

Asthma News This Week

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JOURNAL articles

Parikh, K., et al. Barriers and Facilitators to Asthma Care After Hospitalization as Reported by Caregivers, Health Providers, and School Nurses. *Hospital Pediatrics*. Oct 4, 2018. doi: 10.1542/hpeds.2017-0182. [e-pub ahead of print; abstract only]

OBJECTIVES: To develop a comprehensive understanding of the barriers and/or facilitators for asthma management for the health professionals and caregivers of children with >1 hospitalization. **METHODS:** Individual interviews were conducted with family caregivers and health professionals. Focus groups were conducted with school nurses. The interview and focus group guide were used to probe for barriers and facilitators of asthma management. Interviews were recorded, transcribed, and coded by using qualitative software. Themes were identified by using content analysis in the interviews and descriptive qualitative

analysis in the focus groups. RESULTS: Caregivers (n = 10), asthma educators (n = 4), physicians (n = 4), and a payer (n = 1) were individually interviewed. School nurses were interviewed via a focus group (n = 10). Children had a median age of 7 years, mean length of stay of 1.9 days, and 56% had a previous hospitalization in the previous 12 months. **The "gaps in asthma knowledge" theme (which includes an inadequate understanding of asthma chronicity, activity restrictions, and management with controller medications) emerged as a theme for both caregivers and health professionals but with different health beliefs. School nurses reinforced the difficulty they have in managing children who have asthma in schools, and they identified using the asthma action plan as a facilitator.** CONCLUSIONS: Caregivers and health professionals have different health beliefs about asthma knowledge, which raises challenges in the care of a child who has asthma. In addition, school nurses highlight specific barriers that are focused on medication use in schools. A comprehensive understanding of the barriers and facilitators of asthma management that families experience after hospital discharge is crucial to design better efforts to support families.

Associations between prenatal maternal urinary concentrations of personal care product chemical biomarkers and childhood respiratory and allergic outcomes in the CHAMACOS study. *Environmental International*. Oct 4, 2018; 121(1): 538-549. doi: 10.1016/j.envint.2018.09.027. [e-pub ahead of print]

BACKGROUND: Personal care product chemicals may be contributing to risk for asthma and other atopic illnesses. The existing literature is conflicting, and many studies do not control for multiple chemical exposures. METHODS: We quantified concentrations of three phthalate metabolites, three parabens, and four other phenols in urine collected twice during pregnancy from 392 women. We measured T helper 1 (Th1) and T helper 2 (Th2) cells in their children's blood at ages two, five, and seven, and assessed probable asthma, aeroallergies, eczema, and lung function at age seven. We conducted linear and logistic regressions, controlling for additional biomarkers measured in this population as selected by Bayesian Model Averaging. RESULTS: **The majority of comparisons showed null associations.** Mono-n-butyl phthalate (MnBP) was associated with higher Th2% (RR: 10.40, 95% CI: 3.37, 17.92), and methyl paraben was associated with lower Th1% (RR: -3.35, 95% CI: -6.58, -0.02) and Th2% at borderline significance (RR: -4.45, 95% CI: -8.77, 0.08). Monoethyl phthalate was associated with lower forced expiratory flow from 25 to 75% of forced vital capacity (FEF25-75%) (RR: -3.22 L/s, 95% CI: -6.02, -0.34). Propyl paraben (OR: 0.86, 95% CI: 0.74, 0.99) was associated with decreased odds of probable asthma. CONCLUSIONS: **While some biomarkers, particularly those from low molecular weight phthalates, were associated with an atopic cytokine profile and poorer lung function, no biomarkers were associated with a corresponding increase in atopic disease.**

Pérez-Losada, Marcos, et al. Pediatric asthma comprises different phenotypic clusters with unique nasal microbiotas. *Microbiome*. Oct 4, 2018; 6(1): 179. doi: 10.1186/s40168-018-0564-7.

BACKGROUND: Pediatric asthma is the most common chronic childhood disease in the USA, currently affecting ~ 7 million children. This heterogeneous syndrome is thought to encompass various disease phenotypes of clinically observable characteristics, which can be statistically identified by applying clustering approaches to patient clinical information. Extensive evidence has shown that the airway microbiome impacts both clinical heterogeneity and pathogenesis in pediatric asthma. Yet, so far, airway microbiotas have been consistently neglected in the study of asthma phenotypes. Here, we couple extensive clinical information with 16S rRNA high-throughput sequencing to characterize the microbiota of the nasal cavity in 163 children and adolescents clustered into different asthma phenotypes. **RESULTS:** Our clustering analyses identified three statistically distinct phenotypes of pediatric asthma. Four core OTUs of the pathogenic genera *Moraxella*, *Staphylococcus*, *Streptococcus*, and *Haemophilus* were present in at least 95% of the studied nasal microbiotas. Phyla (Proteobacteria, Actinobacteria, and Bacteroidetes) and genera (*Moraxella*, *Corynebacterium*, *Dolosigranulum*, and *Prevotella*) abundances, community composition, and structure varied significantly ($0.05 < P \leq 0.0001$) across asthma phenotypes and one of the clinical variables (preterm birth). Similarly, microbial networks of co-occurrence of bacterial genera revealed different bacterial associations across asthma phenotypes. **CONCLUSIONS:** This study shows **that children and adolescents with different clinical characteristics of asthma also show different nasal bacterial profiles, which is indicative of different phenotypes of the disease.** Our work also shows how clinical and microbial information could be integrated to validate and refine asthma classification systems and develop biomarkers of disease.

Jang, Hoon, et al. Factors Associated With First Medication Time for Children Treated in the Emergency Department for Asthma. *Pediatric Emergency Care*. Oct 2, 2018; doi: [10.1097/PEC.0000000000001609](https://doi.org/10.1097/PEC.0000000000001609). [e-pub ahead of print]

OBJECTIVES: Acute asthma exacerbations are among the most common reasons for childhood emergency department (ED) visits and hospitalizations. Although early ED administration of asthma medication has been shown to decrease hospitalizations, studies of factors associated with early ED asthma medication delivery have been limited. The objective of our study was to identify patient- and ED-related factors associated with early medication delivery among children treated in the ED for asthma exacerbations. **METHODS:** This **retrospective study** used electronic health record data from all encounters for a primary diagnosis of asthma in an academic children's hospital ED during the study period 2009 to 2013. Using multivariate logistic regression, **we identified the association between patient- and ED-related factors and the time to first medication** defined as a binary outcome using a threshold of 1 hour from ED arrival. We then stratified our analysis by triage level (Emergency Severity Index [ESI]). **RESULTS:** Of the 4846 encounters during the study period, 62% were male, mean age was 7.30 years, 76% had public insurance, and 57% had an ESI level of 3. Medication was administered within 1 hour of arrival in 2236 encounters (46%). After adjusting for covariates, multivariate logistic regression revealed that patients were less likely to have medications within 1 hour when they had less severe ESI (ESI 2 vs ESI 4: odds ratio [OR], 0.139; confidence interval [CI], 0.114-

0.170), arrived via non-emergency medical services (OR, 0.525; CI, 0.413-0.665), or arrived to a crowded ED (OR, 0.574; CI, 0.505-0.652). Age, sex, and insurance type were not associated with timeliness of initial medication administration. Stratified analyses demonstrated that the crowding effect was larger for less severely ill patients. **CONCLUSIONS:** Our study found that patient severity (acuity level, arrival mode) and level of ED crowding-but not demographic factors-are associated with the administration of medication in the first hour to pediatric patients with asthma. Our findings may be helpful in redesigning asthma care management strategies.

Landigran, P.J., et al. Pollution and Children's Health. *Science of the Total Environment*. Oct 2, 2018; 650(2): 2389-2394. doi: 10.1016/j.scitotenv.2018.09.375. [e-pub ahead of print]

FINDINGS: The Lancet Commission on Pollution and Health found that pollution - air, water, soil, and chemical pollution - was responsible in 2016 for 940,000 deaths in children worldwide, two-thirds of them in children under the age of 5. Pollution is inequitably distributed, and the overwhelming majority of pollution-related deaths in children occurred in low- and middle-income countries (LMICs). Most were due to respiratory and gastrointestinal diseases caused by polluted air and water. **Pollution is linked also to multiple non-communicable diseases (NCDs) in children including low birth weight, asthma, cancer and neurodevelopmental disorders, and these diseases are on the rise.** The full impact of pollution, especially chemical pollution on the global burden of pediatric disease is not yet known, but almost certainly is undercounted because patterns of chemical exposure are not well charted and the potential toxicity of many chemical pollutants has not been characterized. The list of pediatric NCDs attributed to pollution will likely expand as the health effects of newer chemical pollutants are better defined and additional associations between pollution and disease are discovered.

CONCLUSION: Pollution prevention presents a major, largely unexploited opportunity to improve children's health and prevent NCDs, especially in LMICs. Failure to incorporate pollution prevention into NCD control programs is a major missed opportunity for disease prevention.

ARIA Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology. *Journal of Asthma and Clinical Immunology*. Sept 28, 2018. doi: [10.1016/j.jaci.2018.08.049](https://doi.org/10.1016/j.jaci.2018.08.049). [e-pub ahead of print]

Allergic Rhinitis and its Impact on Asthma (ARIA) has evolved from a guideline using the best approach to integrated care pathways (ICPs) using mobile technology in AR and asthma multimorbidity. **The proposed next phase of ARIA is Change Management (CM) with the aim of providing an active and healthy life to rhinitis sufferers and to those with asthma multimorbidity across the life cycle whatever their gender or socio-economic status in order to reduce health and social inequities incurred by the disease.** ARIA has followed the 8-step model of Kotter to assess and implement the impact of rhinitis on asthma multimorbidity and to propose multimorbid guidelines. A second change management strategy is proposed by ARIA Phase 4 to increase self-medication and shared decision making in rhinitis and asthma

multimorbidity. An innovation of ARIA has been the development and validation of IT evidence-based tools (MASK: Mobile Airways Sentinel Network) that can inform patient decisions on the basis of a self-care plan proposed by the health care professional.

Pennington, Audrey F., et al. Caesarean delivery, childhood asthma, and effect modification by sex: An observational study and meta-analysis. *Paediatric Perinatal Epidemiology*. Sept 28, 2018. doi: [10.1111/ppe.12510](https://doi.org/10.1111/ppe.12510). [e-pub ahead of print]

BACKGROUND: Numerous studies indicate caesarean delivery is associated with childhood asthma. Sex-specific associations were reported in four of these studies, and in all four studies, the estimated association between caesarean delivery and asthma was of greater magnitude among girls, although most report a lack of evidence of multiplicative interaction. **METHODS:** **We assessed potential effect modification by sex, on the additive and multiplicative scales, of the association between caesarean delivery and asthma** by ages 2 through 6 in up to 17 075 racially diverse children from a retrospective birth cohort, the Kaiser Air Pollution and Pediatric Asthma (KAPPA) Study. **We also conducted a random-effects meta-analysis**, combining our sex-stratified results (using the odds ratio for compatibility with previous studies) with previously published results. **RESULTS: Adjusted risk differences for caesarean delivery and asthma in the KAPPA cohort were higher among girls than boys at every follow-up age.** By age 5, caesarean delivery was associated with an absolute 3.8% (95% confidence interval [CI] 0.4%, 7.3%) higher asthma risk among girls and a 1.9% (95% CI -1.7, 5.4) higher risk among boys. The summary odds ratio from the meta-analysis for caesarean delivery and asthma among girls was 1.26 (95% CI 1.14, 1.39) and 1.08 (95% CI 0.98, 1.20) among boys ($P = 0.036$). **CONCLUSIONS:** Higher, but imprecise, estimates for females across five studies should motivate investigators to estimate sex-specific associations for caesarean delivery and asthma and to explore biological mechanisms or sex-dependent biases that could explain this possible heterogeneity. (*NOTE: "In four out of five studies that assessed these sex-specific associations (including ours), statistical tests of interaction were not significant (ie, $P < 0.05$).")*)

Tattersall, Matthew C., et al. Asthma is associated with carotid arterial injury in children: The Childhood Origins of Asthma (COAST) Cohort. *PLoS One*. Sept 27, 2018; 13(9): e0204708. doi: [10.1371/journal.pone.0204708](https://doi.org/10.1371/journal.pone.0204708)

BACKGROUND: Asthma is associated with an increased cardiovascular disease (CVD) risk in adults, but the impact of asthma and atopic conditions on CVD risk in children is less well established. We hypothesized that children in the Childhood Origins of Asthma (COAST) Cohort with asthma and atopic conditions would have early carotid arterial injury. **METHODS:** **The COAST study is a longitudinal birth cohort of children at increased risk of developing asthma. Children underwent ultrasonography measuring far wall right carotid bifurcation (RCB) and common carotid artery (RCCA) intima-media thickness (IMT; a measure of arterial injury).** Multivariable linear regression models adjusted for age, gender, race, blood pressure, and body-mass index were used to assess associations of asthma and markers of arterial

injury. RESULTS: The 89 participants were a mean (standard deviation) 15.3 (0.6) years old and 42% were female; 28 asthmatics had atopic disease, 34 asthmatics were without other atopic disease, and 15 non-asthmatics had atopic disease. This study population was compared to 12 controls (participants free of asthma or atopic disease). Compared to controls (589 μm), those with atopic disease (653 μm , $p = 0.07$), asthma (649 μm , $p = 0.05$), or both (677 μm , $p = 0.005$) had progressively higher RCB IMT values ($p_{\text{trend}} = 0.011$). In adjusted models, asthmatic and/or atopic participants had significantly higher RCB IMT than those without asthma or atopic disease (all $p \leq 0.03$). Similar relationships were found for RCCA IMT. CONCLUSION: **Adolescents with asthma and other atopic diseases have an increased risk of subclinical arterial injury compared to children without asthma or other atopic disease.**

Fitzpatrick, A.M., et al. Phenotypes of Recurrent Wheezing in Preschool Children: Identification by Latent Class Analysis and Utility in Prediction of Future Exacerbation. *Journal of Allergy and Clinical Immunology*. Sept 26, 2018. doi: 10.1016/j.jaip.2018.09.016. [e-pub ahead of print; abstract only]

BACKGROUND: Recurrent preschool wheezing is a heterogeneous disorder with significant morbidity, yet little is known about phenotypic determinants and their impact on clinical outcomes. OBJECTIVE: **Latent class analysis (LCA) was used to identify latent classes of recurrent preschool wheeze and their association with future exacerbations and inhaled corticosteroid (ICS) treatment response.** METHODS: Data from five clinical trials of 1,708 children age 12-71 months with recurrent wheezing were merged. LCA was performed on 10 demographic, exposure and sensitization variables to determine the optimal number of latent classes. The primary outcome was the annualized rate of wheezing exacerbations requiring systemic corticosteroids during the study intervention period; the secondary outcome was the time to first exacerbation. Exploratory analyses examined the effect of daily ICS treatment on exacerbation outcomes. RESULTS: Four latent classes of recurrent wheezing were identified; these were not distinguished by current symptoms or historical exacerbations but differed with regard to allergen sensitization and/or exposures. Annualized exacerbation rates (mean \pm SEM/year) were 0.65 ± 0.06 for class 1 ("minimal sensitization"), 0.93 ± 0.10 for **class 2 ("sensitization with indoor pet exposure")**, 0.60 ± 0.07 for class 3 ("sensitization with tobacco smoke exposure"), and 0.81 ± 0.10 for **class 4 ("multiple sensitization and eczema")** ($p < 0.001$). In a research setting of high adherence, **daily ICS treatment improved exacerbation rates in classes 2 and 4 but not the other groups.** CONCLUSION: Sensitization and exposure assessments are useful in the prediction of future exacerbation and may identify children most likely to respond favorably to daily ICS treatment.

Lin, J., et al. Effects of supplementation with omega-3 fatty acids during pregnancy on asthma or wheeze of children: A Systematic Rev and meta-analysis. *The Journal of Maternal-fetal and Neonatal Medicine*. Set 25, 2018: 1-151. doi: 10.1080/14767058.2018.1529161. [e-pub ahead of print; abstract only]

OBJECTIVE: To evaluate the effects of omega-3 fatty acids during pregnancy on the incidence of wheeze and asthma of children. **METHODS:** A search was conducted in PubMed, Embase and CENTRAL until September 2017. Randomized controlled trials (RCTs) assessing the effects of omega-3 fatty acids during pregnancy on wheeze/asthma of children were included. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. Outcomes of relative risks were pooled. Subgroup analyses were conducted. **RESULTS:** **Seven RCTs involving 2047 children were included. The pooled data revealed the supplementation during pregnancy reduced the incidence of wheeze/asthma** (risk ratio (RR) 0.81; 95% CI 0.66-0.99; p 0.04), **but the incidence of childhood asthma was not significantly reduced** (RR 0.89; 95%CI 0.67-1.17; p 0.40). Subgroup analyses indicated that the risk of childhood wheeze/asthma was significantly decreased 1) in studies located in Europe (RR 0.67 95% CI 0.51 0.88), 2) in children whose first-degree relatives were diagnosed with allergic disease (RR 0.65 95% CI 0.49 0.85), 3) when a dose of omega - 3 fatty acids \geq 2000mg/d was applied (RR 0.61 95% CI 0.45 0.81), 4) in wheeze/asthma without sensitivity (RR 0.71 95% CI 0.54 0.94). **CONCLUSION:** The available low-quality evidence indicated that omega-3 fatty acids supplementation during pregnancy may reduce the incidence of wheeze/asthma of children, but incidence of asthma was not reduced after omega-3 fatty acids supplementation during pregnancy. More well-designed RCTs with large sample sizes need to be conducted to better understand the effectiveness of omega-3 fatty acids supplementation during pregnancy with asthma in childhood.

In the NEWS

- ❖ Jacobs, Sheila. [Montelukast Plus Levocetirizine vs Monotherapy in Asthma, Allergic Rhinitis](#). *Pulmonology Advisor*. Oct 8, 2018.
- ❖ [Complementary Alternative Medicine in Asthma Use Varies Among Racial/Ethnic Groups](#). *Pulmonology Advisor*. Oct 7, 2018.
- ❖ Rowan, Harriet. [Dirty Air And Disasters Sending Kids To The ER For Asthma](#). *California Healthline*. Oct 4, 2018.
- ❖ [Higher Childhood Asthma Risk From Recurring Acute Respiratory Infections](#). *Pulmonology Advisor*. Oct 5, 2018.
- ❖ Jacobs, Sheila. [Paraben Exposure and Childhood Asthma-Related Outcomes](#). *Pulmonology Advisor*. Oct 2, 2018.
- ❖ Yuen, Laura. [Minneapolis community funds focus on lead poisoning, asthma](#). *MPR News*. Sept 25, 2018.
- ❖ Slaughter, Erica. [Effects of Environmental Air Pollution on Childhood Asthma Rates](#). *MD Magazine*. Sept 27, 2018.
- ❖ O'Hare, Ryan. [Exposure to farmyard bugs reduces immune overreaction found in childhood asthma](#). *Medical Xpress*. Sept 24, 2018.