>
<td>Peak Expiratory Flow</td>
<td>Longitudinal</td>
<td>Children (n=846) 4-9 years of age</td>
<td>To examine the effect of daily ambient air pollution among children residing in urban areas.</td>
<td>Data collected over 4 months for respiratory symptoms, air pollutant concentrations and lung function</td>
<td>Exposure to Ozone was associated with a 59% decline in PEFR (95% CI 0.13-1.05). Even at levels below then current USA air quality standards, summer air pollution was linked to decreased pulmonary function among the children.</td>
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<tr>
<td>Chronic exposure to ambient ozone</td>
<td>Hospital</td>
<td>Asthma admission</td>
<td>Longitudinal</td>
<td>Children (n=1204396) 1-6</td>
<td>To investigate impact of high ozone levels on</td>
<td>Data collected on ozone concentrations and</td>
<td>Chronic exposure to Ozone may increase risk</td>
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<td>and asthma hospital admissions among children (2008)</td>
<td>record of admission with asthma (infants excluded)</td>
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<td>years of age</td>
<td>childhood asthma admissions.</td>
<td>asthma admissions.</td>
<td>of asthma admissions (OR 1.16, 95% CI 1.15-1.17).</td>
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### Particulates

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<tr>
<th>Study</th>
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<tbody>
<tr>
<td>In-home particulate concentrations and childhood asthma morbidity (2009)</td>
<td>Physician diagnosed asthma plus medication/symptoms in previous 6 months</td>
<td>Symptoms and reliever medication use</td>
<td>Longitudinal</td>
<td>150 children aged 2-6 years. 91% African Americans</td>
<td>Relate bedroom PM$<em>{2.5}$ and PM$</em>{2.5-10}$ exposures at baseline and 3 and 6 months afterwards to daily diary scores</td>
<td>Particulate exposures were measured at 3 month intervals over 6 months. Parents completed daily diaries.</td>
<td>Each increase of 10microg/m$^3$ PM$<em>{2.5-10}$ exposure was associated with a 6% increase in asthma symptoms [95% CI 1-12] and 6% increase in reliever medication [95% CI 1-10]. 3% and 4% increase in symptoms and reliever use were associated with a 10microg/m$^3$ increase in PM$</em>{2.5}$ exposure.</td>
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<tr>
<td>Indoor particulate matter increases asthma morbidity in children with non-atopic and atopic asthma (2011)</td>
<td>Same cohort as above$^8$</td>
<td>Same cohort as above$^8$</td>
<td>Same cohort as above$^8$</td>
<td>Same cohort as above$^8$. 31% skin prick test negative</td>
<td>Same cohort as above$^8$</td>
<td>Same cohort as above$^8$</td>
<td>PM$<em>{2.5-10}$ exposures were comparable for atopic and non-atopic children. PM$</em>{2.5}$ exposures were higher for non-atopic compared to atopic children (36 vs 28 μg/m$^3$). Increasing PM exposure was associated with increased risk for symptoms in atopic and...</td>
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<td>Household levels of nitrogen dioxide and pediatric asthma severity (2013)</td>
<td>At least two out of the following: Physician diagnosed asthma, asthma symptoms in previous 12 months, asthma treatment within the previous 12 months</td>
<td>Symptoms and reliever medication use</td>
<td>Longitudinal study</td>
<td>1342 children aged 5-10 years (52% aged &lt;8 years)</td>
<td>To relate indoor NO2 exposure to asthma outcomes in children</td>
<td>NO2 was measured over one month using Palms tubes at baseline and at 3 months intervals over the next 12 months. Asthma outcomes were determined by telephone interviews which were held at the end of each NO2 measurement period. Exposure to indoor allergens including HDM, cat, dog and cockroach was also measured</td>
<td>non atopic children although the study was underpowered for non-atopic analysis (eg rescue medication increased by 5% and 7% for each 10 microg/m³ increase in PM2.5,10 for non atopic and atopic children).</td>
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<tr>
<td>Association of indoor nitrogen dioxide exposure</td>
<td>Physician diagnosed asthma</td>
<td>Symptoms</td>
<td>Cross sectional</td>
<td>728 children aged &lt;12 years (67%&lt;6 years)</td>
<td>Relate indoor NO2 concentrations to symptoms over the previous month</td>
<td>Respiratory symptoms over the previous month were determined by</td>
<td>NO2 concentrations were higher in homes with gas stoves. Each 20 ppb</td>
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**Nitrogen dioxide**
### Study

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<tr>
<th>Study</th>
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<tbody>
<tr>
<td>children with respiratory symptoms in asthma (2006) <strong>11</strong> USA</td>
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<td>whose newborn sibling had been recruited onto a trial (inclusion criteria were older sibling with asthma)</td>
<td>previous month</td>
<td>research administered questionnaire. NO2 was measured over the following 10-14 days using (Palms tubes).</td>
<td>increase in NO2 was associated with increased wheeze (OR 1.5 [1.0, 2.2]) and chest tightness (OR 1.6 [1.0, 2.5])</td>
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<tr>
<td>Damp housing, mould</td>
<td>Presentation to emergency department of primary care or hospitalisation with acute asthma</td>
<td>Symptoms</td>
<td>RCT, follow-up period one year</td>
<td>Children with asthma (n=62) 2-17 years of age. Intervention n=29, Controls n=33</td>
<td>To examine the changes in asthma morbidity in children following home remediation aimed at moisture sources.</td>
<td>Both groups received an asthma intervention (action plan, education and individualized problem solving). Intervention group also received household repair, removal of water damaged building materials and heating, ventilation and air conditioning alterations.</td>
<td>There was a significant decrease in symptom days in the intervention group (p=0.003)</td>
</tr>
<tr>
<td>Differential effects of outdoor versus indoor fungal spores on asthma morbidity in inner-city children (2010) <strong>13</strong> USA</td>
<td>Moderate-to-severe asthma with positive skin test to at least one fungal allergen</td>
<td>Symptom score (daytime, night time and exertional symptoms) and unschedule d ED or</td>
<td>Longitudinal study</td>
<td>469 children aged 5-11 years (mean 7.7 years) out of 936 children screened (467 with no positive skin test)</td>
<td>To relate indoor and outdoor fungal exposures to asthma symptoms over 2 years.</td>
<td>Fungal exposures were measured at baseline and 6 monthly thereafter. Symptoms were obtained from 2 monthly telephone consultations</td>
<td>Indoor and outdoor fungal exposures were positively associated with outcome. When both were considered, only indoor exposures were associated with outcomes. A 10-fold increase in total fungal exposure was positively related to risk for</td>
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<tr>
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<tr>
<td>House Dust Mite-Free Pillow on Clinical Course of Asthma and IgE Level—A Randomized, Double-Blind, Controlled Study. (2008)</td>
<td>Medical follow up for asthma in hospital clinic. HDM sensitised.</td>
<td>Symptoms</td>
<td>Intervention 12 months</td>
<td>Intervention (n=10) mean age 7, range 5-11 years and controls (n=10) mean age 6; range (4-8).</td>
<td>To investigate HDM and fungi contamination of HDM-free pillows and the effects of these pillows on clinical courses of asthmatic children with house dust allergy.</td>
<td>Intervention group were provided with HDM free pillows and control group used new common pillows with HDM permeable fabrics. Samples were collected for fungi and HDM allergen Der 1 detection at three intervals.</td>
<td>Asthma symptoms did not differ between intervention and control groups. There were no significant differences in the levels of HDM allergen Der 1 between the groups. Among children with high HD-IgE levels (≥ 50 U/mL) before the study, the levels had decreased after 12 months in all six subjects in the intervention group (p=0.030; paired t-test) and in four of seven subjects in the placebo group (p=0.481; paired t-test).</td>
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**Inhaled allergens (house dust mite, pets, pollens)**

<table>
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<tbody>
<tr>
<td>Effect of mattress</td>
<td>Level of Interventions</td>
<td>Children (n=60)</td>
<td>To investigate whether</td>
<td>Active treatment group</td>
<td>Significant reduction in</td>
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<td>and pillow encasings on children with asthma and house dust mite allergy (2003)</td>
<td>Physician diagnosed asthma, HDM skin prick positive and BHR to inhaled HDM</td>
<td>mattress and pillow encasings resulted in an effective long-term control of HDM allergen levels, thereby reducing the need for asthma medication in children with asthma and HDM allergy.</td>
<td>n with one year follow-up period</td>
<td>6-15 years old with asthma and allergy to house dust mite.</td>
<td>was provided mattress and pillow encasings coated with semi permeable polyurethane. Control group received a placebo mattress and pillow covers.</td>
<td>HDM allergen was observed in the active treatment group (p=0.032). After 12 months there was a reduction in the dose of inhaled steroids by 50% in significantly more children in the active treatment group vs. the control group (73% vs. 24%, p&lt;0.001).</td>
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<tr>
<td>Does a multifaceted environmental intervention alter the impact of asthma on inner-city children? (2006)</td>
<td>Asthma admission or presentation to emergency department</td>
<td>Children (5-12 years of age, trial period one year</td>
<td>RCT</td>
<td>To evaluate the impact of an environmental and educational intervention on the indoor environment and health in children with asthma living in urban environments.</td>
<td>Children were randomized into intervention (n=84) and delayed intervention (n=77) groups. Interventions were delivered by trained community health workers and focused on reduction of HDM and cockroach allergen, reduction in exposure to ETS, professional cleaning and health education. Asthma severity scores were determined, house dust assays were carried out and blood samples were collected from children</td>
<td>There was no change in the asthma severity scores between the groups.</td>
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<td>Results of a home-based environmental intervention among urban children with asthma. (2004) USA <em>STRONG STUDY DESIGN</em></td>
<td>Asthma diagnosed by study physician, exacerbation in past 6 months and skin prick positive.</td>
<td>Symptoms</td>
<td>Intervention RCT one year</td>
<td>Children (n=937) aged 5-11 years of age with mild to moderate asthma. Intervention n=469, control n=468.</td>
<td>To determine whether an environmental intervention tailored to each child’s allergic sensitization and environmental risk factors could improve asthma-related outcomes.</td>
<td>Baseline data were collected for complications related to asthma and information on home environment (dust samples). Carers of children in the intervention group received education, skills, motivation, equipment and supplies to perform environmental remediation. Control group received visits only every six months.</td>
<td>Intervention group had significantly fewer days with symptoms compared to the control group both during the intervention year (3.39 vs. 4.20 days, p&lt;0.001) and in the follow-up year (2.62 vs. 3.21 days, p&lt;0.001).</td>
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<tr>
<td>Environmental intervention for house dust mite control in childhood bronchial asthma (2012) Egypt</td>
<td>Physician diagnosed asthma and asthma treatment within the last 6 months and skin prick positive to HDM</td>
<td>Asthma severity and spirometry (FEV₁)</td>
<td>RCT</td>
<td>160 children aged 5-12 (mean 7.7 years)</td>
<td>To determine whether chemical HDM measures (twice weekly sparing with tannic acid) or physical measures (multiple including ventilation, HDM impermeable bedding) or both are superior to standard care</td>
<td>A 16 week trial. After randomisation, home visits each 2 weeks to ensure compliance. Outcomes measures at 8 and 16 weeks.</td>
<td>No significant difference in severity- evidence for reduced prevalence of most severe symptoms. Improvement of approximately 2% in FEV₁ for children in each of the 3 active arms of the trial.</td>
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<td>Healthy Homes University: a home-based environmental intervention and education program for families with pediatric asthma in Michigan (2011)</td>
<td>Care giver reported asthma</td>
<td>Symptoms seeking unscheduled health care</td>
<td>Single arm intervention study</td>
<td>243 households, index case aged under 12 in 80%</td>
<td>To determine whether complex intervention improved asthma outcomes</td>
<td>Complex intervention including removing asthma triggers, asthma education and also addressing injury hazards. Interventions included removing moisture from the house, removing carpets, air filter unit, HDM impermeable bedding, smoking education. 4 visits to encourage compliance over 6 months</td>
<td>Improved reported symptoms after 6 months (between 1-7% for different symptoms). 47% reduction in unscheduled healthcare visits.</td>
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<tr>
<td>Effects of ambient pollen concentrations on frequency and severity of asthma symptoms among asthmatic children (2012)</td>
<td>Physician diagnosed asthma and symptoms in previous 6 months</td>
<td>Symptom score and reliever medication use</td>
<td>Longitudinal study</td>
<td>430 children aged 4-12 (44% &lt;8 years) sensitised and not sensitised to pollens (predominantly ragweed)</td>
<td>To relate asthma symptoms and rescue medication use to changes in pollen exposure during one pollen season (April-September)</td>
<td>At recruitment sensitisation status and use of maintenance treatment were established. Pollen exposure was estimated using a previously validated model. Ambient PM$_{2.5}$, O$_3$, NO$_2$ and SO$_2$ were included in the analysis</td>
<td>Among children on maintenance treatment and sensitised to grass and weed, risk for symptoms and rescue medication use were increased in all quintile of exposure compared to the lowest quintile. The greatest risk was seen among those exposure to the second highest quintile of pollen exposure: OR for wheeze 2.4 [95%CI 1.5, 3.7] and OR for rescue medication</td>
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<tr>
<td>Influence of early and current environmental exposure factors on sensitization and outcome of asthma in pre-school children. (2001)</td>
<td>≥3 episodes of wheeze</td>
<td>Longitudinal study</td>
<td>Children (n=183) age 1-4 years diagnosed with asthma.</td>
<td>To evaluate the importance of early exposure to pets and other environmental risk factors in asthmatic children.</td>
<td>Questionnaire data were collected for family history of atopic disease and indoor environmental conditions. Serum IgE antibodies to cat and dog were measured. Asthma severity scored at structured interview with a parent. Floor dust collected from home and analyzed for FelD1 and Can f 1.</td>
<td>Children with exposure to cats during the first 2 years of life were more likely to have developed sensitisation by 4 years of age compared to unexposed children (OR 5.6 [95% CI 1.06, 29.0]. High levels of cat allergen (Fel D1≥8 μg/g dust) were associated with an increased risk of sensitisation to cat and in combination with ETS with more severe asthma.</td>
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<td>Industrial incineration, coal- No evidence</td>
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<td>Fireworks- No evidence</td>
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<td>Domestic combustion (solid fuel, gas and candles)</td>
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<td>Effects of improved home heating on asthma in community dwelling children: randomised controlled trial. (2008)</td>
<td>Physician diagnosed asthma and symptoms in the past 12 months.</td>
<td>Symptoms Spirometry</td>
<td>RCT</td>
<td>Children (n=349) Intervention n=175, control n=174.</td>
<td>To assess whether non-polluting, more effective home heating has a positive effect on the health of children with asthma.</td>
<td>Intervention group received a non polluting more effective home heater before winter. Control group received a replacement heater at the end of the trial.</td>
<td>No significant improvements observed in lung function. There was a significant reduction in asthma symptoms (OR=0.48, 95% CI 0.31-0.74, p&lt;0.001)</td>
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*STRONG STUDY
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<td>Randomized controlled trial of unflued gas heater replacement on respiratory health of asthmatic schoolchildren (2004) 23 Australia <em>POOR STUDY DESIGN</em></td>
<td>Physician diagnosed asthma</td>
<td>Symptoms</td>
<td>RCT</td>
<td>Intervention (n=45) mean age 8.4, SD 2.2; Control (n=68) mean age 8.7, SD 2.3.</td>
<td>To investigate the effect of replacing unflued gas heaters on respiratory health of asthmatic children.</td>
<td>In intervention schools unflued gas heaters were replaced with flued gas or electric heaters. No heaters were replaced in the control school. Information on symptoms was collected using daily diaries, lung function tests were carried out and data on NO2 was collected using passive diffusion badge monitors.</td>
<td>There was a significant reduction in asthma symptoms in the children from intervention schools. 1) Difficulty breathing during day RR=0.41, 95% CI 0.07-0.98. 2) Difficulty breathing during night RR=0.32, 95% CI 0.14-0.69. 3) Daytime asthma attacks RR=0.39, 95% CI 0.17-0.93.</td>
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<td>Humidity control for chronic asthma. Cochrane Database Systematic Rev . (2008) 24 UK</td>
<td>Attending hospital asthma clinic</td>
<td>Systematic Review</td>
<td>One RCT25 (13 adults and 27 children age 4-16 years)</td>
<td>To study the effect of dehumidification of the home environment on asthma control.</td>
<td>Study participants were grouped into those who received 1) fixed humidifiers, 2) MVHR, 3) High efficiency vacuum cleaners and 4) No intervention</td>
<td>Although there was a significant decline in the house dust mite count and antigen levels in group 1 and group 2, no clinical benefit was observed in the asthmatic patients.</td>
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<td>The effects of exclusion of dietary egg and milk in the management of asthmatic children: a pilot study (2004)</td>
<td>Physician diagnosed mild or moderate asthma</td>
<td>Peak expiratory flow</td>
<td>RCT (8 weeks)</td>
<td>Asthmatic children (n=22) aged 3-14 years, Intervention n=13, control n=9.</td>
<td>To determine the potential benefits of dietary avoidance of egg and egg products and milk and milk products in reducing the symptoms of asthma in children.</td>
<td>Intervention group participants were asked to adhere to a diet devoid of egg and egg products and milk and milk products. Those in the control group were asked to continue to eat their usual diet.</td>
<td>Amongst the intervention group the mean value for peak expiratory flow rate (PEFR) measurement had risen by 22% (p&lt;0.05) whereas there was a decrease in mean PEFR value by 0.6% in the control group.</td>
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<td>Study of modifiable risk factors for asthma exacerbations: virus infection and allergen exposure increase the risk of asthma hospital admissions in children . (2006)</td>
<td>Admitted to hospital with asthma or attending hospital asthma clinic</td>
<td>Asthma admission</td>
<td>Case control study</td>
<td>Children aged 3-17 years of age (n=84)</td>
<td>To investigate the importance of allergen exposure in sensitised individuals in combination with viral infections and other potentially modifiable risk factors precipitating asthma admissions in children.</td>
<td>Cases were children admitted over a one year period (acute asthmatics) matched with two groups of controls: those with stable asthma and children admitted with non respiratory conditions.</td>
<td>A combination of virus detection and allergen sensitization significantly increased risk of hospital admission among the acute asthmatics in comparison to the controls (OR 19.4, 95% CI 3.7-101.5, p&lt;0.001)</td>
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<td>Is respiratory viral infection really an important trigger of asthma</td>
<td>Physician diagnosed asthma, symptoms in previous year,</td>
<td>Presence of virus in mild exacerbation</td>
<td>Longitudinal study</td>
<td>114 children aged 6-1 4years (mean age not stated)</td>
<td>To determine whether respiratory viruses were associated with asthma exacerbations</td>
<td>After recruitment, children completed diaries and twice daily peak flow. If peak flow was ≤80% baseline,</td>
<td>Over 12-15 months, there were 305 respiratory illnesses in 98 children presented for clinical assessment. 166 samples</td>
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<td>exacerbations in children? (2011)</td>
<td>no hospitalisation s and on ≤400 microg inhaled steroids daily (BUD equivalent)</td>
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<td>symptom score exceeded the predetermined threshold or parents felt their child had a cold then the child attended an clinical assessment which included collecting samples for viral testing (immune fluorescence and some PCR)</td>
<td>were collected (54% of episodes) from which respiratory virus was identified in only 61. Approximately half of episodes were considered asthma exacerbations, the remainder respiratory infections.</td>
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Table II. Summary of the quality control exercise. Each of the six individual domains and the global rating is scored as follows: 1=strong, 2=moderate and 3=weak. The paper\textsuperscript{25} which was included in the systematic review\textsuperscript{24} for the use of humidification was used for the quality control.

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REFERENCES


Search strategy

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166. 128 or 151 or 153 or 155 or 157 or 159 or 161 or 163 or 165
167. allergens.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
168. aspergillus.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
169. cladosporium.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
170. dust mite*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
171. cat*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
172. dog*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
173. horse*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
174. animal*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
175. pet*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
176. mould.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
177. mold.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
178. alternaria.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
179. cockroach*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
180. mice.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
181. rats.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
182. pollen.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
183. grass.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
184. aeroallergen*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
185. IgE.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
186. fungal spore*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
187. food allerg*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
188. glucan*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
189. peanut*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
190. egg.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
191. milk.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
192. dairy.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
193. 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176 or 177 or 178 or 179 or 180 or 181 or 182 or 183 or 184 or 185 or 186 or 187 or 188 or 189 or 190 or 191 or 192
194. 18 and 193
195. exercise.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
196. 18 and 195
197. lipopolysaccharide.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
198. 18 and 197
199. endotoxin.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
200. 18 and 199
201. respiratory syncitial virus.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
202. 18 and 201
203. rhinovirus.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
204. 18 and 203
205. influenza virus.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
206. 18 and 205
207. corona virus.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
208. 18 and 207
209. 202 or 204 or 206
210. diet.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
211. 18 and 210
212. sulphite*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
213. sulfite*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
214. sodium metabisul*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
215. monosodium glutamate.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
216. MSG.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
217. sodium benzoate.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
218. vitamin D.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
219. vitamin E.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
220. antioxidant*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
221. lipid*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
222. 212 or 213 or 214 or 215 or 216 or 217 or 218 or 219 or 220 or 221
223. 18 and 222
224. 211 or 223
225. breastfeeding.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
226. weaning.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
227. 225 or 226
228. 18 and 227
229. drug*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
230. 18 and 229
231. aspirin.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
232. paracetamol.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
233. antibiotic*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
234. NSAID*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
235. 231 or 232 or 233 or 234
236. 18 and 235
237. obesity.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
238. 18 and 237
239. 29 or 131 or 136 or 149 or 166 or 194 or 196 or 198 or 200 or 209 or 224 or 228 or 236 or 238
240. 9 or 10 or 11
241. 18 and 240
242. 239 or 241
243. 74 or 242
244. limit 243 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)") and english and humans and (case reports or classical article or comparative study or congresses or consensus development conference or consensus development conference, nih or controlled clinical trial or "corrected and republished article" or government publications or guideline or historical article or introductory

...
journal article or journal article or meta analysis or multicenter study or patient education handout or periodical index or randomized controlled trial or research support, nih, extramural or research support, nih, intramural or research support, non us gov't or research support, us gov't, non phs or research support, us gov't, phs or "review" or "scientific integrity review" or twin study or validation studies))

245. from 244 keep 6033,6045,6055,6062,6065,6091,6122,6150,6166,6172,6179,6225,6229-6230,6245,6249,6304,6307-6309,6315,6317,6346,6413-6414,6428,6435,6441,6453,6516,6551-6552,6574,6581,6585,6588,6599,6622,6641,6660,6699

246. from 244 keep 6710,6783