



# Childhood Asthma Leadership Coalition

## Journal articles

Merckx, Joanna, et al. Respiratory Viruses and Treatment Failure in Children With Asthma Exacerbation. *Pediatrics*. July 2018; 142(1): <http://pediatrics.aappublications.org/content/early/2018/05/31/peds.2017-4105>

**OBJECTIVES:** Respiratory pathogens commonly trigger pediatric asthma exacerbations, but their impact on severity and treatment response remains unclear.

**METHODS:** We performed a secondary analysis of the Determinants of Oral Corticosteroid Responsiveness in Wheezing Asthmatic Youth (DOORWAY) study, a prospective cohort study of children (aged 1–17 years) presenting to the emergency department with moderate or severe exacerbations. Nasopharyngeal specimens were analyzed by RT-PCR for 27 respiratory pathogens. We investigated the association between pathogens and both exacerbation severity (assessed with the Pediatric Respiratory Assessment Measure) and treatment failure (hospital admission, emergency department stay >8 hours, or relapse) of a standardized severity-specific treatment. Logistic multivariate regressions were used to estimate average marginal effects (absolute risks and risk differences [RD]).

**RESULTS:** Of 958 participants, 61.7% were positive for  $\geq 1$  pathogen (rhinovirus was the most prevalent [29.4%]) and 16.9% experienced treatment failure. The presence of any pathogen was not associated with higher baseline severity but with a higher risk of treatment failure (20.7% vs 12.5%; RD = 8.2% [95% confidence interval: 3.3% to 13.1%]) compared to the absence of a pathogen. Nonrhinovirus pathogens were associated with an increased absolute risk (RD) of treatment failure by 13.1% (95% confidence interval: 6.4% to 19.8%), specifically, by 8.8% for respiratory syncytial virus, 24.9% for influenza, and 34.1% for parainfluenza.

**CONCLUSIONS:** Although respiratory pathogens were not associated with higher severity on presentation, they were associated with increased treatment failure risk, particularly in the presence of respiratory syncytial virus, influenza, and parainfluenza. This supports influenza prevention in asthmatic children, consideration of pathogen identification on presentation, and exploration of treatment intensification for infected patients at higher risk of treatment failure.

Dor, Avi, et al. Cost-effectiveness of an Evidence-Based Childhood Asthma Intervention in Real-World Primary Care Settings. *Journal of Ambulatory Care Management*. July/Sept 2018. 41(3): 213-224. DOI: [10.1097/JAC.0000000000000231](https://doi.org/10.1097/JAC.0000000000000231).

We present an incremental cost-effectiveness analysis of an evidence-based childhood asthma intervention (Community Healthcare for Asthma Management and Prevention of Symptoms [CHAMPS]) to usual management of childhood asthma in community health centers. Data used in the analysis include household surveys, Medicaid insurance claims, and community health center expenditure reports. We combined our incremental cost-effectiveness analysis with a difference-in-differences multivariate regression framework. We found that CHAMPS reduced symptom days by 29.75 days per child-year and was cost-effective (incremental cost-effectiveness ratio: \$28.76 per symptom-free days). Most of the benefits were due to reductions in direct medical costs. Indirect benefits from increased household productivity were relatively small.

Bonato, Matteo, et al. Clinical and Pathologic Factors Predicting Future Asthma in Wheezing Children. A Longitudinal Study. *American Journal of Respiratory Cell and Molecular Biology*. May 2018. DOI: [doi.org/10.1165/rcmb.2018-0009OC](https://doi.org/10.1165/rcmb.2018-0009OC).

**RATIONALE:** Wheeze is a common symptom in infants, but not all wheezers develop asthma. Indeed, up to 50% of wheezing children outgrow their symptoms by school age. How to predict if early wheeze will become asthma is still a matter of vivid debate.

**AIM:** To assess the clinical and pathological factors possibly predicting the future development of asthma in children. **Methods:** 80 children (mean age 3.8±1 yrs) undergoing a clinically indicated bronchoscopy were followed prospectively for a median of 5 yrs. At baseline clinical characteristics with a particular focus on wheezing and its presentation (episodic, multitrigger) were collected; structural and inflammatory changes were quantified in bronchial biopsies.

**RESULTS:** Follow-up data were available in 74/80 children. Children presenting with multitrigger wheeze were more likely to be asthmatics at follow-up than those with episodic (p=0.04) or without wheeze (p <0.0001). Children with asthma also had lower birthweight (p=0.02), lower prevalence of breast-feeding (p=0.02) and a trend for increased IgE (p=0.07) at baseline than those with no asthma. Basement membrane thickness and airway eosinophils at baseline were increased in children who developed asthma at follow-up (p=0.001 and p=0.026, respectively). Multivariate analysis showed that, among all clinical and pathological factors, multitrigger wheezing, basement membrane thickening and reduced birth weight were predictive of future asthma development.

**CONCLUSIONS:** Multitrigger wheeze and reduced birth-weight are clinical predictors of asthma development. Basement membrane thickening in early childhood is closely associated with asthma development, highlighting the importance of airway remodeling in early life as a risk for future asthma.

Agusala, V., et al. Can interactive parental education impact health care utilization in pediatric asthma: A study in rural Texas. *Journal of Internal Medicine Research*. May 2018. DOI: [10.1177/0300060518773621](https://doi.org/10.1177/0300060518773621).

**OBJECTIVE:** It is well known that parent/patient education helps to reduce the burden of asthma in urban areas, but data are scarce for rural areas. This study explored the impact of asthma education in Ector County, a rural part of Health Services Region 9 in Texas, which has one of the highest prevalence rates of asthma in the state.

**METHODS:** This prospective study investigated an interactive asthma education intervention in pediatric patients aged 2-18 years and their caregivers. Change in parental/caregiver knowledge about their child's asthma along with frequency of missed school days, emergency department (ED) visits and hospital admissions was obtained via telephone surveys before and after the educational intervention was delivered.

**RESULTS:** The study enrolled 102 pediatric patients and their parents/caregivers. Asthma education was associated with significantly fewer school absences, ED visits and hospitalizations. Parents/caregivers reported feeling better educated, knowing what triggers an asthma exacerbation, identifying the signs of a severe asthma attack in their child, feeling confident about managing asthma and feeling that the asthma was under control.

**CONCLUSION:** Asthma education of caregivers and children was associated with better symptom management and fewer acute exacerbations, pointing to the relevance and importance of asthma education among pediatric patients in rural areas.

Petsky, Helen L., et al. Tailoring asthma treatment on eosinophilic markers (exhaled nitric oxide or sputum eosinophils): a systematic review and meta-analysis. *Thorax*. June 2018. DOI: [10.1136/thoraxjnl-2018-211540](https://doi.org/10.1136/thoraxjnl-2018-211540). [Epub ahead of print]

**BACKGROUND:** Asthma guidelines guide health practitioners to adjust treatments to the minimum level required for asthma control. As many people with asthma have an eosinophilic endotype, tailoring asthma medications based on airway eosinophilic levels (sputum eosinophils or exhaled nitric oxide, FeNO) may improve asthma outcomes.

**OBJECTIVE:** To synthesise the evidence from our updated Cochrane systematic reviews, for tailoring asthma medication based on eosinophilic inflammatory markers (sputum analysis and FeNO) for improving asthma-related outcomes in children and adults.

**DATA SOURCES:** Cochrane reviews with standardised searches up to February 2017.

**STUDY SELECTION:** The Cochrane reviews included randomised controlled comparisons of tailoring asthma medications based on sputum analysis or FeNO compared with controls (primarily clinical symptoms and/or spirometry/peak flow).

**RESULTS:** The 16 included studies of FeNO-based management (seven in adults) and 6 of sputum-based management (five in adults) were clinically heterogeneous. On follow-up, participants randomised to the sputum eosinophils strategy (compared with controls) were significantly less likely to have exacerbations (62 vs 82/100 participants with  $\geq 1$  exacerbation; OR 0.36, 95% CI 0.21 to 0.62). For the FeNO strategy, the respective numbers were adults OR 0.60 (95% CI 0.43 to 0.84) and children 0.58 (95% CI 0.45 to 0.75). However, there were no significant group differences for either strategy on daily inhaled corticosteroids dose (at end of study), asthma control or lung function.

**CONCLUSION:** Adjusting treatment based on airway eosinophilic markers reduced the likelihood of asthma exacerbations but had no significant impact on asthma control or lung function.

Reid, KM, Forrest, JR, and L. Porter. Tobacco Product Use Among Youths With and Without Lifetime Asthma - Florida, 2016. *Morbidity and Mortality Weekly Report*. June 2018; 67(21): 599-601. DOI: [10.15585/mmwr.mm6721a2](https://doi.org/10.15585/mmwr.mm6721a2).

The increasing availability of diverse tobacco products has led to complex tobacco product use patterns among youths (1). Use by youths of products containing nicotine in any form is unsafe (2); among young persons with asthma, use of combustible tobacco products, particularly cigarettes, is associated with worsening symptoms, poor asthma control, and an increased need for medical management (3,4). Studies suggest that youths with asthma adopt health risk behaviors, including tobacco product use, at rates similar to or higher than those of youths without asthma (3-7); however, these studies are often limited to a partial list of tobacco product types among high school students. To assess current use ( $\geq 1$  days during the past 30 days) of one or more of five tobacco product types (cigarettes, electronic cigarettes [defined as e-cigarettes, e-cigars, vape pipes, vaping pens, e-hookah, and hookah pens], hookah, smokeless tobacco, or cigars) among Florida middle school (grades 6-8) and high school (grades 9-12) students with or without a previous medical diagnosis of asthma, the Florida Department of Health analyzed data from the 2016 Florida Youth Tobacco Survey (FYTS). In 2016, 11.1% of middle school and 27.9% of high school students with asthma, and 7.9% of middle school and 24.2% of high school students without asthma, reported any current tobacco product use. Current use of each tobacco product type was considerably higher among students with asthma than among those without asthma. E-cigarettes were the most commonly used tobacco product type reported by middle and high school students with asthma (7.9% and

19.6%, respectively) and without asthma (5.8% and 17.2%, respectively). Statewide tobacco prevention strategies could help reduce all forms of tobacco product use among youths, particularly among those with asthma.

Gangadharan, A., et al. Recovery of hypothalamo-pituitary-adrenal axis suppression during treatment with inhaled corticosteroids for childhood asthma. *Journal of Asthma and Allergy*. 2018; 10(15): 317-326. DOI: [10.2147/JAA.S142874](https://doi.org/10.2147/JAA.S142874)

**OBJECTIVE:** To describe recovery of adrenal insufficiency in asthmatic children treated with inhaled corticosteroids (ICS) and cortisol replacement therapy.

**DESIGN:** Retrospective, observational study.

**PATIENTS:** A total of 113 patients, 74 male; age 10.4 (3.3-16.5) years; beclomethasone-equivalent ICS dose, 800 µg, (100-1,000), tested by low dose short Synacthen (tetracosactide) test (LDSST), were studied. Test results were classified by basal and peak cortisol concentration: “normal” (basal >100 nmol/L, peak >500 nmol/L), “suboptimal” (basal >100 nmol/L, peak 350-499 nmol/L), “abnormal” (basal <100 nmol/L and/or peak <350 nmol/L). Patients with suboptimal results received hydrocortisone during periods of stress only, and those with abnormal responses received daily hydrocortisone, increased during periods of stress. A total of 73 patients (68%) had ≥2 LDSSTs over 2.2 years (0.2-7.7).

**MEASUREMENTS:** Change in cortisol response to repeat LDSST (movement between diagnostic groups, difference in basal and peak cortisol >15% [2× the inter-assay coefficient of variation]), change in BMI and height standard deviation score (SDS).

**RESULTS:** Baseline test results were abnormal in 17 patients (15%) and all of them had repeat tests. In 13 patients (76%), test results improved (normal in six, suboptimal in seven) and four (24%) remained abnormal. Baseline tests results were suboptimal in 54 patients (48%), of whom 50 (93%) were retested. Repeat tests were normal in 36 patients (72%), remained suboptimal in 11 (22%), and were abnormal in three (6%). Baseline tests results were normal in 42 patients, of whom six patients (14%) were retested. Results remained normal in three (50%), were suboptimal in two (33%), and abnormal in one (17%). Basal and peak cortisol levels increased by >15% in 33/73 (45%) and 42/73 (57%) patients, respectively, and decreased by >15% in 14/73 (19%) and 7/73 (10%), respectively. There was no significant change in height or BMI SDS.

**CONCLUSION:** Recovery of adrenal function is common and occurs during continued ICS and cortisol replacement therapy.

Hayashi, F., et al. Hopkins syndrome following the first episode of bronchial asthma associated with enterovirus D68: a case report. *BMC Neurology*. 2018; 18(71). DOI: [10.1186/s12883-018-1075-7](https://doi.org/10.1186/s12883-018-1075-7)

**BACKGROUND:** Hopkins syndrome (HS) is a rare disorder presenting with acute flaccid paralysis of the limbs following an asthma attack. Neurologists encounter a diagnostic challenge if patients without a history of bronchial asthma develop neurologic features mimicking HS following acute respiratory distress. We report a case of HS occurring after a first episode of bronchial asthma associated with enterovirus D68 infection.

**CASE PRESENTATION:** A 5-year-old girl developed acute respiratory distress. On the fourth hospital day, both her legs became paralyzed except for slight muscle contraction in the right lower limb. Tendon reflexes in the lower limbs were diminished and there was a positive Babinski sign on the right. Sensation was normal in all modalities, and there was no uro-rectal disturbance. Spinal magnetic resonance imaging identified T2-hyperintense lesions with spinal cord edema, mainly involving the bilateral T11 to L1

anterior horns, with left side dominance extending to the left posterior horn. The neurological and neuro-radiological findings of our case were suggestive of HS; however, she had no history of bronchial asthma. An acetylcholine inhalation challenge eventually proved the presence of reversible airway hyper-responsiveness, allowing us to diagnose HS. We identified enterovirus D68 in the patient's intratracheal aspirates using a sensitive polymerase chain reaction assay. Intravenous immunoglobulin administrations at 2 g/kg<sup>2</sup> for 5 consecutive days were repeated every month up to four times. After these treatments, the muscle strength of her right lower limb slightly improved while her left lower leg remained completely paralyzed.

**CONCLUSION:** This case emphasizes the importance of provocation tests to reveal the presence of airway hyper-responsiveness when a child shows neurological signs mimicking HS following acute respiratory distress. Furthermore, the present case suggests a possible link between HS and acute flaccid paralysis following lower respiratory tract infection by enterovirus D68.

Montoya-Williams, D., et al. The Neonatal Microbiome and Its Partial Role in Mediating the Association between Birth by Cesarean Section and Adverse Pediatric Outcomes. *Neonatology*. May 2018; 114(2): 103-111. DOI: [10.1159/000487102](https://doi.org/10.1159/000487102)

**BACKGROUND:** Cesarean sections (CS) are among the most commonly performed surgical procedures in the world. Epidemiologic data has associated delivery by CS with an increased risk of certain adverse health outcomes in children, such as asthma and obesity.

**OBJECTIVE:** To explore what is known about the effect of mode of delivery on the development of the infant microbiome and discuss the potentially mediating role of CS-related microbial dysbiosis in the development of adverse pediatric health outcomes. Recommendations for future inquiry are also provided.

**METHODS:** This study provides a narrative overview of the literature synthesizing the findings of literature retrieved from searches of PubMed and other computerized databases and authoritative texts.

**RESULTS:** Emerging evidence suggests that mode of delivery is involved in the development of the neonatal microbiome and may partially explain pediatric health outcomes associated with birth by CS. Specifically, the gut microbiome of vaginally delivered infants more closely resembles their mothers' vaginal microbiome and thus more commonly consists of potentially beneficial microbiota such as *Lactobacillus*, *Bifidobacterium*, and *Bacteroides*. Conversely, the microbiome of infants born via CS shows an increased prevalence of either skin flora or potentially pathogenic microbial communities such as *Klebsiella*, *Enterococcus*, and *Clostridium*.

**CONCLUSIONS:** Mode of delivery plays an important role in the development of the postnatal microbiome but likely tells only part of the story. More comprehensive investigations into all the pre- and perinatal factors that have the potential to contribute to the neonatal microbiome are warranted.

Turner, S., et al. Variants in genes coding for glutathione S-transferases and asthma outcomes in children. *Pharmacogenomics*. June 2018; 19(8): 707-713. DOI: [10.2217/pgs-2018-0027](https://doi.org/10.2217/pgs-2018-0027)

Our hypothesis was that children with mutations in genes coding for glutathione S-transferases (GST) have worse asthma outcomes compared with children with active type genotype. Data were collected in five populations. The rs1695 single nucleotide polymorphism (GSTP1) was determined in all cohorts (3692 children) and GSTM1 and GSTT1 null genotype were determined in three cohorts (2362 children). GSTT1 null (but not other genotypes) was associated with a minor increased risk for asthma attack and there were no significant associations between GST genotypes and asthma severity. Interactions between

GST genotypes and SHS exposure or asthma severity with the study outcomes were nonsignificant. We find no convincing evidence that the GST genotypes studied are related to asthma outcomes.

Lê-Scherban, F., et al. Intergenerational Associations of Parent Adverse Childhood Experiences and Child Health Outcomes. *Pediatrics*. May 2018. DOI: [10.1542/peds.2017-4274](https://doi.org/10.1542/peds.2017-4274)

**BACKGROUND:** Adverse childhood experiences (ACEs) robustly predict future morbidity and mortality. Researchers are just beginning to investigate intergenerational effects. We hypothesize there are intergenerational associations between parent ACE exposure and worse child health, health behaviors, and health care access and use.

**METHODS:** We linked data from 2 population-based cross-sectional telephone surveys in Philadelphia, Pennsylvania, that were used to ask parents about their past exposure to ACEs and their child's health, respectively. Participants were 350 parent-child dyads. Logistic regression models adjusted for parent and child characteristics. Parent ACE score was used to summarize indicators of parents' childhood adversity. Child health outcomes were poor overall health status, asthma diagnosis, obesity, low fruit and vegetable consumption, any soda consumption, inadequate physical activity, excessive television watching, no health insurance, no usual source of health care, and no dental examination in past 12 months.

**RESULTS:** Of adult participants, 80% were female participants and 45% were non-Latino African American. Eighty-five percent of parents had experienced  $\geq 1$  ACE and 18% had experienced  $\geq 6$  ACEs. In adjusted models, each additional parent ACE was associated with higher odds of poor child overall health status (odds ratio [OR] = 1.19; 95% confidence interval [CI]: 1.07-1.32), asthma (OR = 1.17; 95% CI: 1.05-1.30), and excessive television watching (OR = 1.16; 95% CI: 1.05-1.28).

**CONCLUSIONS:** The full scope of the health effects of ACEs may not be limited to the exposed individual, highlighting the need for a 2-generation approach to addressing the social determinants of child health.

Petrovich, LJ., et al. Reporting to parents on children's exposures to asthma triggers in low-income and public housing, an interview-based case study of ethics, environmental literacy, individual action, and public health benefits. *Environmental Health*. May 2018; 17(1): 48. DOI: [10.1186/s12940-018-0395-9](https://doi.org/10.1186/s12940-018-0395-9)

**BACKGROUND:** Emerging evidence about the effects of endocrine disruptors on asthma symptoms suggests new opportunities to reduce asthma by changing personal environments. Right-to-know ethics supports returning personal results for these chemicals to participants, so they can make decisions to reduce exposures. Yet researchers and institutional review boards have been reluctant to approve results reports in low-income communities, which are disproportionately affected by asthma. Concerns include limited literacy, lack of resources to reduce exposures, co-occurring stressors, and lack of models for effective reporting. To better understand the ethical and public health implications of returning personal results in low-income communities, we investigated parents' experiences of learning their children's environmental chemical and biomonitoring results in the Green Housing Study of asthma.

**METHODS:** The Green Housing Study measured indoor chemical exposures, allergens, and children's asthma symptoms in "green"-renovated public housing and control sites in metro-Boston and Cincinnati in 2011-2013. We developed reports for parents of children in the study, including results for their child and community. We observed community meetings where results were reported, and metro-Boston residents participated in semi-structured interviews in 2015 about their report-back experience. Interviews were systematically coded and analyzed.

**RESULTS:** Report-back was positively received, contributed to greater understanding, built trust between researchers and participants, and facilitated action to improve health. Sampling visits and community

meetings also contributed to creating a positive study experience for participants. Participants were able to make changes in their homes, such as altering product use and habits that may reduce asthma symptoms, though some faced roadblocks from family members. Participants also gained access to medical resources, though some felt that clinicians were not responsive. Participants wanted larger scale change from government or industry and wanted researchers to leverage study results to achieve change. **CONCLUSIONS:** Report-back on environmental chemical exposures in low-income communities can enhance research benefits by engaging residents with personally relevant information that informs and motivates actions to reduce exposure to asthma triggers. Ethical practices in research should support deliberative report-back in vulnerable communities.

Reynolds, KC., et al. Multiple Comorbid Conditions, Sleep Quality and Duration, and Academic Performance in Urban Children With Asthma. *Journal of Pediatric Psychology*. May 2018. DOI: [10.1093/jpepsy/jsy027](https://doi.org/10.1093/jpepsy/jsy027)

**OBJECTIVE:** Common comorbid medical conditions including allergic rhinitis (AR), obesity, and sleep disordered breathing (SDB) have been linked with asthma exacerbations; however, these conditions also impact sleep and academic functioning. The current study sought to examine unique and combined associations of these common comorbidities on sleep and academic performance among urban minority children with persistent asthma. We expected additional comorbid diagnoses would be associated with poorer sleep and academic functioning.

**METHOD:** Urban children 7-9 years old (n = 249) with persistent asthma from African American, Latino, and non-Latino White backgrounds participated in this cross-sectional study. Asthma and AR were assessed using guidelines-based approaches. Overweight/obesity was assessed using body mass index and parents reported on SDB risk. Sleep quality (sleep efficiency) and sleep duration were assessed via 4 weeks of actigraphy. A cumulative risk index (CRI) score of asthma-related comorbidities (i.e., number of comorbidities for which each child met criteria) was calculated.

**RESULTS:** Comorbid conditions were prevalent (AR, 85%; overweight/obese, 39%; SDB risk, 44%). Lower SDB risk and better AR control were both associated with fewer school absences. A higher CRI score was associated with shorter sleep duration and more absences. For children with 1 comorbid condition, better lung function was associated with better sleep efficiency.

**CONCLUSION:** Findings suggest increased risk of shorter sleep and more frequent school absences among urban minority children with asthma and more comorbid conditions. Assessment and treatment of this high-risk group must consider how comorbid conditions exacerbate children's asthma and may affect sleep and daytime functioning.

O'Byrne, PM., et al. Inhaled Combined Budesonide-Formoterol as Needed in Mild Asthma. *New England Journal of Medicine*. May 2018; 378(20): 1865-1876. DOI: [10.1056/NEJMoa1715274](https://doi.org/10.1056/NEJMoa1715274)

**BACKGROUND:** In patients with mild asthma, as-needed use of an inhaled glucocorticoid plus a fast-acting  $\beta$ 2-agonist may be an alternative to conventional treatment strategies.

**METHODS:** We conducted a 52-week, double-blind trial involving patients 12 years of age or older with mild asthma. Patients were randomly assigned to one of three regimens: twice-daily placebo plus terbutaline (0.5 mg) used as needed (terbutaline group), twice-daily placebo plus budesonide-formoterol (200  $\mu$ g of budesonide and 6  $\mu$ g of formoterol) used as needed (budesonide-formoterol group), or twice-daily budesonide (200  $\mu$ g) plus terbutaline used as needed (budesonide maintenance group). The primary objective was to investigate the superiority of as-needed budesonide-formoterol to as-needed terbutaline

with regard to electronically recorded weeks with well-controlled asthma.

**RESULTS:** A total of 3849 patients underwent randomization, and 3836 (1277 in the terbutaline group, 1277 in the budesonide-formoterol group, and 1282 in the budesonide maintenance group) were included in the full analysis and safety data sets. With respect to the mean percentage of weeks with well-controlled asthma per patient, budesonide-formoterol was superior to terbutaline (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30;  $P=0.046$ ) but inferior to budesonide maintenance therapy (34.4% and 44.4%, respectively; odds ratio, 0.64; 95% CI, 0.57 to 0.73). The annual rate of severe exacerbations was 0.20 with terbutaline, 0.07 with budesonide-formoterol, and 0.09 with budesonide maintenance therapy; the rate ratio was 0.36 (95% CI, 0.27 to 0.49) for budesonide-formoterol versus terbutaline and 0.83 (95% CI, 0.59 to 1.16) for budesonide-formoterol versus budesonide maintenance therapy. The rate of adherence in the budesonide maintenance group was 78.9%. The median metered daily dose of inhaled glucocorticoid in the budesonide-formoterol group (57  $\mu\text{g}$ ) was 17% of the dose in the budesonide maintenance group (340  $\mu\text{g}$ ).

**CONCLUSIONS:** In patients with mild asthma, as-needed budesonide-formoterol provided superior asthma-symptom control to as-needed terbutaline, assessed according to electronically recorded weeks with well-controlled asthma, but was inferior to budesonide maintenance therapy. Exacerbation rates with the two budesonide-containing regimens were similar and were lower than the rate with terbutaline. Budesonide-formoterol used as needed resulted in substantially lower glucocorticoid exposure than budesonide maintenance therapy. (*Funded by AstraZeneca; SYGMA 1 ClinicalTrials.gov number, NCT02149199*).

Werder, RB., et al. PGD2/DP2 receptor activation promotes severe viral bronchiolitis by suppressing IFN- $\lambda$  production. *Science Translational Medicine*. May 2018; 10(440). DOI: [10.1126/scitranslmed.aao0052](https://doi.org/10.1126/scitranslmed.aao0052)

Prostaglandin D2 (PGD2) signals through PGD2 receptor 2 (DP2, also known as CRTH2) on type 2 effector cells to promote asthma pathogenesis; however, little is known about its role during respiratory syncytial virus (RSV) bronchiolitis, a major risk factor for asthma development. We show that RSV infection up-regulated hematopoietic prostaglandin D synthase expression and increased PGD2 release by cultured human primary airway epithelial cells (AECs). Moreover, PGD2 production was elevated in nasopharyngeal samples from young infants hospitalized with RSV bronchiolitis compared to healthy controls. In a neonatal mouse model of severe viral bronchiolitis, DP2 antagonism decreased viral load, immunopathology, and morbidity and ablated the predisposition for subsequent asthma onset in later life. This protective response was abolished upon dual DP1/DP2 antagonism and replicated with a specific DP1 agonist. Rather than mediating an effect via type 2 inflammation, the beneficial effects of DP2 blockade or DP1 agonism were associated with increased interferon- $\lambda$  (IFN- $\lambda$ ) [interleukin-28A/B (IL-28A/B)] expression and were lost upon IL-28A neutralization. In RSV-infected AEC cultures, DP1 activation up-regulated IFN- $\lambda$  production, which, in turn, increased IFN-stimulated gene expression, accelerating viral clearance. Our findings suggest that DP2 antagonists or DP1 agonists may be useful antivirals for the treatment of viral bronchiolitis and possibly as primary preventatives for asthma.

Montgomery, MP., et al. Association between pediatric asthma care quality and morbidity and English language proficiency in Ohio. *Journal of Asthma*. May 2018; 8: 1-24. DOI: [10.1080/02770903.2018.1474364](https://doi.org/10.1080/02770903.2018.1474364)

**OBJECTIVE:** Limited English proficiency can be a barrier to asthma care and is associated with poor outcomes. This study examines whether pediatric patients in Ohio with limited English proficiency experience lower asthma care quality or higher morbidity.

**METHODS:** We used electronic health records for asthma patients aged 2-17 years from a regional, urban, children's hospital in Ohio during 2011-2015. Community-level demographics were included from U.S. Census data. By using chi-square and t-tests, patients with limited English proficiency and bilingual English-speaking patients were compared with English-only patients. Five asthma outcomes—two quality and three morbidity measures—were modeled using generalized estimating equations with a logit link function.

**RESULTS:** The study included 15 352 (84%) English-only patients, 1744 (10%) patients with limited English proficiency, and 1147 (6%) bilingual patients. Recommended pulmonary function testing (quality measure) and multiple exacerbation visits (morbidity measure) did not differ by language group. Compared with English-only patients, bilingual patients had higher odds of ever having an exacerbation visit (morbidity measure) (adjusted odds ratio [aOR], 1.4; 95% confidence interval [CI], 1.2-1.6) but lower odds of admission to intensive care (morbidity measure) (aOR, 0.3; 95% CI, 0.2-0.7), while patients with limited English proficiency did not differ on either factor. Recommended follow-up after exacerbation (quality measure) was higher for limited English proficiency (aOR, 1.8; 95% CI, 1.4-2.3) and bilingual patients (aOR, 1.6; 95% CI, 1.3-2.1), compared with English-only patients.

**CONCLUSIONS:** In this urban, pediatric population with reliable interpreter services, limited English proficiency was not associated with worse asthma care quality or morbidity.

Amat, F. and A. Labbé. Biomarkers for severe allergic asthma in children: could they be useful to guide disease control and use of omalizumab? *Expert Review of Respiratory Medicine*. May 2018; 16: 1-8. DOI: [10.1080/17476348.2018.1475233](https://doi.org/10.1080/17476348.2018.1475233)

Although symptom controls in asthmatic children can be achieved through compliant use of conventional medication, some children have uncontrolled severe persistent asthma, especially if they are allergic. For these children, omalizumab (approved by the EMA and FDA in children aged > 6 years) could be a therapeutic option. However, response to omalizumab varies from one child to another. Predictive biomarkers of omalizumab effectiveness could be useful to monitor response to treatment. Area covered: The authors searched in the PubMed database for publications related to the use of biomarkers in allergic asthma. Supported by their own experience in phenotyping asthma in children, they analyzed whether these biomarkers could be useful in assessing response to omalizumab. Expert commentary: Th2 inflammation in children with allergic asthma can be assessed by measuring several biomarkers (blood eosinophil, serum ECP or periostin, FeNO). While a single measurement may be insufficient, a combination of biomarkers assessments may improve the follow-up of children treated by omalizumab.

## NEWS

Campbell, Ruth. [Tech shows off remodeled pediatric clinic; spotlights asthma awareness month](#). *Odessa American News Online*. June 2, 2018.

Showcasing its spruced up pediatric clinic, Texas Tech University Health Sciences Center in Odessa took the opportunity to spotlight asthma awareness month....Dr. Bhargavi Kola runs an

asthma awareness program and conducts a lot of student outreach. About five years ago, Kola said two students died who suffered from asthma.

“And those were easily preventable. That ignited our department to do something for our community and that’s when we started this program. So basically what we do here is we screen them; we educate them; we empower them with the knowledge of asthma. We give them the tools to check and take care of their asthma at their house and when to call a doctor,” Kola said.

Stutzman, Stephanie. [Port Of Long Beach Awards \\$600,000 Grant Toward Asthma Research, Care](#). *The Grunion*. Jun 1, 2018.

The Port of Long Beach Community Grant Program has awarded \$600,000 to the Long Beach Alliance for Children with Asthma, a community coalition that's part of MemorialCare Miller Children's and Women's Hospital. The grant will support the organization's Community Health Workers and Community Education Program.

[DOH: Brooklyn asthma rates among highest in city](#). *News 12 Brooklyn*. May 31, 2018.

Asthma rates in parts of Brooklyn are higher than most of New York City, according to the Department of Health. It says Downtown Brooklyn neighborhoods have worse air pollution rates, which is an environmental factor of asthma, compared to the city average. Child asthma rates are also higher.

Wolfram, Joel. [Your child’s allergies could be caused by acid reflux](#). *WHYY*. May 29, 2018.

When reflux reaches the respiratory system, it can cause congestion and breathing problems that, when chronic, might at first appear to be asthma or a lingering infection. Adults are prone to respiratory reflux too, but Zur said the condition can begin during infancy.

Klass, Perri. [Asthma Doesn’t Take a Vacation](#). *The New York Times*. May 21, 2018.

Many parents do know that they have to be especially vigilant about their child’s medication in pollen season, when the air is thick with allergens. But some think they can take a vacation from the inhalers during the summer, and their children's doctors would really like to be consulted before the regimen is changed.

Basco, William T. [Inhaled Steroids in Childhood Asthma: Does Dose Matter?](#) *Medscape*. May 21, 2018. [Paywall]

An uncertainty in the management of children with poorly controlled asthma is whether increasing the inhaled glucocorticoid dose when asthma symptoms first begin to worsen can help to prevent asthma exacerbations. A recent study explored this strategy. The randomized, double-blind, parallel-group trial enrolled children at 17 sites in the United States...

Grygotis, Lauren. [Antibiotic Use During Pregnancy May Increase Risk for Childhood Asthma](#). *Pulmonary Advisor*. May 21, 2018.

Frequent maternal antibiotic use during pregnancy is associated with increased risk for childhood asthma, according to data presented at the American Thoracic Society (ATS) 2018 International Conference, held May 18 to 23, 2018, in San Diego, California.

Boyles, Salynn. [Ozone Exposure at Birth May Influence Asthma Risk](#). *Medpage Today*. May 20, 2018.

Exposure to ozone air pollution at birth was associated with a significantly increased risk of developing asthma, allergic rhinitis, and eczema later in childhood, researchers reported here. Each 10 parts per billion (ppb) increase in exposure to ozone at birth was associated with an 82% increased risk for developing asthma in the 10-year follow up to the 2006 Toronto Child Health Evaluation Questionnaire (T-CHEQ), according to Teresa To, PhD, of the Hospital for Sick Children in Toronto, and colleagues.

Bender, Kenneth. [Antibiotics in Infancy Linked to Childhood Atopic Asthma](#). *MD Magazine*. May 18, 2018.

An association between antibiotic treatment in the first week of life and atopic asthma in childhood found in a long-term study suggests an immune-mediated effect, possibly from early disturbance of gastrointestinal microbiota, according to researchers.

Stern, Melissa. [Missouri schools now have access to live-saving medications for kids with asthma attacks](#). *Fox 4 Kansas City*. May 16, 2018.

Missouri schools now have access to certain medications that could save lives, and it's helping some breathe easier in class... With the help of Children's Mercy Hospital, KC public schools now have access to medications that can treat asthma attacks. Even more importantly, school nurses can give students having attacks those medications as they wait for an ambulance to arrive.

Rambaldi, Camilla. [New coalition hopes to help families learn how to manage a child's asthma](#). *News 4 San Antonio*. May 9, 2018.

May is Asthma Awareness Month, and in San Antonio, the condition is the reason dozens of children are sent to the hospital every year. But one local coalition is working to decrease the growing rate. At 10 a.m. today, Councilwoman Ana Sandoval will commemorate the South Texas Asthma Coalition - a community-based organization.

[Low Neighborhood Walkability Increases Risk of Asthma in Kids](#). *Clinical Advisor*. May 8, 2018.

Children living in neighborhoods with low walkability are at increased risk of asthma, according to a study published online April 17 in the *Annals of the American Thoracic Society*. The researchers found that 21% of children (69,628) developed incident asthma and were followed longitudinally in the Ontario Asthma Surveillance Information System (OASIS) asthma database. There was an increased incidence of asthma among birth home neighborhoods with low walkability (hazard ratio, 1.11). Low walkability in a given year of a child's life was associated with greater odds of ongoing asthma in the same year (odds ratio, 1.12).

Beth Israel Deaconess Medical Center. Traffic-related pollution linked to risk of asthma in children. *Science Daily*. May 1, 2018.

New research suggests that long-term exposure to traffic-related pollution significantly increases the risk of pediatric asthma, especially in early childhood. Children living within a football field's length of major roadways had nearly three times the odds of pediatric asthma compared to children who lived four times farther away.