

Interventions for pediatric asthma a literature review of efficacy and safety in pharmacological and non-pharmacological modalities

Intervenciones para el asma pediátrica una revisión de la literatura sobre eficacia y seguridad en modalidades farmacológicas y no farmacológicas

Mónica Thalía Yépez Cujilema

<https://orcid.org/0009-0000-4216-0676>

Universidad Nacional de Chimborazo, Ecuador

Tiffany Ivanna Guerrero Solorzano

<https://orcid.org/0009-0006-8723-3772>

Universidad de Especialidades Espíritu Santo, Ecuador

Galo Fernando Tulcanaza Ochoa

<https://orcid.org/0000-0002-6254-8624>

Hospital Misereor de Gualaquiza, Ecuador

Chamorro Martínez Gina Jessica

<https://orcid.org/0009-0007-5643-654X>

Universidad Nacional de Chimborazo, Ecuador

Jose Alberto Naspud Peña

<https://orcid.org/0009-0001-7312-3613>

Universidad Católica Santiago de Guayaquil, Ecuador

ABSTRACT

Asthma continues to be a major global health concern due to its related morbidity and healthcare utilization, especially in children. Pharmaceutical treatments are crucial for managing asthma, but non-pharmacological therapies are now increasingly recognized for their complimentary benefits in enhancing quality of life and lowering medication reliance. This review examines the many methods for managing asthma that involve both non-pharmacological and pharmacological techniques. The review underscores the significance of environmental triggers, including dust mites, pet dander, and mold, and shows practical strategies for mitigating allergy symptoms and adjusting living environments. It also covers how enhancing indoor air quality using smoke-free zones and HEPA air filters might lessen asthma attacks, particularly in kids who are exposed to secondhand smoke and urban air pollution. The objective is to maximize the care of asthma and reduce the worldwide prevalence of this chronic respiratory disorder by implementing comprehensive approaches that incorporate both non-pharmacological and pharmaceutical interventions.

Keywords: Asthma, Management, Pharmacological Interventions, Non-pharmacological Interventions, Environmental.

RESUMEN

El asma sigue siendo un importante problema de salud mundial debido a la morbilidad relacionada y la utilización de la atención médica, especialmente en los niños. Los tratamientos farmacéuticos son cruciales para controlar el asma, pero las terapias no farmacológicas son cada vez más reconocidas por sus beneficios complementarios para mejorar la calidad de vida y reducir la dependencia de los medicamentos. Esta revisión examina los muchos métodos para controlar el asma que involucran técnicas tanto farmacológicas como no farmacológicas. La revisión subraya la importancia de los desencadenantes ambientales, incluidos los ácaros del polvo, la caspa de las mascotas y el moho, y muestra estrategias prácticas para mitigar los síntomas de las alergias y ajustar los entornos de vida. También cubre cómo mejorar la calidad del aire interior utilizando zonas libres de humo y filtros de aire HEPA podría disminuir los ataques de asma, particularmente en niños que están expuestos al humo de segunda mano y a la contaminación del aire urbano. El objetivo es maximizar la atención del asma y reducir la prevalencia mundial de este trastorno respiratorio crónico mediante la implementación de enfoques integrales que incorporen intervenciones farmacéuticas y no farmacológicas.

Palabras clave: Asma, Manejo, Intervenciones Farmacológicas, Intervenciones No Farmacológicas, Ambiental.

INTRODUCTION

No Airway obstruction that occurs frequently and either resolves on its own or requires medication treatment is one of the primary features of asthma. At the other end of the scale, asthma can be more severe and costly for healthcare systems because of refractoriness to existing medicines and comorbidities that overlap with COPD.¹ When it comes to the top 20

chronic conditions globally in terms of children's disability-adjusted life years, asthma is one of the top 10 causes throughout the mid-childhood years, which span from 5 to 14 years of age.²

There are between 0.0 and 0.7 asthma-related deaths per 100,000 children worldwide. In spite of the fact that asthma symptoms are more common in many high-income countries (HICs), several low- and middle-income countries (LMICs) also have high rates of these symptoms. Children in LMICs, not HICs, were more likely to have experienced severe asthma symptoms among those who had wheezed in the preceding year.²

Therapeutic approaches mild to moderate asthma symptoms

Inhaled corticosteroids, either by themselves or in combination with long-acting beta agonists, remain the cornerstone of pharmacological treatment for mild to moderate asthma. When taken as directed, inhaled corticosteroids efficiently improve lung function, lessen the chance of exacerbations, and control everyday asthma symptoms.³ Controlled trials have consistently shown that inhaled corticosteroids are superior to leukotriene receptor antagonists, including montelukast, at symptom control, lung function improvement, and exacerbation reduction. However, montelukast may be just as effective as inhaled corticosteroids, according to the findings of a pragmatic trial that aimed to replicate standard medical practice.⁴ According to community-based study, up to 20% of patients adhere to this type of therapy. Participants do not take more than 50% of the prescribed dosages after several months of the experiment; adherence is quite high initially but gradually decreases in carefully monitored trials.⁵

There was some improvement in the asthma outcomes of children undergoing supervised therapy, which involved using inhaled corticosteroids under the supervision of study staff members every school day for 15 months. Patients with less severe asthma who moved from a daily dose of inhaled corticosteroids to an as-needed combination of inhaled corticosteroids and albuterol showed similar exacerbation rates to those seen with daily inhaled corticosteroids, as well as improved rates of asthma exacerbations when compared to placebo.⁶

In individuals who still experience symptoms after having inhaled corticosteroids, adding a LABA has been demonstrated to be helpful in several clinical trials. Moreover, a greater percentage of these individuals react more favorably to the addition of LABA than to leukotriene receptor antagonists or higher doses of inhaled corticosteroids.¹⁴ The hunt for additional medications has been spurred by safety concerns for those whose asthma is not adequately managed by inhaled corticosteroids alone.⁷

Therapeutic approaches to severe asthma

Patients with severe asthma who do not react to high-dose inhaled corticosteroids plus LABA or who often have exacerbations of their disease still face significant challenges in receiving corticosteroids as a form of treatment.¹⁶ Individuals who suffer from severe asthma, particularly in younger patients, frequently experience atopic issues. In a large inner-city research with patients of all severity, omalizumab, a humanized monoclonal antibody against IgE, reduced asthma exacerbations by thirty percent. The most significant effects were seen in patients who had been exposed to cockroaches and had been sensitized to them.⁸

Pharmacological Interventions

Environmental management and pharmaceutical therapy are the two main facets of asthma treatment.⁹ Treating patients with severe asthma who take oral corticosteroids or high-dose inhaled corticosteroids plus LABA but nevertheless have uncontrollable symptoms and frequent exacerbations remains a significant challenge. The potential course of treatment for severe asthma has significantly changed as a result of our expanding knowledge of the pathophysiology of the condition.¹⁰ According to one theory, distinct pathogenic mechanisms underlie each asthma subphenotype, and pinpointing these mechanisms may enable more specialized and targeted treatment.

Atopic disorders are common in people with severe asthma, particularly in children. An important inner city trial with patients of all severity levels found that omalizumab, a humanized monoclonal antibody against IgE, reduced asthma exacerbations by thirty percent.¹¹ It has been discovered that a number of asthma subphenotypes exhibit sputum eosinophilia symptoms and are more prone to exacerbations. This research revealed that the use of humanized monoclonal antibodies against interleukin, the most powerful eosinophil stimulant and chemo-attractor, may be part of the strategy to prevent these exacerbations.¹²

Non - Pharmacological Interventions

The use of non-pharmacological therapies is a fundamental component in the treatment of a wide range of medical disorders in modern healthcare practices. Sensitization to and exposure to indoor allergens, such as dust mites, rats, cockroaches, and pet allergens, might impair the regulation of childhood asthma and lung function due to increased morbidity and inflammation of the airways.¹³

Dermatophagoides farinae and *Dermatophagoides pteronyssinus*, the two most prevalent species of home dust mites, are the source of allergens Der f 1 and Der p 2, respectively. Dust mite sensitization affects between 30 and 60 percent of kids who suffer from persistent asthma.¹⁴ Three strategies have been found to be effective in reducing exposure to dust mites: (1) washing all bed linens in hot water on a regular basis; (2) using allergen-impermeable mattresses and pillow encasements; and (3) concentrating on other dust mite allergen reservoirs by vacuuming, scraping off carpet, and taking stuffed toys off the bed. Furthermore, there's little evidence that air filtration significantly reduces exposure to dust mites.¹⁵

Furry animal allergens are carried on minuscule particles (less than 10–20 μm), which allows them to hang out in the atmosphere for extended periods of time. Subsequently, these particles stick to upholstered surfaces including clothes, furniture, and walls. Due to the passive transfer of allergy from owners of furry pets into places lacking furry critters, sensitization to allergens from pets can happen through direct or indirect exposure.¹⁶ The first line of protection against exposure to pet allergies is the removal of the pet and the cleaning that follows to remove any reservoirs. Remember that it may take many months for there to be a noticeable decrease in allergy levels, even in cases where pets have been removed.¹⁷

Bla g 1 and Bla g 2 are the main allergens associated with cockroaches. Two of the main mouse proteins that cause allergies are Mus m 1 and Mus m 2. Urine, hair follicles, and mouse dander all include these allergens. Removing residents and neighbors from their homes is one method of managing cockroaches and rodents, however this tactic is ineffective on its own. It has been researched as a pest-related allergen intervention technique to reduce allergen levels. Four key principles are involved in this approach: (1) using sticky traps to track pest populations and identify their hiding places (reservoirs); (2) obstructing pest access and entryways; (3) removing food and water sources to promote the growth of predators; and (4) applying low-toxicity insecticides sparingly.¹⁸

A little over 12.2% of kids with chronic asthma had a mold sensitivity. Molds can be found both indoors and outdoors, and each species has a different set of allergenic proteins. It is common to find *Aspergillus* and *Penicillium* species of mold inside. Certain kinds of mold, such as *Cladosporium*, *Alternaria*, and *Epicoccum*, are frequently found outside. There must be moisture for mold to grow. Children are most frequently exposed to and sensitized to *Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium* species.¹⁹

Research suggests that HEPA air filters may be beneficial, especially for children who are unable to avoid secondhand smoke. Children with asthma who were known to be exposed to secondhand environmental tobacco smoke participated in a double-blind, randomized controlled trial. According to numerous studies, establishing smoke-free public areas helps lessen the harmful effects of secondhand smoke on asthmatic children. A recent meta-analysis found that the rate of preterm deliveries, hospital admissions for pediatric respiratory tract infections, and asthma flare-ups decreased when smoke-free laws were put into place, as recommended by the World Health Organization (MPOWER).²⁰

Urban air pollution, which can enter buildings and have a negative impact on school interior air quality, is primarily caused by traffic pollution. Gaseous pollutants from this form of pollution, including ozone, NO₂, and SO₂, can aggravate asthma by inducing oxidative stress that damages and inflames the lungs.

Using multipollutant models it is shown that children's asthma symptoms increase in response to brief exposures to ozone, NO₂, and SO₂. A photochemical interaction between sunlight and precursors of pollution, such as nitrogen oxide, creates ozone. There is proof that short-term ozone exposure causes asthma exacerbations in both adults and children.²¹

METHODOLOGY

Data Search Strategy

In order to find relevant research on Interventions for pediatric asthma as a review of efficacy and safety in pharmacological and non-pharmacological modalities, a systematic and comprehensive search strategy was employed. The following electronic databases were searched: Google Scholar, PubMed/MEDLINE, semanticscholar. To effectively combine search terms, the search strategy included a combination of keywords and medical topic headings (MeSH) linked to asthma, pediatric asthma, pharmacological interventions, non-pharmacological interventions, and HEPA air filters. The search results were filtered and limited based on language, study design, and publication type. The search parameters were limited to peer-reviewed research and articles published in the English language. The reference lists of relevant papers and systematic reviews were hand-searched in order to locate further research that satisfied the inclusion criteria.

Table 1. MeSH terms and keywords used in the systematic review

Category	Keywords/MeSH Phrases
Asthma	"pediatric asthma" OR "lungs disease " OR " COPD "
Treatment	" Pharmacological intervention " OR " Non-Pharmacological Interventions " OR "Therapy"
SHS	" Second Hand Smoke " OR " HEPA filters"

Source: the authors.

Inclusion Criteria:

Included were studies that fulfilled the following criteria:

- Studies evaluating Asthma / Pediatric Asthma
- Studies that offer in-depth information regarding pharmacological and non-pharmacological interventions
- studies that provide a brief relationship between interventions, efficacy and safety of modalities

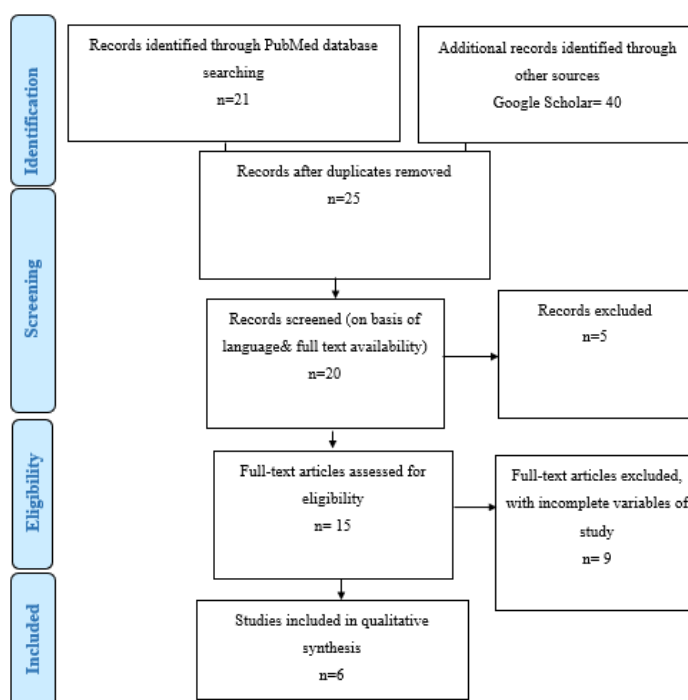
Exclusion Criteria:

Studies mentioned below were excluded:

- Studies that did not specifically address asthma
- studies that did not fully report their findings
- animal research; in vitro testing
- Studies that are not full text available in English.

Data Extraction:

An extensive evaluation of the therapies for pediatric asthma was carried out using a methodical approach to data extraction and synthesis. This required evaluating specific articles that met predetermined criteria, compiling pertinent information from full-text journals, and analyzing significant findings. A narrative approach was used in the method to highlight significant discoveries, trends, and patterns that were found in multiple investigations. The methodological methodology allowed for a full study of the literature, which led to significant findings on the pharmacological and non-pharmacological therapies for juvenile asthma. The meticulous data management system, which guaranteed the authenticity and dependability of the review findings, made the rigorous selection and analysis of publications easier. The PRISMA-compliant data extraction procedure utilized for this systematic review is shown in Figure.

Figure 1. Prisma

Source: the authors.

RESULTS AND DISCUSSION

Out of all pertinent studies that matched the inclusion requirements for this systematic review were found using the systematic search approach. Three of these research particularly examined the pharmacological interventions, while the remaining four studies concentrated on non-pharmacological interventions of asthma based on efficacy and safety parameter. Table 2 provides a summary of the features and major conclusions of these investigations.

Table 2. Characteristics of Studies Included in the Systematic Review

Study	Study Design	Intervention	Key Findings
Jarjour et al., 2012	Longitudinal Cohort Study	Pharmacological	patients who take oral corticosteroids or high-dose inhaled corticosteroids plus LABA but nevertheless have uncontrollable symptoms and frequent exacerbations remains a significant challenge
Hanania et al., 2011	placebo-controlled trial	Pharmacological	Atopic disorders are common in people with severe asthma, particularly in children.
Moore et al., 2010	Cluster analysis	Pharmacological	Use of humanized monoclonal antibodies against interleukin, eosinophil stimulant and chemo-attractor, part of the strategy to prevent exacerbations.
Weisse et al., 2001	CAMP study	Non pharmacological	Der f 1 and Der p 2 the two most prevalent species of home dust mites, are the source of allergens
Human verification. (n.d.).	PEACE study	Non pharmacological	Air filtration significantly reduces exposure to dust mites.
Pongracic et al., 2010	Longitudinal study	Non pharmacological	Bla g 1 and Bla g 2 are the main allergens associated with cockroaches.
Naja et al., 2018	Retrospective analysis	Non pharmacological	Short-term ozone exposure causes asthma exacerbations in both adults and children.

Source: the authors.

After a careful review of the literature, the effectiveness and safety of interventional therapy for childhood asthma have been brought to the attention of scholars. These methods offer prospective solutions to some of the many obstacles associated with treating this illness. Through the SARP collaboration Comprehensive clinical, physiologic, genetic, and radiological assessments were performed It's still very difficult to treat people with severe asthma who take oral corticosteroids or high-dose inhaled corticosteroids together with LABA but nevertheless have unmanageable symptoms and frequent exacerbations. The burden this places on society and the highly incapacitating nature of severe asthma justify ongoing efforts to develop novel therapies, since these individuals bear a disproportionate share of the direct costs associated with having the condition. Our growing understanding of the pathophysiology of severe asthma has led to substantial changes in the possible treatment plan. There's no shortage of evidence that severe asthma is heterogeneous, since unbiased hierarchical clustering techniques have been used to identify several subphenotypes in both adults and children.¹⁰ Patients with severe asthma that was not well managed with high-dose ICS, LABAs, and, frequently, additional controller drugs reported a 25% reduction in asthma exacerbations when treated with omalizumab. Omalizumab add-on therapy also enhanced the quality of life for those with asthma. Omalizumab consistently outperformed a placebo in terms of the change from baseline in the overall asthma symptom score and the utilization of rescue 2-agonists.¹² Clinical strategies that employ these cellular indicators to direct asthma care have been developed as a result of numerous investigations that have shown eosinophilic or noneosinophilic inflammation in asthma. Although sputum eosinophilia is a biomarker that seems to be helpful in directing corticosteroid therapy, most clinical settings may not have access to induced sputum analysis due to the technique's complexity and challenges in doing this analysis accurately. As a noninvasive biomarker for asthma diagnosis and treatment response assessment, FENO has been employed in clinical settings; however, newer research indicates that its predictive power may be limited.¹³ Three methods have been found to be effective in reducing exposure to dust mites: (1) regularly washing all bed linens in hot water; (2) utilizing allergen-impermeable mattresses and pillow encasements; and (3) focusing on other dust mite allergen reservoirs by vacuuming, removing stuffed toys from the bed, and scraping off carpet. Sadly, maintaining indoor humidity levels low enough to prevent dust mite reproduction and survival may prove to be

challenging. Moreover, there isn't much proof that air filtration greatly lowers dust mite exposure.¹⁵ Allergens from furry animals can linger in the atmosphere for a long time because they are carried on tiny particles (less than 10–20 μm). These particles then adhere to upholstered surfaces, such as walls, furniture, and clothing. Sensitization to pet allergens can occur through direct or indirect exposure due to the passive transmission of allergy from owners of furry pets into regions without furry critters.¹⁶ The mold sensitivity rate in children with chronic asthma was little above 12.2%. Both indoor and outdoor molds are common, and each species contains a unique combination of allergenic proteins. Mold species such as *Aspergillus* and *Penicillium* are frequently found inside. Some molds are commonly found outside, including *Cladosporium*, *Alternaria*, and *Epicoccum*. Mold can only grow in a damp environment. The kitchen and bathroom vents should be opened, broken items should be replaced, leaks should be fixed, a dehumidifier should be kept in the basement, the air conditioner should be run during the summer, and moldy areas should be treated with fungicide. The species of *Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium* that most commonly expose and sensitize children are those.¹⁸ Traffic pollution is the main source of urban air pollution, which can infiltrate buildings and lower the interior air quality in schools. This type of pollution produces gaseous pollutants such as ozone, NO₂, and SO₂, which can exacerbate asthma by causing oxidative stress, which damages and irritates the lungs.

It is demonstrated using multipollutant models that children's asthma symptoms worsen after short exposure to SO₂, NO₂, and ozone. This is important since schools are usually located in the midst of communities, close to business and industrial buildings, busy roads, and highways.

Ozone is produced by the photochemical reaction of sunlight with pollution precursors like nitrogen oxide. Research indicates that children and adults who are exposed to short-term ozone suffer from exacerbations of their asthma.²¹

CONCLUSION

The effects of asthma on morbidity and healthcare utilization, especially in children, highlight the importance of asthma as a global health issue. Pharmaceutical therapies are essential for managing asthma, but non-pharmacological approaches are also becoming more important due to their complimentary benefits, which include improvement in quality of living standards and lowering medication reliance. The goal of comprehensive asthma management is to treat environmental triggers such mold, dust mites, and pet dander while integrating pharmaceutical and non-pharmacological therapies. Studies indicate that strategies to reduce exposure to certain allergens, like avoiding allergies and making changes to the surroundings, can improve general health and lessen symptoms of asthma. It has also been demonstrated that better indoor air quality helps to promote better respiratory health and reduce asthma exacerbations, particularly in children who are exposed to secondhand smoking and urban air pollution. The usage of HEPA air filters and the creation of smoke-free areas are two examples of these endeavors. Optimizing asthma care and reducing the worldwide burden of this chronic respiratory condition can be accomplished by implementing holistic methods to asthma management that incorporate both pharmaceutical and non-pharmacological treatments. Asthma sufferers can receive comprehensive support from this integrated strategy, which targets underlying triggers in addition to symptoms.

REFERENCE

1. Martínez, F. D., & Vercelli, D. (2013). Asthma. *Lancet*, 382(9901), 1360–1372. [https://doi.org/10.1016/s0140-6736\(13\)61536-6](https://doi.org/10.1016/s0140-6736(13)61536-6)
2. Asher, I., & Pearce, N. (2014). Global burden of asthma among children. *The International Journal of Tuberculosis and Lung Disease*, 18(11), 1269–1278. <https://doi.org/10.5588/ijtld.14.0170>
3. Martínez, F. D., Chinchilli, V. M., Morgan, W. J., Boehmer, S. J., Lemanske, R. F., Mauger, D. T., Strunk, R. C., Szeffler, S. J., Zeiger, R. S., Bacharier, L. B., Bade, E., Covar, R., Friedman, N., Guilbert, T. W., Heidarian-Raissy, H., Kelly, H. W., Malka-Rais, J., Mellon, M., Sorkness, C. A., & Taussig, L. M. (2011). Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. *Lancet*, 377(9766), 650–657. [https://doi.org/10.1016/s0140-6736\(10\)62145-9](https://doi.org/10.1016/s0140-6736(10)62145-9)
4. Price, D., Musgrave, S. D., Shepstone, L., Hillyer, E. V., Sims, E., Gilbert, R., Juniper, E. F., Ayres, J. G., Kemp, L., Blyth, A., Wilson, E., Wolfe, S., Freeman, D., Mugford, H. M., Murdoch, J., & Harvey, I. (2011). Leukotriene antagonists as First-Line or add-on Asthma-Controller therapy. *New England Journal of Medicine/the New England Journal of Medicine*, 364(18), 1695–1707. <https://doi.org/10.1056/nejmoa1010846>
5. Nikander, K., Turpeinen, M., Pelkonen, A., Bengtsson, T., Selroos, O., & Haahtela, T. (2010). True adherence with the Turbuhaler in young children with asthma. *Archives of Disease in Childhood*, 96(2), 168–173. <https://doi.org/10.1136/adc.2010.187724>
6. Papi, A., Canonica, G. W., Maestrelli, P., Paggiaro, P., Olivieri, D., Pozzi, E., Crimi, N., Vignola, A. M., Morelli, P., Nicolini, G., & Fabbri, L. M. (2007). Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma. *New England Journal of Medicine/the New England Journal of Medicine*, 356(20), 2040–2052. <https://doi.org/10.1056/nejmoa063861>

7. Lemanske, R. F., Mauger, D. T., Sorkness, C. A., Jackson, D. J., Boehmer, S. J., Martínez, F. D., Strunk, R. C., Szeffler, S. J., Zeiger, R. S., Bacharier, L. B., Covar, R., Guilbert, T. W., Larsen, G. L., Morgan, W. J., Moss, M. H., Spahn, J. D., & Taussig, L. M. (2010). Step-up Therapy for Children with Uncontrolled Asthma Receiving Inhaled Corticosteroids. *New England Journal of Medicine/the œNew England Journal of Medicine*, 362(11), 975–985. <https://doi.org/10.1056/nejmoa1001278>
8. Peters, S. P., Kunselman, S. J., Icitovic, N., Moore, W. C., Pascual, R. M., Ameredes, B. T., Boushey, H. A., Calhoun, W. J., Castro, M., Cherniack, R. M., Craig, T. J., Denlinger, L. C., Engle, L., DiMango, E., Fahy, J. V., Israel, E., Jarjour, N. N., Kazani, S., Kraft, M., . . . Bleecker, E. R. (2010). Tiotropium Bromide Step-Up Therapy for Adults with Uncontrolled Asthma. *New England Journal of Medicine/the œNew England Journal of Medicine*, 363(18), 1715–1726. <https://doi.org/10.1056/nejmoa1008770>
9. Zar, H. J., & Levin, M. (2012). Challenges in treating pediatric asthma in developing countries. *Paediatric Drugs*, 14(6), 353–359. <https://doi.org/10.2165/11597420-000000000-00000>
10. Jarjour, N. N., Erzurum, S. C., Bleecker, E. R., Calhoun, W. J., Castro, M., Comhair, S., Chung, K. F., Curran-Everett, D., Dweik, R. A., Fain, S. B., Fitzpatrick, A. M., Gaston, B., Israel, E., Hastie, A. T., Hoffman, E. A., Holguín, F., Levy, B. D., Meyers, D. A., Moore, W. C., . . . Busse, W. W. (2012). Severe asthma. *American Journal of Respiratory and Critical Care Medicine*, 185(4), 356–362. <https://doi.org/10.1164/rccm.201107-1317pp>
11. Busse, W. W., Morgan, W. J., Gergen, P. J., Mitchell, H., Gern, J. E., Liu, A. H., Gruchalla, R. S., Kattan, M., Teach, S. J., Pongracic, J. A., Chmiel, J. F., Steinbach, S., Calatroni, A., Togias, A., Thompson, K. M., Szeffler, S. J., & Sorkness, C. A. (2011). Randomized trial of omalizumab (Anti-IgE) for asthma in Inner-City children. *New England Journal of Medicine/the œNew England Journal of Medicine*, 364(11), 1005–1015. <https://doi.org/10.1056/nejmoa1009705>
12. Hanania, N. A., Alpan, O., Hamilos, D. L., Condemi, J. J., Reyes-Rivera, I., Zhu, J., Rosén, K., Eisner, M. D., Wong, D. A., & Busse, W. W. (2011). Omalizumab in severe allergic asthma inadequately controlled with standard therapy. *Annals of Internal Medicine*, 154(9), 573. <https://doi.org/10.7326/0003-4819-154-9-201105030-00002>
13. Moore, W. C., Meyers, D. A., Wenzel, S. E., Teague, W. G., Li, H., Li, X., D'Agostino, R., Castro, M., Curran-Everett, D., Fitzpatrick, A. M., Gaston, B., Jarjour, N. N., Sorkness, R. L., Calhoun, W. J., Chung, K. F., Comhair, S., Dweik, R. A., Israel, E., Peters, S. P., . . . Bleecker, E. R. (2010). Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. *American Journal of Respiratory and Critical Care Medicine*, 181(4), 315–323. <https://doi.org/10.1164/rccm.200906-0896oc>
14. Sheehan, W. J., & Phipatanakul, W. (2016). Indoor allergen exposure and asthma outcomes. *Current Opinion in Pediatrics, With Evaluated MEDLINE/Current Opinion in Pediatrics*, 28(6), 772–777. <https://doi.org/10.1097/mop.0000000000000421>
15. Weiss, S. T., Horner, A. A., Shapiro, G. G., & Sternberg, A. L. (2001). The prevalence of environmental exposure to perceived asthma triggers in children with mild-to-moderate asthma: Data from the Childhood Asthma Management Program (CAMP). *the œJournal of Allergy and Clinical Immunology/Journal of Allergy and Clinical Immunology/the œJournal of Allergy and Clinical Immunology*, 107(4), 634–640. <https://doi.org/10.1067/mai.2001.113869>
16. Human verification. (n.d.). <https://www.semanticscholar.org/paper/Worsening-of-asthma-in-children-allergic-to-cats%2C-Almqvist-Wickman/9870366d8c19f7a7d197738e5a266cb7df0c1ee7>
17. Wood, R. A., Chapman, M. D., Adkinson, N. F., & Eggleston, P. A. (1989). The effect of cat removal on allergen content in household-dust samples. *the œJournal of Allergy and Clinical Immunology/Journal of Allergy and Clinical Immunology/the œJournal of Allergy and Clinical Immunology*, 83(4), 730–734. [https://doi.org/10.1016/0091-6749\(89\)90006-7](https://doi.org/10.1016/0091-6749(89)90006-7)
18. Phipatanakul, W., Eggleston, P. A., Wright, E. C., & Wood, R. A. (2000). Mouse allergen. I. The prevalence of mouse allergen in inner-city homes. *the œJournal of Allergy and Clinical Immunology/Journal of Allergy and Clinical Immunology/the œJournal of Allergy and Clinical Immunology*, 106(6), 1070–1074. <https://doi.org/10.1067/mai.2000.110796>
19. Pongracic, J. A., O'Connor, G., Muilenberg, M. L., Vaughn, B., Gold, D. R., Kattan, M., Morgan, W. J., Gruchalla, R. S., Smartt, E., & Mitchell, H. (2010). Differential effects of outdoor versus indoor fungal spores on asthma morbidity in inner-city children. *The Journal of Allergy and Clinical Immunology*, 125(3), 593–599. <https://doi.org/10.1016/j.jaci.2009.10.036>
20. Faber, T., Kumar, A., Mackenbach, J. P., Millett, C., Basu, S., Sheikh, A., & Been, J. V. (2017). Effect of tobacco control policies on perinatal and child health: A systematic review and meta-analysis. *The Lancet. Public Health*, 2(9), e420–e437. [https://doi.org/10.1016/s2468-2667\(17\)30144-5](https://doi.org/10.1016/s2468-2667(17)30144-5)
21. Naja, A. S., Permaul, P., & Phipatanakul, W. (2018). Taming Asthma in School-Aged Children: A Comprehensive Review. *Journal of Allergy and Clinical Immunology: In Practice*, 6(3), 726–735. <https://doi.org/10.1016/j.jaip.2018.01.023>