

# Asthma News This Week

April 1<sup>st</sup>, 2019

---

## CONTENTS

### JOURNAL ARTICLES

- ❖ Montelukast linked to neuropsychiatric events in children
- ❖ Tertiary interventions may be necessary to target individual asthma triggers
- ❖ Healthy lifestyles may help prevent and control asthma symptoms
- ❖ Wheezing phenotypes vary but consistently predict poorer lung function
- ❖ As treatment options for childhood asthma emerge, a need for efficacy evidence
- ❖ Chicago trial links families to home-based asthma CHW interventions
- ❖ Need identified for methods to predict severe therapy-resistant childhood asthma
- ❖ Indoor particulate matter (PM) may be a worse asthma trigger than outdoor PM
- ❖ Certain antioxidant flavonoids may reduce lung inflammation
- ❖ Poor methodologies in environmental allergen control intervention research
- ❖ Reverse causation unlikely to confound asthma risk factors
- ❖ Vitamin D may mitigate correlation between maternal and child asthma
- ❖ Condition-response interactions identified between health outcomes and pollution
- ❖ AAP highlights disparities in child hospitalization outcomes
- ❖ AAP updates clinical report on maternal and infant diet and asthma/allergy
- ❖ Indoor cannabis smoke might exacerbate childhood asthma symptoms

### IN THE NEWS

- ❖ Albany highlights childhood asthma on April 2, National Healthy Schools Day
- ❖ Study finds potential link between parental asthma and child autism
- ❖ Omega-3 and -6 may reduce and increase risk of asthma, respectively
- ❖ Britain's NHS to launch first national database of child mortality
- ❖ Asthma and other diseases used by some to justify forgoing vaccination
- ❖ Children's Hospital of Philadelphia to create Pediatric Cell Atlas
- ❖ AOC cites childhood asthma disparities in Green New Deal speech
- ❖ Precision medicine aims at reducing asthma disparities
- ❖ Low umbilical blood flow may indicate childhood asthma risk
- ❖ More mixed findings about prenatal vitamin D and childhood asthma
- ❖ Asthma medication use varies among Latino youth

---

## JOURNAL articles

**Glockler-Lauf, S.D., et al. Montelukast and Neuropsychiatric Events in Children with Asthma: A Nested Case-Control Study. *J Pediatr.* 2019 Mar 21. pii: S0022-3476(19)30198-2. doi: 10.1016/j.jpeds.2019.02.009. [Epub ahead of print]**

**OBJECTIVE:** To examine the association between montelukast prescription and neuropsychiatric events in children with asthma. **STUDY DESIGN:** A matched, nested case-control design was used to identify cases and controls from a cohort of children aged 5-18 years with physician-diagnosed asthma from 2004 to 2015, in Ontario, Canada, prescribed an asthma maintenance medication. Cases were children with a hospitalization or emergency department visit for a neuropsychiatric event. Cases were matched to up to 4 controls on birth year, year of asthma diagnosis, and sex. The exposures were dispensed prescriptions for montelukast (yes/no) and number of dispensed montelukast prescriptions in the year before the index date. Conditional logistic regression was used to measure the unadjusted OR and aOR and 95% CIs for montelukast prescription and neuropsychiatric events. Covariates in the adjusted model included sociodemographic factors and measures of asthma severity. **RESULTS:** In total, 898 cases with a neuropsychiatric event and 3497 matched controls were included. Children who experienced a new-onset neuropsychiatric event had nearly 2 times the odds of having been prescribed montelukast, compared with controls (OR 1.91, 95% CI 1.15-3.18; P = .01). Most cases presented for anxiety (48.6%) and/or sleep disturbance (26.1%). **CONCLUSIONS:** Children with asthma who experienced a new-onset neuropsychiatric event had nearly twice the odds of having been prescribed montelukast in the year before their event. Clinicians should be aware of the association between montelukast and neuropsychiatric events in children with asthma, to inform prescribing practices and clinical follow-up.

**Conrad, L. and M.S. Perzanowski. The Role of Environmental Controls in Managing Asthma in Lower-Income Urban Communities. *Clin Rev Allergy Immunol.* 2019 Mar 22. doi: 10.1007/s12016-019-08727-y. [Epub ahead of print]**

Children living in lower-income urban communities are at much greater risk of developing asthma, going to the emergency department for an asthma attack and being hospitalized for asthma than children living in upper- and middle-income communities. For many asthmatic children living in urban communities, especially those with greater morbidity, the allergic pathway is important in the etiology of the disease. The stages of developing allergic disease can be divided into the onset of allergic sensitization, development of allergic disease and subsequent exacerbations, and it is useful to consider the relevance of interventions at each of these stages. Indoor allergens and environmental exposures are a major contributor to allergic disease, particularly among lower socioeconomic status, urban, minority communities. These exposures include allergens, environmental tobacco smoke, combustion by-products, and mold, all of which can play an important role in asthma progression as well as morbidity. These exposures are often not found in isolation and thus these concomitant exposures need to be considered when conducting environmental interventions. There have been numerous studies looking at both primary and tertiary prevention strategies and the impact on allergic sensitization and asthma with varied results. While the outcomes of these studies have been mixed, what has emerged is the need for tertiary interventions to be targeted to the individual and to reduce all relevant

exposures to which an asthmatic child is exposed and sensitized. In addition, effective intervention strategies must also consider other social determinants of asthma morbidity impacting low socioeconomic, urban communities.

**Morales, E., et al. Combined impact of healthy lifestyle factors on risk of asthma, rhinoconjunctivitis and eczema in school children: ISAAC phase III. *Thorax*. 2019 Mar 21. pii: thoraxjnl-2018-212668. doi: 10.1136/thoraxjnl-2018-212668. [Epub ahead of print]**

**BACKGROUND:** Asthma is not the key focus of prevention strategies. A Healthy Lifestyle Index (HLI) was developed to examine the combined effect of modifiable lifestyle factors on asthma, rhinoconjunctivitis and eczema using data from the International Study of Asthma and Allergies in Childhood (ISAAC) phase III. **METHODS:** Information on symptoms of asthma, rhinoconjunctivitis, eczema and several lifestyle factors was obtained from children aged 6-7 years through written questionnaires. The HLI combined five lifestyle factors: no parental smoking, child's adherence to Mediterranean diet, child's healthy body mass index, high physical activity and non-sedentary behaviour. The association between the HLI and risk of asthma, rhinoconjunctivitis and eczema was evaluated using multilevel mixed-effects logistic regression models. **FINDINGS:** Data of 70 795 children from 37 centres in 19 countries were analysed. Each additional healthy lifestyle factor was associated with a reduced risk of current wheeze (OR 0.87, 95% CI 0.84 to 0.89), asthma ever (OR 0.89, 95% CI 0.87 to 0.92), current symptoms of rhinoconjunctivitis (OR 0.95, 95% CI 0.92 to 0.97) and current symptoms of eczema (OR 0.92, 95% CI 0.92 to 0.98). Theoretically, if associations were causal, a combination of four or five healthy lifestyle factors would result into a reduction up to 16% of asthma cases (ranging from 2.7% to 26.3 % according to region of the world). **CONCLUSIONS:** These findings should be interpreted with caution given the limitations to infer causality from cross-sectional observational data. Efficacy of interventions to improve multiple modifiable lifestyle factors to reduce the burden asthma and allergy in childhood should be assessed.

**Oksel, C., et al. Distinguishing Wheezing Phenotypes from Infancy to Adolescence: A Pooled Analysis of Five Birth Cohorts. *Ann Am Thorac Soc*. 2019 Mar 19. doi: 10.1513/AnnalsATS.201811-837OC. [Epub ahead of print]**

**RATIONALE:** Pooling data from multiple cohorts and extending the time-frame across childhood should minimize study-specific effects, enabling better characterization of the childhood wheezing. **OBJECTIVE:** To analyze wheezing patterns from early childhood to adolescence using combined data from five birth cohorts. **METHODS:** We used latent class analysis to derive wheeze phenotypes among 7719 participants from five birth cohorts with complete report of wheeze at five time-periods. We tested the association of derived phenotypes with late asthma outcomes and lung function, and investigated the uncertainty in phenotype assignment. **RESULTS:** We identified five phenotypes: Never/Infrequent wheeze (52.1%), Early-onset pre-school remitting (23.9%), Early-onset mid-childhood remitting (9%), Persistent (7.9%) and Late-onset wheeze (7.1%). Compared to the Never/infrequent wheeze, all phenotypes had higher odds of asthma and lower FEV1 and FEV1/FVC in adolescence. The association with asthma was strongest for Persistent wheeze (adjusted odds ratio 56.54, 95% CI 43.75-73.06). We observed considerable within-class heterogeneity at individual level, with 913 (12%) children

having low membership probability (<0.60) of any phenotype. Class membership certainty was highest in Persistent and Never/infrequent, and lowest in Late-onset wheeze (with 51% of participants having membership probabilities<0.80). Individual wheezing patterns were particularly heterogeneous in Late-onset wheeze, while many children assigned to Early-onset pre-school remitting class reported wheezing at later time points. CONCLUSIONS: All wheeze phenotypes had significantly diminished lung function in school-age, suggesting that the notion that early-life episodic wheeze has a benign prognosis may not be true for a proportion of transient wheezers. We observed considerable within-phenotype heterogeneity in individual wheezing patterns.

**Ahmed, H. and S. Turner. Severe asthma in children-a review of definitions, epidemiology, and treatment options in 2019. *Pediatr Pulmonol.* 2019 Mar 18. doi: 10.1002/ppul.24317. [Epub ahead of print]**

Severe asthma is a relatively uncommon condition in children but one which causes morbidity, occasionally mortality, and is a challenging condition to manage. There are several definitions of severe asthma, which have a common theme of poor control despite high dose inhaled corticosteroid treatment. Depending on the definition chosen, the prevalence of severe childhood asthma may be up to 5% within populations with asthma. Collectively, there is some evidence that the treatments used in severe asthma are beneficial, but a solid evidence-base is lacking for many treatments and some treatments have recognized side effects. Evidence supporting the use of maintenance oral prednisolone and intramuscular triamcinolone is weak. Response to systemic corticosteroids is heterogeneous and recognizing phenotypes or endotypes may identify those most likely to gain maximal benefit from treatment. For children aged 6 to 11 years, the anti-IgE biologic omalizumab is effective and anti-IL-5 agent (mepolizumab) has recently been licenced in Europe (but not the US). Biologics, which are licenced for >11 year olds include omalizumab, mepolizumab, benralizumab, reslizumab, and dupilumab. There is plenty that the clinician can offer to the child and adolescent with severe asthma in 2019, including nontherapeutic and therapeutic interventions. To manage severe asthma, practitioners from broad specialities must establish and maintain a close therapeutic relationship with patients. Looking beyond 2019, more treatment options will emerge for severe childhood asthma, and clinical teams will need to continue weighing up benefits and harms.

**Mosnaim, G.S., et al. Design and baseline characteristics of a low-income urban cohort of children with asthma: The Asthma Action at Erie Trial. *Contemp Clin Trials.* 2019 Apr;79:55-65. doi: 10.1016/j.cct.2019.02.006. Epub 2019 Feb 14.**

OBJECTIVE: To describe the methodology of a randomized controlled trial comparing the efficacy of integrated asthma community health workers (CHW) and a certified asthma educator (AE-C) to improve asthma outcomes in low-income minority children in Chicago. METHODS: Child/caregiver dyads were randomized to CHW home visits or education in the clinic from an AE-C. Intervention was delivered in the first year after enrollment. Data collection occurred at baseline, 6-, 12-, 18, and 24-months. The co-primary outcomes included asthma control using the Asthma Control Test/childhood Asthma Control Test (ACT/cACT) and activity limitation over the past 14 days. RESULTS: A total of 223 participants ages 5-16 years were randomized. The

majority of children were in the 5-11 year old range (78.9%). Most caregivers (96.9%) and 44% of children were female. Approximately 85% of caregivers and children reported Hispanic ethnicity and 62.3% reported a household income of  $\leq$  \$59,000. Over half (55.7%) had uncontrolled asthma as measured by ACT/cACT; 13.9% had a normal ACT/cACT score but were uncontrolled using the Asthma Control Questionnaire and 20.2% were controlled on both measures but had received oral steroids in the past year for asthma. **CONCLUSION:** The Asthma Action at Erie Trial successfully recruited a largely Hispanic cohort of children with uncontrolled or high-risk asthma to study the differential effects of clinic-based AE-C and home-based CHW interventions. Strengths of the trial include its comparative effectiveness design that integrates interventionists and intervention delivery into a clinical setting. Categorizing asthma control in community settings for research purposes presents unique challenges. **CLINICAL TRIAL REGISTRATION:** University of Illinois at Chicago Protocol Record R01HL123797, Asthma Action at Erie Trial [ClinicalTrials.gov](https://clinicaltrials.gov) Identifier: NCT02481986 "ClinicalTrials.gov Registration" [register@clinicaltrials.gov](mailto:register@clinicaltrials.gov).

**Selby, L. and S. Saglani. Severe asthma in children: therapeutic considerations. *Curr Opin Allergy Clin Immunol.* 2019 Apr;19(2):132-140. doi: 10.1097/ACI.0000000000000521.**

**PURPOSE OF REVIEW:** Children with poor asthma control despite maximal maintenance therapy have problematic severe asthma (PSA). A step-wise approach including objective adherence monitoring and a detailed multidisciplinary team assessment to identify modifiable factors contributing to poor control is needed prior to considering therapy escalation. Pathophysiological phenotyping in those with true severe therapy-resistant asthma (STRA) and the current array of add-on therapies will be discussed. **RECENT FINDINGS:** Adherence monitoring using electronic devices has shown that only 20-30% of children with PSA have STRA and need additional therapies. Omalizumab and mepolizumab are licensed for children with STRA aged 6 years and older. Although robust safety and efficacy data, with reduced exacerbations, are available for omalizumab, biomarkers predicting response to treatment are lacking. Paediatric safety data are available for mepolizumab, but efficacy data are unknown for those aged 6-11 years and minimal for those 12 years and older. A sub-group of children with STRA have neutrophilia, but the clinical significance and contribution to disease severity remains uncertain. **SUMMARY:** Most children with PSA have steroid sensitive disease which improves with adherence to maintenance inhaled corticosteroids. Add-on therapies are only needed for the minority with STRA. Paediatric efficacy data of novel biologics and biomarkers that identify the optimal add-on for each child are lacking. If we are to progress toward individualized therapy for STRA, pragmatic clinical trials of biologics in accurately phenotyped children are needed.

**Iuigo, K., et al. Indoor particulate matter and lung function in children. *Sci Total Environ.* 2019 May 1;663:408-417. doi: 10.1016/j.scitotenv.2019.01.309. Epub 2019 Jan 24.**

People generally spend more time indoors than outdoors resulting in a higher proportion of exposure to particulate matter (PM) occurring indoors. Consequently, indoor PM levels, in contrast to outdoor PM levels, may have a stronger relationship with lung function. To test this hypothesis, indoor and outdoor PM<sub>2.5</sub> and fungal spore data were simultaneously collected from

the homes of forty-four asthmatic children aged 10-16 years. An optical absorption technique was utilized on the collected PM<sub>2.5</sub> mass to obtain concentrations of black carbon (BC) and ultraviolet light absorbing particulate matter, (UVPM; a marker of light absorbing PM<sub>2.5</sub> emitted from smoldering organics). Enrolled children completed spirometry after environmental measurements were made. Given the high correlation between PM<sub>2.5</sub>, BC, and UVPM, principal component analysis was used to obtain uncorrelated summaries of the measured PM. Separate linear mixed-effect models were developed to estimate the association between principal components of the PM variables and spirometry values, as well as the uncorrelated original PM variables and spirometry values. A one-unit increase in the first principal component variable representing indoor PM (predominantly composed of UVPM and PM<sub>2.5</sub>) was associated with 4.1% decrease (99% CI = -6.9, -1.4) in FEV<sub>1</sub>/FVC ratio. 11.3 µg/m<sup>3</sup> increase in indoor UVPM was associated with 6.4% and 14.7% decrease (99% CI = -10.4, -2.4 and 99% CI = -26.3, -2.9, respectively) in percent predicted FEV<sub>1</sub>/FVC ratio and FEF<sub>25-75</sub> respectively. Additionally, 17.7 µg/m<sup>3</sup> increase in indoor PM<sub>2.5</sub> was associated with 6.1% and 12.9% decrease (99% CI = -10.2, -1.9 and 99% CI = -24.9, -1.0, respectively) in percent predicted FEV<sub>1</sub>/FVC ratio and FEF<sub>25-75</sub>, respectively. Outdoor PM, indoor BC, and indoor fungal spores were not significantly associated with lung function. The results indicate that indoor PM is more strongly associated with lung function in children with asthma as compared with outdoor PM.

Ma, B., et al. Cyanidin-3-O-β-glucoside attenuates allergic airway inflammation by modulating the IL-4Rα-STAT6 signaling pathway in a murine asthma model. *Int Immunopharmacol*. 2019 Apr;69:1-10. doi: 10.1016/j.intimp.2019.01.008. Epub 2019 Jan 17.

Cyanidin-3-O-β-glucoside (Cy-3-g), a typical and abundant monomer of anthocyanins, exhibits a variety of biological activities, such as anti-atherosclerosis, anti-obesity, and anticancer effects. However, to date little is known about its effects on asthma. This study aimed to investigate the efficacy of dietary Cy-3-g on allergic asthma in an animal model. BALB/c mice were sensitized and challenged with ovalbumin (OVA) to induce allergic asthma. The pathological changes of the lung tissues, type 2 helper (Th<sub>2</sub>)-associated cytokine production in bronchoalveolar lavage fluid (BALF), and the interleukin 4 receptor alpha (IL-4Rα)-signal transducer and activator of transcription 6 (STAT6) signaling pathway activities were assessed. We found that Cy-3-g significantly inhibited OVA-induced inflammatory cell infiltration and mucus hyper-production in lung tissues, reduced the production of interleukin 4 (IL-4), interleukin 5 (IL-5) and interleukin 13 (IL-13) in BALF. Furthermore, Cy-3-g effectively suppressed OVA-induced up-regulation of the IL-4Rα-STAT6 signaling pathway activity of the lung tissues. These results demonstrated that dietary Cy-3-g could attenuate allergic airway inflammation in a murine asthma model, and Cy-3-g might be used as an agent for asthma prevention and/or treatment in the future.

**va Boven, F.E., et al. A reintroduction of environmental mite allergen control strategies for asthma treatment and the debate on their effectiveness. *Clin Exp Allergy*. 2019 Apr;49(4):400-409. doi: 10.1111/cea.13340. Epub 2019 Feb 11.**

Asthma affects three hundred million people worldwide. The effectiveness of house dust mite allergen control for asthma treatment is debatable. One aspect that has been little discussed in

existing meta-analyses is the possible role of environmental strategies. Here, we reintroduce the previously defined strategies for mite allergen control and discuss their importance to the debate on clinical effectiveness. The strategy of concurrent bedroom interventions is related to the combined use of a priori defined interventions, while the strategy of exposure-based control relates to the treatment of relevant textiles after assessing exposure. The air purification strategy aims to purify the human breathing zone of airborne allergens. In Western European patient practice, the use of these strategies differs. A post hoc study of the dominant Cochrane review by Gøtzsche and Johansen (Cochrane Database of Systematic Reviews, 2008, Art. No: CD001187) appears to indicate that a majority of the underlying trials reported on the strategy of concurrent bedroom interventions, which were mainly executed in a minimal manner. Some trials have reported on the air purification strategy and may potentially alter the debate on effectiveness. No trial has reported on the strategy of exposure-based control. We therefore hypothesize that the absence of evidence for the effectiveness of mite allergen control for asthma treatment applies to the strategy of concurrent bedroom interventions. The evidence-based effectiveness of the exposure-based control strategy appears to be undetermined. The results of our post hoc reanalysis urge that future meta-analyses of mite allergen control should a priori define the environmental strategy under study. Future trials of mite allergen control are warranted to test the exposure-based strategy as well as the sparsely tested strategy of air purification.

**Silverwood, R.J., et al. Are environmental risk factors for current wheeze in the International Study of Asthma and Allergies in Childhood (ISAAC) phase three due to reverse causation? *Clin Exp Allergy*. 2019 Apr;49(4):430-441. doi: 10.1111/cea.13325. Epub 2019 Jan 23.**

**BACKGROUND:** Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC) measured the global prevalence of symptoms of asthma in children. We undertook comprehensive analyses addressing risk factors for asthma symptoms in combination, at both the individual and the school level, to explore the potential role of reverse causation due to selective avoidance or confounding by indication. **OBJECTIVE:** To explore the role of reverse causation in risk factors of asthma symptoms. **METHODS:** We compared two sets of multilevel logistic regression analyses, using (a) individual level exposure data and (b) school level average exposure (ie prevalence), in two different age groups. In individual level analyses, reverse causation is a possible concern if individual level exposure statuses were changed as a result of asthma symptoms or diagnosis. School level analyses may suffer from ecologic confounding, but reverse causation is less of a concern because individual changes in exposure status as a result of asthma symptoms would only have a small effect on overall school exposure levels. **RESULTS:** There were 131 924 children aged 6-7 years (2428 schools, 25 countries) with complete exposure, outcome and confounder data. The strongest associations in individual level analyses (fully adjusted) were for current paracetamol use (odds ratio = 2.06; 95% confidence interval 1.97-2.16), early life antibiotic use (1.65; 1.58-1.73) and open fire cooking (1.44; 1.26-1.65). In school level analyses, these risk factors again showed increased risks. There were 238 586 adolescents aged 13-14 years (2072 schools, 42 countries) with complete exposure, outcome and confounder data. The strongest associations in individual level analyses (fully adjusted) were for current paracetamol use (1.80; 1.75-1.86), cooking on an open fire (1.32; 1.22-1.43) and

maternal tobacco use (1.23; 1.18-1.27). In school level analyses, these risk factors again showed increased risks. **CONCLUSIONS & CLINICAL RELEVANCE:** These analyses strengthen the potentially causal interpretation of previously reported individual level findings, by providing evidence against reverse causation.

**Mirsakhani, H., et al. Impact of parental asthma, prenatal maternal asthma control, and vitamin D status on risk of asthma and recurrent wheeze in 3-year-old children. *Clin Exp Allergy*. 2019 Apr;49(4):419-429. doi: 10.1111/cea.13320. Epub 2019 Jan 3.**

**BACKGROUND:** While familial clustering of asthma is known, few studies have reported on the relative roles of paternal and maternal asthma and the role of maternal asthma control in pregnancy on the risk for asthma in the child. **OBJECTIVE:** We aimed to investigate the relative roles of paternal asthma, maternal asthma, and maternal asthma control during pregnancy on the risk of asthma or recurrent wheeze in 3-year-old children and how prenatal and cord blood vitamin D status might affect this risk. **METHODS:** Data from 806 women, their partners (biologic fathers of the infants), and their children participated in the Vitamin D Antenatal Asthma Reduction Trail (VDAART, clinicaltrials.gov identification number NCT00920621) were used for this cohort analysis. The parental report of physician-diagnosed asthma or recurrent wheeze in offspring was the main outcome. Weibull regression models for interval-censored event times were used to estimate the main variables of interests and additional covariates on the outcome. **RESULTS:** The highest risk was observed among children with both parents being asthmatic relative to non-asthmatic parents (aHR = 2.30, 95% CI: 1.35-3.84), and less so if only the mother was asthmatic (aHR = 1.70, 95% CI: 1.17-2.40). In the subset of children born to asthmatic mothers, the risk for asthma was higher in those who were born to mothers whose asthma was uncontrolled (aHR = 1.60, 95% CI: 1.02-2.54). Children whose mothers had sufficient vitamin D status (25Hydroxyvitamin D  $\geq$  30 ng/mL) at early and late pregnancy and had cord blood vitamin D sufficiency demonstrated a lower risk of asthma/recurrent wheeze than children who had insufficient cord blood vitamin D status at birth (aHR = 0.47, 95% CI: 0.27-0.83). **CONCLUSION AND CLINICAL RELEVANCE:** Careful attention to maternal asthma control, monitoring vitamin D status, and correcting insufficiency at early pregnancy and maintaining the sufficiency status throughout pregnancy have potential preventive roles in offspring asthma or recurrent wheeze.

**McKay, Shaunte, and Victoria Parente. Health Disparities in the Hospitalized Child. *Hospital Pediatrics*. April 2019: special article.**

Health care disparities exist along the continuum of care for children admitted to the hospital; they start before admission, impact hospital course, and continue after discharge. During an acute illness, risk of admission, length of stay, hospital costs, communication during family-centered rounds, and risk of readmission have all been shown to vary by socioeconomic status, race, and ethnicity. Understanding factors beyond the acute illness that increase a child's risk of admission, increase hospital course complications, and lower discharge quality is imperative for the new generation of pediatric hospitalists focused on improving health for a population of children. In this article, we describe a framework to conceptualize socioeconomic, racial, and

ethnic health disparities for the hospitalized child. Additionally, we offer actions pediatric hospitalists can take to address disparities within their practices.

**Perera, F., et al. Towards a fuller assessment of benefits to children's health of reducing air pollution and mitigating climate change due to fossil fuel combustion. *Environmental Research*. 2019 May; 55-72. DOI: 10.1016/j.envres.2018.12.016**

Background: Fossil fuel combustion by-products, including particulate matter (PM 2.5 ), polycyclic aromatic hydrocarbons (PAH), nitrogen dioxide (NO<sub>2</sub> ) and carbon dioxide (CO<sub>2</sub> ), are a significant threat to children's health and equality. Various policies to reduce emissions have been implemented to reduce air pollution and mitigate climate change, with sizeable estimated health and economic benefits. However, only a few adverse outcomes in children have been considered, resulting in an undercounting of the benefits to this vulnerable population. Objectives: Our goal was to expand the suite of child health outcomes addressed by programs to assess health and economic benefits, such as the Environmental Protection Agency (EPA) Benefits Mapping and Analysis Program (BenMAP), by identifying concentration-response (C-R) functions for six outcomes related to PM 2.5 , NO<sub>2</sub> , PAH, and/or PM 10 : preterm birth (PTB), low birthweight (LBW), autism, attention deficit hyperactivity disorder, IQ reduction, and the development of childhood asthma. Methods: We conducted a systematic review of the literature published between January 1, 2000 and April 30, 2018 to identify relevant peer-reviewed case-control and cohort studies and meta-analyses. In some cases meta-analyses were available that provided reliable C-R functions and we assessed their consistency with subsequent studies. Otherwise, we reviewed all eligible studies published between our search dates. Results: For each pollutant and health outcome, we present the characteristics of each selected study. We distinguish between C-R functions for endpoints having a causal or likely relationship (PTB, LBW, autism, asthma development) with the pollutants for incorporation into primary analyses and endpoints having a suggestive causal relationship with the pollutants (IQ reduction, ADHD) for secondary analyses. Conclusion: We have identified C-R functions for a number of adverse health outcomes in children associated with air pollutants largely from fossil fuel combustion. Their incorporation into expanded assessments of health benefits of clean air and climate mitigation policies will provide an important incentive for preventive action.

**Greer, F.R., Sicherer, S.H., and A.W. Burks. The Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Hydrolyzed Formulas, and Timing of Introduction of Allergenic Complementary Foods. *Pediatrics*. 2019 April; 143(4).**

This clinical report updates and replaces a 2008 clinical report from the American Academy of Pediatrics, which addressed the roles of maternal and early infant diet on the prevention of atopic disease, including atopic dermatitis, asthma, and food allergy. As with the previous report, the available data still limit the ability to draw firm conclusions about various aspects of atopy prevention through early dietary interventions. Current evidence does not support a role for maternal dietary restrictions during pregnancy or lactation. Although there is evidence that exclusive breastfeeding for 3 to 4 months decreases the incidence of eczema in the first 2 years of life, there are no short- or long-term advantages for exclusive breastfeeding beyond 3 to 4

months for prevention of atopic disease. The evidence now suggests that any duration of breastfeeding  $\geq 3$  to 4 months is protective against wheezing in the first 2 years of life, and some evidence suggests that longer duration of any breastfeeding protects against asthma even after 5 years of age. No conclusions can be made about the role of breastfeeding in either preventing or delaying the onset of specific food allergies. There is a lack of evidence that partially or extensively hydrolyzed formula prevents atopic disease. There is no evidence that delaying the introduction of allergenic foods, including peanuts, eggs, and fish, beyond 4 to 6 months prevents atopic disease. There is now evidence that early introduction of peanuts may prevent peanut allergy.

**Posis, A., et al. Indoor cannabis smoke and children's health. *Preventive Medicine Reports*. 2019 June; 14. Article number 100853. DOI: 10.1016/j.pmedr.2019.100853**

Cannabis use is increasing and cannabis is typically consumed by smoking. This study explored how indoor secondhand cannabis smoke (SCS) was associated with child health. As part of a larger trial, air particle monitors were placed in 298 homes of families with at least one cigarette smoker and one child under 14 years old in San Diego County, California. Assessment included past 7-day indoor cigarette and cannabis use, the youngest child's exposure to cigarette smoke, and 5 smoke-related past-year child health outcomes: emergency department use for coughing/difficulty breathing; physician diagnosis of ear infection, bronchitis/bronchiolitis, asthma, or eczema/atopic dermatitis. An ordinal measure of adverse health outcomes (0, 1, or  $\geq 2$ ) was regressed on reported indoor cannabis smoking—the main measure of exposure (yes/no). Of 221 parents/guardians asked about cannabis use, 192 (86.9%) provided all required data, and 29 (15.1%) reported indoor cannabis smoking; reports were supported by air particle data. Homes without indoor smoking had lower average 7-day particle concentrations (1968 particles/0.01ft<sup>3</sup>) than homes with cannabis smoking only (3131 particles/0.01ft<sup>3</sup>), cigarette smoking only (3095 particles/0.01ft<sup>3</sup>), or both cigarette and cannabis smoking (6006 particles/0.01ft<sup>3</sup>). Odds of reporting a greater number of adverse health outcomes were 1.83 (95% CI = 0.89–3.80,  $p = 0.10$ ) times higher for children of families with indoor cannabis smoking vs families without cannabis smoking, after controlling for exposure to cigarette smoke and other covariates. Our results do not indicate a statistically significant association. However, the magnitude of the (non-significant) association between indoor cannabis smoking and adverse health outcomes warrants more studies.

---

## In the NEWS

Press release: [A Healthy School For Every Child](#). *Digital Journal*. April 1, 2019.

Furfaro, Hannah. [Asthma in parents shows slim link to autism in children](#). *Spectrum*. April 1, 2019.

Tanna, Shreyas. [The Role Played By Omega-3 And Omega-6 In Childhood Asthma](#). *Health Gazette*. April 1, 2019.

Mole, Beth. [Bogus medical exemptions sought by anti-vaxxers may get revoked in Calif.](#) *ARS Technica*. March 28, 2019.

Children's Hospital of Philadelphia. [Pediatric cell atlas will map single-cell changes for a deeper view of child health and disease.](#) *Science Daily*. Mar 28, 2019.

Guardian staff and agencies. [Green New Deal: Senate defeats proposal as Democrats unite in protest.](#) *The Guardian*. March 26, 2019.

McQuaid, John. [Asthma takes a hard toll on African-Americans. Can precision medicine ease the burden?](#) *Stat News*. March 26, 2019.

Moeller, Bryant. [Childhood Asthma Not Affected by High-Dose Vitamin D Given in Pregnancy.](#) *Pulmonolgy Advisor*. March 22, 2019.

May, Brandon. [Childhood Asthma Risk May Be Affected by Umbilical Artery Flow.](#) *Pulmonolgy Advisor*. March 22, 2019.

Lisa Rapaport. [Asthma medication use varies among Latino youth.](#) *Reuters Health News*. March 19, 2019.