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# Pediatric Year in Review Bibliography

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Atlanta, GA

**Erick Forno, MD, MPH, ATSF**  
University of Pittsburgh School of Medicine  
Pediatric Pulmonary Medicine  
Pittsburgh, PA

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# The Pediatric Exposome

Stephanie Lovinsky-Desir, MD, MS

Columbia University Medical Center – NY Presbyterian  
Department of Pediatric Pulmonology  
New York, NY

## GENERAL EXTERNAL EXPOSOME – SOCIAL FACTORS

Banwell, E, Collaco, JM, Oates, GR, et al. **Area deprivation and respiratory morbidities in children with bronchopulmonary dysplasia.** *Pediatric Pulmonology*. 2022; 57: 2053- 2059. doi:10.1002/ppul.25969

### Summary

Composite indices of socioeconomic disadvantage allow for assessment of risk to a multitude of social and community level factors that may disadvantage individuals based on the communities where they live. In this study of infants with bronchopulmonary dysplasia (BPD, 911 recruited from Johns Hopkins in Baltimore and 125 from Children’s Hospital of Philadelphia), investigators used the area deprivation index (ADI) to investigate the association between neighborhood-level disadvantage and clinical outcomes. The ADI is a composite index constructed from 17 neighborhood-level socioeconomic variables tabulated from the United States census. Authors observed that infants and young children with BPD (ages 0-3 years) who lived in deprived areas were more likely to have adverse respiratory outcomes including visits to the emergency department, re-hospitalization, and activity limitations. Additionally, authors observed that greater social disadvantage, as measured by the ADI was associated with earlier gestational age, suggesting that children born in deprived neighborhoods are at greater risk of preterm birth. Risk factors such as poor air quality, lower household income, poor quality and crowded housing, and reduced access to health care have all been associated with respiratory illness and may contribute to worse outcomes among premature infants.

### Comments

1. Premature infants with BPD who are born in neighborhoods with greater social disadvantage have worse clinical outcomes.
2. Composite indices that combine a multitude of neighborhood-level social and environmental exposures offer insight on the general external exposome.

3. One limitation of the current study and similar analyses is the use of ADI at a single time point that may not capture changes in neighborhood exposure over time.
4. Future research is needed to develop more comprehensive social environmental exposure indices that can capture greater variability across neighboring communities.

Najjar N, Opolka C, Fitzpatrick AM, Grunwell JR.

**Geospatial Analysis of Social Determinants of Health Identifies Neighborhood Hot Spots Associated With Pediatric Intensive Care Use for Acute Respiratory Failure Requiring Mechanical Ventilation.** *Pediatr Crit Care Med*. 2022 Aug 1;23(8):606-617. doi: 10.1097/PCC.0000000000002986.

### Summary

Several different types of multi-dimensional composite measures of social and community level disadvantage have been developed. In this study investigators used 2 composite indices of neighborhood vulnerability: the social vulnerability index (SVI) that seeks to identify potential negative effects on communities caused by external stresses on human health and the childhood opportunity index (COI) that assesses the quality of resources and conditions that matter for children to live healthy lives in the neighborhoods where they live. This retrospective, population based ecological study evaluated 3,514 children who were mechanically ventilated in the pediatric intensive care units (PICU) of 2 free-standing children’s hospitals in Atlanta, GA. They identified PICU admission ‘hot spots’ as the census tracts with the greatest rate of PICU admissions requiring mechanical ventilation (at the 90<sup>th</sup> percentile). They observed that 9.7% of the children admitted with respiratory failure lived in PICU hot spots. PICU hot spot census tracts had greater social vulnerability and less childhood opportunity than non-hot spot census tracts. Also, mechanically ventilated children who lived in PICU hot spots had greater PICU lengths of stay compared to children in non-hot spots. Overall duration of hospitalization, mortality, and PICU readmission rates did not differ by hot spot designation.

### Comments

1. Social vulnerability and childhood opportunity are composite variables that capture multi-dimensional aspects of social determinants of health.
2. Children who lived in communities of Atlanta that had high social vulnerability and low childhood opportunity had a higher frequency of admission for acute respiratory failure with mechanical ventilation and longer PICU stays.
3. Neighborhood level social deterrents of health were examined in this study rather than individual level assessments; thus, the study is subject to ecological fallacy.
4. Geospatial analysis can be a powerful tool to identify neighborhoods at greatest risk for social vulnerability and health disparities.

### SPECIFIC EXTERNAL EXPOSOME – ENVIRONMENTAL EXPOSURES

Lu C, Yang W, Liu Z, Liao H, Liu Q. **Effect of preconceptional, prenatal and postnatal exposure to home environmental factors on childhood pneumonia: A key role in early life exposure.** *Environmental Research*. 2022; 21 (3): 114098. doi: 10.1016/j.envres.2022.114098

### Summary

Childhood pneumonia is the most common respiratory illness worldwide and has been linked to environmental exposures. The authors of this retrospective cohort study evaluated 8,689 kindergarteners across 6 districts in Changsha, China. They examined personal exposure to 12 indoor environmental factors assessed by detailed questionnaire focusing on 4 exposure windows: 1 year prior to pregnancy, during pregnancy, first year life and 1 year prior to survey. Additionally, they used air quality monitoring data to determine outdoor exposure to ambient pollutants near participants' homes across the same 4 windows of exposure. The main outcome of interest was lifetime incidence of physician diagnosed pneumonia. Pneumonia in pre-school children was significantly related with exposure of new furniture, redecoration, mold/damp stains, and mold or damp clothing or bedding exposure experienced in all 4 exposure windows, with the strongest associations observed for exposure in the 1 year before pregnancy. Also, exposure to environmental tobacco smoke in the prenatal and post-natal periods and the presence of non-flowering plants in the 1 year prior to survey were associated with pre-school pneumonia. Associations between indoor environmental exposures and childhood pneumonia were stronger among children

who lived near traffic sources and had greater exposure to outdoor pollutants.

### Comments

1. Both indoor and outdoor environmental exposures contribute to the specific external exposome and are associated with pediatric pneumonia.
2. One year prior to pregnancy represents a specific exposure window that may contribute to increased risk for future childhood pneumonia but may be often under-recognized.
3. Study limitations include the reliance on questionnaire data that can be subject to recall bias and the lack of indoor measure of chemical exposures.
4. Assessment of environmental exposures at multiple stages of life is an important aspect of exposome research.

Altman MC, Kattan M, O'Connor GT, Murphy RC, Whalen E, LeBeau P, Calatroni A, Gill MA, Gruchalla RS, Liu AH, Lovinsky-Desir S, Pongracic JA, Kercksmar CM, Khurana Hershey GK, Zoratti EM, Teach SJ, Bacharier LB, Wheatley LM, Sigelman SM, Gergen PJ, Togias A, Busse WW, Gern JE, Jackson DJ; National Institute of Allergy and Infectious Disease's Inner City Asthma Consortium.

### Associations between outdoor air pollutants and non-viral asthma exacerbations and airway inflammatory responses in children and adolescents living in urban areas in the USA: a retrospective secondary analysis.

*Lancet Planet Health*. 2023 Jan;7(1):e33-e44. doi: 10.1016/S2542-5196(22)00302-3.

### Summary

In this retrospective analysis, investigators evaluate specific factors in the external exposome (air pollution) and the influence on a specific component of the internal exposome (the transcriptome). The field of transcriptomics uses high-throughput sequencing methods to analyze the expression of multiple RNA transcripts across different physiologic and pathologic conditions. They recruited 208 children with asthma from 9 urban US centers (ages 6-17 years) and a validation cohort of 419 children with asthma from 8 urban centers (age 6-20 years). Exposure to environmental air pollution was captured from the Environmental Protection Agency's daily air quality index (AQI) that is a composite score based on the 6 criteria pollutants. Transcriptomics analysis was conducted on upper airway nasal samples collected during a respiratory illness. A significant proportion of asthma exacerbations were observed in the absence of

respiratory virus (30%). Higher AQI values were associated with asthma exacerbations and decreases in pulmonary function in the absence of respiratory viral infection. Additionally, increased exposure to air pollutants was associated with altered gene expression in inflammatory pathways assessed by transcriptomics. PM<sub>2.5</sub> was associated with increased epithelial inflammatory responses, mucus hypersecretion, and airway remodeling pathways and O<sub>3</sub> with type-2 inflammatory responses.

### Comments

1. Air pollution in urban communities is an important risk factor for asthma exacerbations, independent of respiratory viral infections.
2. Air pollution is associated with specific transcriptomic pathways that likely contribute to asthma exacerbations and reduced lung function.
3. Combined effects of multiple asthma triggers (e.g. air pollution and viral infections) were not examined in this study.
4. Linkages between specific components of the external exposome and the internal exposome offer greater insight into underlying mechanisms that contribute to environmentally triggered respiratory diseases such as asthma.

### INTERNAL EXPOSOME

O'Connor JB, Mottlowitz M, Kruk ME, Mickelson A, Wagner BD, Harris JK, Wendt CH, Laguna TA. **Network Analysis to Identify Multi-Omic Correlations in the Lower Airways of Children With Cystic Fibrosis.** *Front Cell Infect Microbiol.* 2022 Mar 10;12:805170. doi: 10.3389/fcimb.2022.805170. PMID: 35360097; PMCID: PMC8960254.

### Summary

The microbiome is one example of the internal exposome. Metabolomics, or the study of metabolites (intermediary or end products of metabolism) can be interrogated with the microbiome to understand complex interactions between infection and inflammation. Bronchoalveolar lavage fluid (BALF) was obtained during bronchoscopy for this cross-sectional observational study and examined for 68 persons with cystic fibrosis compared to 22 control participants who did not have CF. Metabolomic profiles were assessed with the Biocrates platform and microbiome data were acquired through 16S sequencing. There were 409 metabolomic features measured in the BALF. Higher concentrations of amino acids and lower concentrations of acylcarnitines were observed in the BALF of participants with CF compared to controls

whereas control participants had higher levels of glycerophospholipids and sphingomyelin compared to those with CF. Additionally, 50 metabolomic features in CF BALF were correlated with blood inflammatory markers. There were weak associations between metabolomic features and microbial taxa identified in the airway microbiome including correlations between specific metabolomic markers and *Staphylococcus*, among other pathogens. L-methionine-S-oxide was one of the strongest predictors of CF status and was strongly correlated with *Staphylococcus* suggesting that the CF metabolome may be defined by the polymicrobial bacterial communities within it.

### Comments

1. Metabolomics can be used to understand how features of the internal exposome (e.g., the microbiome) contribute to infection and inflammation for people with cystic fibrosis, a disease that is characterized by recurrent pulmonary infection.
2. Strong metabolomic signatures were identified among individuals with cystic fibrosis compared to disease free controls and associated with both blood inflammatory markers and airway microbiota.
3. One limitation of this study is that the diagnosis free control participants underwent bronchoscopy for a different clinically indicated reason; thus, they do not represent a completely healthy population.
4. Metabolomic signatures that distinguish individuals with specific respiratory disease, such as cystic fibrosis, may be considered as a promising biomarker in future research and clinical practice.

### EXPOSOME AND MULTI-OMIC PROFILING

Maitre L, Bustamante M, Hernández-Ferrer C, Thiel D, Lau CE, Siskos AP, Vives-Usano M, Ruiz-Arenas C, Pelegrí-Sisó D, Robinson O, Mason D, Wright J, Cadiou S, Slama R, Heude B, Casas M, Sunyer J, Papadopoulou EZ, Gutzkow KB, Andrusaityte S, Grazuleviciene R, Vafeiadi M, Chatzi L, Sakhi AK, Thomsen C, Tamayo I, Nieuwenhuijsen M, Urquiza J, Borràs E, Sabidó E, Quintela I, Carracedo Á, Estivill X, Coen M, González JR, Keun HC, Vrijheid M. **Multi-omics signatures of the human early life exposome.** *Nat Commun.* 2022 Nov 21;13(1):7024. doi: 10.1038/s41467-022-34422-2. PMID: 36411288; PMCID: PMC9678903.

## Summary

Large-scale attempts have been made to capture a multitude of factors within the human exposome and integrate them with various measures of biologic function in a multi-omic approach to identify potential biomarkers of the exposome. The Human Early Life Exposome (HELIX) project is a multi-center, longitudinal population-based cohort of 1,301 mother-child pairs from 6 countries (Spain, UK, France, Lithuania, Norway and Greece). The investigators assessed 91 environmental exposures during pregnancy and 116 exposures during childhood (between 6-11 years). Exposures were assessed using a multi-dimensional approach including chemical exposure monitors, geospatial methods, questionnaires, and others to capture a multitude of factors in the exposome of the children including socio-economic, built environment, air and chemical pollutants, diet and activity, among others. In depth multi-omic molecular phenotyping was performed on blood and urine samples between 6-11 years of age to develop an integrated assessment of the children's epigenetic, transcriptomic, proteomic, and metabolomic profiles. Key observations from the integrated analysis include associations between exposures in pregnancy (e.g., maternal smoking, cadmium, and molybdenum) and changes in DNA methylation. Additionally, childhood exposures (e.g., diet, toxic chemical compounds, essential trace elements, and weather conditions) were associated with all omics layers, particularly the metabolome.

## Comments

1. Multi-omic approaches provide information on thousands of biologic functions and are now being used to study how the exposome impacts human health.
2. This study identified 249 associations in pregnancy and 921 associations in childhood that reveal potential biologic responses and sources of exposure.
3. Most participants included in the study were of European ancestry thus replication in cohorts with different ancestral origins and in regions of the world that may experience different environmental exposures is warranted.
4. The entire catalogue of all results of this study have been made publicly available, thus providing a valuable resource that can be used for future research to develop and validate biomarkers of exposure.

## OTHER ARTICLES OF INTEREST

### General External Exposome

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2. Mutic AD, Mauger DT, Grunwell JR, Opolka C, Fitzpatrick AM. **Social Vulnerability Is Associated with Poorer Outcomes in Preschool Children With Recurrent Wheezing Despite Standardized and Supervised Medical Care.** *J Allergy Clin Immunol Pract.* 2022 Apr;10(4):994-1002. doi: 10.1016/j.jaip.2021.12.043. Epub 2022 Feb 2. PMID: 35123099; PMCID: PMC9007879.
3. Deschamps J, Boucekine M, Fayol L, Dubus JC, Nauleau S, Garcia P, Boubred F. **Neighborhood Disadvantage and Early Respiratory Outcomes in Very Preterm Infants with Bronchopulmonary Dysplasia.** *J Pediatr.* 2021 Oct;237:177-182.e1. doi: 10.1016/j.jpeds.2021.06.061. Epub 2021 Jun 30. PMID: 34216631.
4. Zanobetti A, Ryan PH, Coull B, et al. **Childhood Asthma Incidence, Early and Persistent Wheeze, and Neighborhood Socioeconomic Factors in the ECHO/CREW Consortium.** *JAMA Pediatr.* 2022;176(8):759-767. doi:10.1001/jamapediatrics.2022.1446

### Specific External Exposome

5. Marín D, Orozco LY, Narváez DM, Ortiz-Trujillo IC, Molina FJ, Ramos CD, Rodríguez-Villamizar L, Bangdiwala SI, Morales O, Cuellar M, Hernández LJ, Henao EA, Lopera V, Corredor A, Toro MV, Groot H, Villamil-Osorio M, Muñoz DA, Hincapié RC, Amaya F, Oviedo AI, López L, Morales-Betancourt R, Marín-Ochoa BE, Sánchez-García OE, Marín JS, Abad JM, Toro JC, Pinzón E, Builes JJ, Rueda ZV. **Characterization of the external exposome and its contribution to the clinical respiratory and early biological effects in children: The PROMESA cohort study protocol.** *PLoS One.* 2023 Jan 20;18(1):e0278836. doi: 10.1371/journal.pone.0278836. PMID: 36662732; PMCID: PMC9858469.

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7. Dapas M, Thompson EE, Wentworth-Sheilds W, Clay S, Visness CM, Calatroni A, Sordillo JE, Gold DR, Wood RA, Makhija M, Khurana Hershey GK, Sherenian MG, Gruchalla RS, Gill MA, Liu AH, Kim H, Kattan M, Bacharier LB, Rastogi D, Altman MC, Busse WW, Becker PM, Nicolae D, O'Connor GT, Gern JE, Jackson DJ, Ober C. **Multi-omic association study identifies DNA methylation-mediated genotype and smoking exposure effects on lung function in children living in urban settings.** *PLoS Genet.* 2023 Jan 13;19(1):e1010594. doi: 10.1371/journal.pgen.1010594. PMID: 36638096; PMCID: PMC9879483.

### Internal Exposome

8. El Saie A, Fu C, Grimm SL, Robertson MJ, Hoffman K, Putluri V, Ambati CSR, Putluri N, Shivanna B, Coarfa C, Pammi M. **Metabolome and microbiome multi-omics integration from a murine lung inflammation model of bronchopulmonary dysplasia.** *Pediatr Res.* 2022 Dec;92(6):1580-1589. doi: 10.1038/s41390-022-02002-1. Epub 2022 Mar 25. PMID: 35338351; PMCID: PMC9509498.
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### Measurement of the Exposome – Multi-Omics

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Murua J, Sardón-Prado O, Pino-Yanes M, Potočnik U, Kabesch M, Kraneveld AD, Maitland-van der Zee AH, On Behalf Of The SysPharmPediA Consortium. **A System Pharmacology Multi-Omics Approach toward Uncontrolled Pediatric Asthma.** *J Pers Med.* 2021 May 28;11(6):484. doi: 10.3390/jpm11060484. PMID: 34071272; PMCID: PMC8227234.

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### Exposome and Multi-Omics Profiles

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# Epidemic and Pandemic Respiratory Viruses: Long-term Impact on Respiratory Health

Christian Rosas-Salazar, MD, MPH, ATSF

Vanderbilt University Medical Center

Department of Pediatrics

Nashville, Tennessee

## SARS-COV-2: PREVALENCE AND CHARACTERISTICS OF LONG COVID IN ADOLESCENTS

Stephenson T, Pinto Pereira SM, Shafran R, de Stavola BL, Rojas N, McOwat K, Simmons R, Zavala M, O'Mahoney L, Chalder T, Crawley E, Ford TJ, Harnden A, Heyman I, Swann O, Whittaker E, CLoCk Consortium, Ladhani SN.

**Physical and mental health 3 months after SARS-CoV-2 infection (long COVID) among adolescents in England (CLoCk): a national matched cohort study.** *Lancet Child Adolesc Health.* 2022;6(4):230-239.

### Summary

This study examined the prevalence of post-COVID symptomatology in a population-based, non-hospitalized cohort of adolescents in the United Kingdom (n=6,804). Using a national public health surveillance database, the authors 1) identified adolescents ages 11-17 years who tested positive for SARS-CoV-2 by PCR between January and March 2021 and only required outpatient management, and 2) matched these participants by age, sex, and geographic region to adolescents who tested negative for SARS-CoV-2 by PCR during the same 3-month period and had no prior history of COVID. Participants were then contacted 3 months after the PCR testing to collect data on physical and mental health symptoms at the time of the PCR testing (retrospective) and at the time of contact (cross-sectional). At the time of PCR testing, 35.4% of the adolescents in the SARS-CoV-2 positive group and 8.3% of those in the SARS-CoV-2 negative group were symptomatic. These proportions increased to 66.5% and 53.3%, respectively, after 3 months of the PCR testing (p<0.0001). Persistent respiratory-related symptoms were more common among adolescents in the SARS-CoV-2 positive group than among those in the SARS-CoV-2 negative group, although only loss of smell (13.5% vs. 1.4%, respectively), shortness of breath (23.4% vs. 10.4%, respectively), and chest pain (7.0% vs. 3.5%, respectively) remained significantly different after controlling for multiple comparisons (p<0.0001).

### Comments

1. Long COVID (also known as post-COVID condition or post-acute COVID syndrome) has been extensively described in adults, but there has been limited research in the pediatric population and most studies in children or adolescents have been small, only included hospitalized participants, or lacked a control group.
2. In this study that addresses many of the prior limitations in the field, the prevalence of physical and mental symptoms was higher among adolescents who tested positive for SARS-CoV-2 infection than among those who tested negative for this respiratory virus at both the time of PCR testing and 3 months after this.
3. Symptoms that persisted after SARS-CoV-2 infection involved multiple body organs and systems (e.g., respiratory, nervous, and cardiovascular systems), which suggests that optimal management of long COVID may require a multidisciplinary team of health care providers.
4. The mechanisms leading to the development of persistent symptoms following SARS-CoV-2 infection were not examined in this study and continue to be poorly understood.
5. There is a need to standardize the definition of long COVID, better understand common risk factors for this condition and its underlying pathophysiology, and improve its diagnostic evaluation and management.

## SARS-COV-2: HEALTH CARE USE FOLLOWING COVID IN THE PEDIATRIC POPULATION

Magnusson K, Skyrud KD, Suren P, Greve-Isdahl M, Stordal K, Kristoffersen DT, Telle K. **Healthcare use in 700 000 children and adolescents for six months after COVID-19: before and after register-based cohort study.** *BMJ.* Epub 2022. In press.

### Summary

This study examined health care use up to 6 months after SARS-CoV-2 infection in a population-based, non-



hospitalized cohort of children and adolescents in Norway (n=706,885). Using a national emergency preparedness register, the authors retrospectively identified 2 main groups of participants ages 1-19 years: 1) those who tested positive for SARS-CoV-2 by PCR between August 2020 and February 2021, and 2) those who tested negative for SARS-CoV-2 by PCR during the same 6-month period and had no prior history of COVID. The authors then identified monthly proportions of all cause and cause-specific health care use in primary and specialist care from 6 months before to 6 months after the PCR testing and used difference-in-difference models adjusting for potential confounders to compare groups by age. In comparison to children ages 1-5 years in the SARS-CoV-2 negative group, children ages 1-5 years in the SARS-CoV-2 positive group had increased primary care use up to 6 months after the SARS-CoV-2 testing (adjusted % relative difference [95% CI] = 339 [308-369] at 1-4 weeks, 22 [4-40] at 5-8 weeks, 26 [7-46] at 9-12 weeks, and 13 [0-26] at 13-24 weeks). The increase in primary care use was mainly due to respiratory, general, or unspecified conditions. No increase in specialist care use was noted for any age group.

#### Comments

1. The impact, severity, and persistence of long COVID (also known as post-COVID condition or post-acute COVID syndrome) in the pediatric population continues to be an important area of research.
2. In this study, preschool-aged children had an increased use of health care services up to 6 months following SARS-CoV-2 infection, which suggests that this age group may be at higher risk of long COVID.
3. The increased use in health care services noted for preschool-aged children was mainly related to primary care visits and not to subspecialty care visits, likely due to the mild and non-specific nature of symptoms associated to long COVID in young children.
4. In contrast to other studies, older children and adolescents did not have an increased long-term use of health care services after SARS-CoV-2 infection.
5. This study did not include children or adolescents who require hospitalization for SARS-CoV-2 infection and who may require prolonged subspecialty care and could have increased health care use.
6. If and how SARS-CoV-2 vaccines influence long COVID in the pediatric population remains unknown.

#### HUMAN RHINOVIRUS: BRONCHIOLITIS DUE TO HUMAN RHINOVIRUS AND CHILDHOOD ASTHMA

Dumas O, Erkkola R, Bergroth E, Hasegawa K, Mansbach JM, Piedra PA, Jartti T, Camargo CA Jr. **Severe bronchiolitis profiles and risk of asthma development in Finnish children.** *J Allergy Clin Immunol.* 2022;149(4):1281-1285 e1281.

#### Summary

This study examined the association of severe bronchiolitis profiles with the development of childhood asthma in a multi-center, prospective cohort of young children in Finland (n=408). Children ages <2 years admitted to 3 hospitals during the 2008–2010 winter seasons were enrolled and longitudinally followed to ascertain the outcome of asthma at age 4 years. Extensive clinical and laboratory markers (e.g., sociodemographic characteristics, acute symptoms, past medical history, indicators of disease severity, and results of viral testing) were collected at enrollment. In addition, the outcome of asthma at age 7 years was determined using a national social insurance database. Through latent class analyses, the authors identified 3 distinct severe bronchiolitis profiles: 1) profile “A”, characterized by human rhinovirus (HRV) infection, current wheeze during the acute illness, and a prior history of wheeze or eczema (47.1%), 2) profile “BC”, characterized by respiratory syncytial virus infection and more severe disease (37.9%), and 3) profile “D”, characterized by HRV infection and milder disease without current wheeze during the acute illness (14.9%). In multivariable logistic regression models adjusting for potential confounders, children in profile “A” had higher odds of 4- (adjusted OR=2.42, 95% CI=1.23-4.75) and 7-year (adjusted OR=3.14, 95% CI=1.33-7.42) asthma than those in profile “BC.” There were no differences in the odds of 4- or 7-year asthma between profiles “D” and “BC.”

#### Comments

1. Bronchiolitis is not a single condition but a heterogeneous entity.
2. This study extends prior findings from other studies using unsupervised clustering approaches that demonstrate that severe bronchiolitis comprises several unique phenotypes with distinct clinical and laboratory characteristics and different risks of childhood asthma.
3. Other studies from the same research group have shown that dissimilarities in patterns related to the human microbiome, host gene expression, and metabolic pathways could explain the differences between these unique severe bronchiolitis profiles.

- The finding that children in profile “BC” were more likely to be HRV-infected and had the highest risk of developing asthma, but also were more likely to have a prior history of wheeze and eczema, suggest that HRV bronchiolitis may just represent an initial severe asthma exacerbation in these children.
- Future studies will need to confirm if early-life HRV infection has a causal role on the development of childhood asthma.

#### RESPIRATORY SYNCYTIAL VIRUS: INFANT RESPIRATORY SYNCYTIAL VIRUS INFECTION AND CHILDHOOD ASTHMA

Rosas-Salazar C, Chirkova T, Gebretsadik T, Chappell JD, Peebles RS Jr., Dupont WD, Jadhao SJ, Gergen PJ, Anderson LJ, Hartert TV. **Respiratory syncytial virus during infancy and asthma during childhood.** *The Lancet*. Epub 2023. In press.

##### Summary

This study examined the association of not being infected with RSV in infancy (i.e., the first year of life) with the development of childhood asthma in a population-based, prospective cohort of participants in the United States (n=1,946). Infants were enrolled near birth and longitudinally followed to capture all RSV infections during their first RSV season and to ascertain the outcome of current asthma at age 5 years. RSV infection status in infancy (not infected vs. infected) was determined using a combination of passive and active surveillance with viral identification through molecular and serological techniques. The proportion of 5-year current asthma was lower among infants not infected with RSV than among those infected with this respiratory virus (15.8% vs. 20.8%, respectively, p=0.02). In a multivariable modified Poisson regression model adjusting for potential confounders, not being infected with RSV in infancy decreased the risk of 5-year current asthma by 26% (adjusted RR=0.74, 95% CI=0.58-0.94). In secondary analyses examining specific childhood asthma phenotypes, children not infected with RSV in infancy had a substantial lower risk of non-atopic 5-year current asthma than those infected with RSV in infancy (adjusted RR=0.52, 95% CI=0.32-0.82). The estimated proportion of 5-year current asthma cases that could be prevented by avoiding RSV infection in infancy was 15.0% (95% CI=2.2-26.8).

##### Comments

- Prior studies in the field have focused on the association of RSV bronchiolitis requiring hospitalization with childhood asthma, but this association is confounded by host genetics as there is shared genetic susceptibility between the severity

of the RSV disease and the risk of childhood asthma.

- In contrast, this study focused on the presence vs. absence of RSV infection in infancy, which the authors have previously shown is unlikely to be confounded by host genetics.
- The findings suggest a causal, age-dependent effect of RSV infection in infancy on the onset of childhood asthma (particularly on the onset of non-atopic pediatric asthma phenotypes).
- Other studies from the same research group suggest that RSV infection in infancy may lead to childhood asthma through early-life changes in the human microbiome, programming of the immune response, and disruption of the airway epithelium barrier and function.
- To definitively establish causality, the effect of interventions that prevent, delay, or decrease the severity of the initial RSV infection on the development of childhood asthma will need to be studied.

#### LOWER RESPIRATORY TRACT INFECTIONS: EARLY-LIFE LOWER RESPIRATORY TRACT INFECTIONS AND PREMATURE RESPIRATORY-RELATED ADULT MORTALITY

Allinson JP, Chaturvedi N, Wong A, Shah I, Donaldson GC, Wedzicha JA, Hardy R. **Early childhood lower respiratory tract infection and premature adult death from respiratory disease in Great Britain: a national birth cohort study.** *The Lancet*. Epub 2023. In press.

##### Summary

This study examined the association of early-life lower respiratory tract infections (LRTIs) with premature respiratory-related adult mortality in a population-based, prospective cohort of participants in the United Kingdom (n=3,589). Using a nationally representative cohort recruited at birth and followed longitudinally until age 73 years together with a centralized national mortality database, the authors evaluated if having a LRTI in the first 2 years of life (as identified by parental report) increased the risk of death from any respiratory disease between ages 26 to 73 years. In a multivariable Cox-proportional hazard model adjusting for birthweight, markers of socioeconomic status, first-hand smoking, and other potential confounders, having an early-life LRTI increased the risk of prematurely dying by respiratory disease by 93% (adjusted HR=1.93, 95% CI=1.10-3.37). The results from negative control analyses supported these findings. In secondary analyses examining possible mediators of this relationship, early-life LRTIs were associated with a decreased FEV<sub>1</sub> at age 43 years and a lower FEV<sub>1</sub> in

adulthood was associated with premature respiratory-related adult mortality. The estimated proportion of premature respiratory-related deaths that could be attributed to early-life LRTIs was 20.4% (95% CI=3.8-29.8), corresponding to 179,188 (95% CI=33,806-261,519) excess premature respiratory-related deaths in England and Wales between 1972 and 2019.

### Comments

1. This life-spanning study provides evidence of the long-term impact of early-life LRTIs and the early origins of adult lung diseases.
2. The estimates of premature respiratory-related adult mortality associated to early-life LRTIs may be substantially higher in low-income countries.
3. The study could not answer if the association of early-life LRTIs with premature respiratory-related adult mortality is truly causal or if developing an early-life LRTI is solely a marker of a genetic predisposition to poor pediatric and adult respiratory health.
4. Further research should identify risk factors for long-term complications after early-life LRTIs to enable better risk stratification, close monitoring of high-risk children, and targeted therapeutic interventions.
5. There is also a need to design interventions to prevent long-term morbidity and mortality after early-life LRTIs.

### ADENOVIRUS: RISK FACTORS FOR POST-INFECTIOUS BRONCHIOLITIS OBLITERANS FOLLOWING SEVERE ADENOVIRUS PNEUMONIA

Peng L, Liu S, Xie T, Li Y, Yang Z, Chen Y, Deng L, Huang H, Ding X, Chen M, Lin L, Wei S, Zhong L. **Construction and analysis of a nomogram prediction model for post-infectious bronchiolitis obliterans in children with adenovirus pneumonia after invasive mechanical ventilation.** *BMC Pediatr.* 2023;23(1):81.

### Summary

This study examined risk factors for the development of post-infectious bronchiolitis obliterans (PIBO) following severe adenovirus pneumonia (ADVP) in a single-center, hospitalized cohort of young children in China (n=863). Between January and December 2019, the authors identified children ages <3 years with a prior history of admission to one hospital due to ADVP and ascertained the outcome of PIBO based on persistent symptoms, physical exam findings, chest CT abnormalities, and spirometry results. Extensive clinical, laboratory, and radiological markers (e.g., sociodemographic characteristics, acute symptoms, blood and chest CT

results, indicators of disease severity, and treatments received) obtained during the initial hospitalization were retrospectively collected. The proportion of young children hospitalized with ADVP who developed PIBO was 5.3%, but this proportion was substantially higher (50.0%) among those who required invasive mechanical ventilation (IMV). In a multivariable logistic regression model including several potential predictors, requiring IMV was the strongest independent risk factor for PIBO in this population (adjusted OR=7.6, 95% CI=2.9-19.9). In a similar model restricted to young children hospitalized with ADVP requiring IMV (n=66), being a male, a longer duration of fever, a higher adenovirus load in bronchoalveolar lavage, and the presence of a fungal co-infection were all associated with higher odds of PIBO (p<0.05 for all predictors). A derived score that included these 4 predictors was successful in discriminating young children hospitalized with ADVP requiring IMV who developed PIBO from those who did not develop this condition (AUC=0.86).

### Comments

1. PIBO, although relatively rare, is associated with high morbidity and mortality and its underlying pathophysiology continues to be poorly understood.
2. In this study, requiring IMV was a strong and independent risk factor for the development of PIBO among young children with severe ADVP.
3. The study describes a predictive model that can be used to identify young children hospitalized with ADVP at high risk of developing PIBO, but this model will need further validation in other populations.
4. Based on their high risk of developing PIBO, young children with severe ADVP who require IMV should be monitored closely by pediatric pulmonologists with expertise in the diagnosis, evaluation, and management of PIBO.
5. Further research is needed to better understand the mechanisms underlying the development of PIBO and to develop interventions that can alter the natural history of this condition.

### OTHER ARTICLES OF INTEREST

#### LONG-TERM IMPACT OF SARS-COV-2 ON RESPIRATORY HEALTH

1. Stephenson T, Allin B, Nugawela MD, Rojas N, Dalrymple E, Pinto Pereira S, Soni M, Knight M, Cheung EY, Heyman I, CLoCk Consortium, Shafran R. **Long COVID (post-COVID-19 condition) in children: a modified Delphi process.** *Arch Dis Child.* 2022;107(7):674-680.

2. Pellegrino R, Chiappini E, Licari A, Galli L, Marseglia GL. **Prevalence and clinical presentation of long COVID in children: a systematic review.** *Eur J Pediatr.* 2022;181(12):3995-4009.
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4. Kikkenborg Berg S, Palm P, Nygaard U, Bundgaard H, Petersen MNS, Rosenkilde S, Thorsted AB, Ersboll AK, Thygesen LC, Nielsen SD, Vinggaard Christensen A. **Long COVID symptoms in SARS-CoV-2-positive children aged 0-14 years and matched controls in Denmark (LongCOVIDKidsDK): a national, cross-sectional study.** *Lancet Child Adolesc Health.* 2022;6(9):614-623.
5. Atchison CJ, Whitaker M, Donnelly CA, Chadeau-Hyam M, Riley S, Darzi A, Ashby D, Barclay W, Cooke GS, Elliott P, Ward H. **Characteristics and predictors of persistent symptoms post-COVID-19 in children and young people: a large community cross-sectional study in England.** *Arch Dis Child.* Epub 2023. In press.
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#### LONG-TERM IMPACT OF HUMAN RHINOVIRUS ON RESPIRATORY HEALTH

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#### LONG-TERM IMPACT OF ADENOVIRUS ON RESPIRATORY HEALTH

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## Wellness and Resilience

Heather De Keyser, MD, MSCR

University of Colorado School of Medicine and Children's Hospital Colorado

Department of Pediatric Pulmonology

Aurora, CO

### INCREASES IN BURNOUT AND WORK LIFE INTEGRATION CONCERNS IN US PHYSICIANS IN THE FIRST 2 YEARS OF THE COVID PANDEMIC

Shanafelt TD, West CP, Dyrbye LN, Trockel M, Tutty M, Wang H, Carlasare LE, Sinsky C. **Changes in Burnout and Satisfaction With Work-Life Integration in Physicians During the First 2 Years of the COVID-19 Pandemic.** *Mayo Clin Proc* 2022; 97: 2248-2258.

#### Summary

Authors surveyed 2440 physicians and compared scores with surveys obtained in previous years. There were significant increases in mean emotional exhaustion scores (increased 38%), and mean depersonalization scores (increased 61%) from 2020. Sixty three percent of physicians had at least 1 marker of burnout, significantly increased from previous years. Only 30% of participants surveyed were satisfied with work-life integration in 2021, compared to 46% in 2020. Additionally, though mean depression scores increased over the period studied, they did not rise to the same extent as the dissatisfaction with work-life integration, indicating that "the increase in physician distress was overwhelmingly work related."

#### Comments

1. Burnout has increased significantly, and satisfaction with work-life integration has decreased significantly since the COVID-19 pandemic started.
2. The OR for burnout among women physicians was 2.02 relative to men in 2021 (compared with 1.27 in 2020), indicating an increased risk for burnout and work/life integration challenges in women that has worsened post-pandemic.
3. Given the association of burnout with several negative implications including turnover, errors and increased healthcare costs, these findings have severe implications on the system as a whole.
4. The COVID-19 global pandemic has worsened pre-existing challenges with burnout and wellbeing among physicians.

### ASSOCIATION BETWEEN BURNOUT AND NEGATIVE EXPERIENCES WITH PATIENTS AND FAMILIES

Dyrbye LN, West CP, Sinsky CA, Trockel M, Tutty M, Satele D, Carlasare L, Shanafelt T. **Physicians' Experiences With Mistreatment and Discrimination by Patients, Families, and Visitors and Association With Burnout.** *JAMA Netw Open* 2022; 5: e2213080.

#### Summary

While it is known that burnout is prevalent among physicians, less is known about how negative experiences with patients and their families may be associated with burnout risk. This study sought to evaluate the association of burnout with experiences of mistreatment or discrimination by patients and family members/visitors by certain physician characteristics. 6512 physicians responded to a survey (39.4% female, 70.5% non-Hispanic white). Negative experiences were unfortunately common, including racially and/or ethnically offensive remarks (29.4%), offensive sexist remarks (28.7%) and unwanted sexual advances (20.5%) being the most common. A staggering 1 in 5 physicians reported a refusal to allow them to provide care. Nearly 15% were subjected to some kind of physical violence. Female and ethnic and/or racial minority physicians experienced the highest rates of mistreatment. Mistreatment was associated with higher odds of burnout.

#### Comments

1. Both verbal and physical mistreatment of physicians is shockingly prevalent.
2. More than half of racial and/or ethnic minority physicians had experienced offensive racial and/or ethnic remarks in the last year.
3. Intersectionality is important, as within most racial and/or ethnic groups, female physicians experienced the highest burden of offensive remarks.
4. Organizations must make the protection of physicians from mistreatment a top priority to not only protect physician wellbeing, but to protect the system from all the harms known to occur when burnout levels rise.

## EFFECT OF IMPOSTERISM ON WELLBEING OF TRAINEES

Liu RQ, Davidson J, Van Hooren TA, Van Koughnett JAM, Jones S, Ott MC. **Impostorism and anxiety contribute to burnout among resident physicians.** *Med Teach* 2022; 44: 758-764.

### Summary

Trainees are a population that may be particularly prone to issues related to wellbeing. This study sought to elucidate if there was an association between feelings of imposterism and self-doubt with burnout and anxiety among trainees in family medicine, pediatrics, anesthesiology and general surgery. Of the 269 residents who responded to the survey, 62.7% displayed characteristics of imposterism, with female learners at highest risk. Twenty three percent met the criteria for burnout. Imposterism was associated with anxiety and burnout.

### Comments

1. Imposterism is prevalent among trainees, and rates may be highest in female trainees.
2. The authors posit that imposterism impairs the trainee's ability to develop a sense of accomplishment or share in the "credit" for positive patient outcomes.
3. As imposterism is independently related to both anxiety and burnout levels in this study, program initiatives to address feelings of imposterism may be beneficial both to learner wellbeing and patient outcomes.
4. Participants surveyed stated that speaking with mentors who shared that they also had feelings of self-doubt was instrumental in overcoming these feelings.

## HEALTH AND WELLNESS FOR PEDIATRIC PHYSICIANS: A CLINICAL REPORT FROM THE AMERICAN ACADEMY OF PEDIATRICS

McClafferty HH, Hubbard DK, Foradori D, Brown ML, Profit J, Tawfik DS. **Physician Health and Wellness.** *Pediatrics* 2022; 150.

### Summary

This clinical report recognizes the impact of physician health and wellness as a topic relevant to all pediatricians. The authors describe an increase in burnout rates for both general and specialist pediatricians to just below 50% in 2014. Physicians (especially trainee and mid-career physicians) have higher rates of burnout than the general population, and additionally most pediatricians are women, and

women have higher rates of burnout (as much as 60% higher compared to male counterparts). While there is national emphasis on physician wellbeing and a recognition that burnout is unnecessarily high across medical specialties, there is also recognition that the problem is worsening through pandemic and post-pandemic times. Drivers of burnout include organizational (leadership accountability vacuums, inefficient workflows, lack of representation, value misalignment and lack of support), technology/clerical (primarily electronic health records and documentation concerns), and individual factors. Mental health concerns are unfortunately still stigmatized, and physicians are at higher risk of suicide than the general population.

### Comments

1. There are several demographic factors that are associated with increased risk of burnout, including age less than 55, private practice, mid-career stage, female, having a child less than 21, and having a nonphysician spouse or partner in healthcare.
2. Aggression, sexism, racism and discrimination may all contribute to higher rates of burnout in racial and/or ethnic minority groups.
3. There is little data on effective interventions to improve wellbeing at the individual and organizational levels, but positive psychology interventions, mindfulness/compassion interventions and professional coaching have shown promise.

## INTERVENTIONS BASED IN POSITIVE PSYCHOLOGY SHOW PROMISE FOR HEALTHCARE WORKERS IN PEDIATRICS

Profit J, Adair KC, Cui X, Mitchell B, Brandon D, Tawfik DS, Rigdon J, Gould JB, Lee HC, Timpson WL, McCaffrey MJ, Davis AS, Pammi M, Matthews M, Stark AR, Papile LA, Thomas E, Cotten M, Khan A, Sexton JB. **Randomized controlled trial of the "WISER" intervention to reduce healthcare worker burnout.** *J Perinatol* 2021; 41: 2225-2234.

### Summary

Utilization of positive psychology principles is one potential way to improve well-being in healthcare workers (HCW). This study evaluated HCWs (mostly nurses in the NICU) before and after completing an online positive psychology-based curriculum. The web-based tool consisted of 6 guided modules of about 20 min each, covering: gratitude, three good things, awe, random acts of kindness, identifying and using

signature strengths, and relationship resilience. Participants were compared to waitlist controls, and burnout was measured using a derivative of the Maslach Burnout Inventory. Two hundred seventy-six providers completed the intervention and a 1-month post survey, and 224 completed the 6-month post survey. This study found that the intervention improved emotional exhaustion, work life integration, and measures of depression both at 1 and 6 months post-intervention.

### Comments

1. Positive psychological interventions may be one way in which organizations can support the wellbeing of their employees.
2. This intervention was given in 2 ways, one module per month for 6 months, and a condensed 28-day program: though results were similar, there was more waning of effect in the condensed group.
3. Trials of wellbeing interventions are plagued by selection bias (those already interested in improving wellbeing may be more likely to enroll).
4. Ongoing work should include ways to include all HCWs and to minimize additional time burden required for completing wellbeing work.

### PEER-LED INTERVENTIONS MAY HELP TO ENHANCE PROFESSIONAL FULFILLMENT

Trockel MT, Menon NK, Makowski MS, Wen LY, Roberts R, Bohman BD, Shanafelt TD. **IMPACT: Evaluation of a Controlled Organizational Intervention Using Influential Peers to Promote Professional Fulfillment.** *Mayo Clin Proc* 2023; 98: 75-87.

### Summary

This study used popular opinion leaders (group members that were identified by their peers as someone who was respected by the group) to conduct sessions with their colleagues to encourage evidence-based wellness practices (including specific gratitude, cognitive reframing, and mindfulness). 265 physicians were randomized by clinic to receive either immediate intervention or delayed intervention (control). Pre/post surveys demonstrated an improvement in measures of professional fulfillment and gratitude, and decreased odds of intent to leave the practice.

### Comments

1. Overall engagement was reasonably high, with 75% of physicians attending at least one of the sessions.
2. The cost-benefit ratio if clinical attrition was lessened could be substantial.

3. Continued work is needed to find ways to engage participants while not feeling like they are adding wellness work as another work-related burden.
4. Engaging popular opinion leaders (determined by peers) may be a good strategy for encouraging participation in wellness related activities.

### OTHER ARTICLES OF INTEREST

Walker ZW, Appah M, Aban I, Lindeman BM, Elopre LE, Goepfert AR, Hill SV. **Assessment of lesbian, gay, bisexual, transgender, and questioning experiences within a large southeast training program.** *Med Educ Online* 2022; 27: 2093692.

Mann A, Fainstad T, Shah P, Dieujuste N, Thurmon K, Dunbar K, Jones C. **"We're all going through it": impact of an online group coaching program for medical trainees: a qualitative analysis.** *BMC Med Educ* 2022; 22: 675.

Duva IM, Higgins MK, Baird M, Lawson D, Murphy JR, Grabbe L. **Practical resiliency training for healthcare workers during COVID-19: results from a Randomized controlled trial testing the Community Resiliency Model for well-being support.** *BMJ Open Qual* 2022; 11.

**Addressing Health Worker Burnout: Us Surgeon General's Advisory On Building A Thriving Health Workforce**

<https://www.hhs.gov/sites/default/files/health-worker-wellbeing-advisory.pdf>

Belfer J, Feld L, Jan S, Fishbein J, Young JQ, Barone S. **The Effect of the COVID-19 Pandemic on Pediatric Physician Wellness: A Cross-Sectional Study.** *Int J Environ Res Public Health* 2022; 19.

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Ganesh Kumar N, Khouri AN, Olinger TA, Sen S, Drolet BC, Vercler CJ. **Managing Resident Mental Health: Prevention is Better than Cure.** *J Surg Educ* 2023; 80: 11-14.



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Hill JE, Harris C, Danielle LC, Boland P, Doherty AJ, Benedetto V, Gita BE, Clegg AJ. **The prevalence of mental health conditions in healthcare workers during and after a pandemic: Systematic review and meta-analysis.** *J Adv Nurs* 2022; 78: 1551-1573.

Meredith LS, Bouskill K, Chang J, Larkin J, Motala A, Hempel S. **Predictors of burnout among US healthcare providers: a systematic review.** *BMJ Open* 2022; 12: e054243.

Murthy VH. **Confronting Health Worker Burnout and Well-Being.** *The New England journal of medicine* 2022; 387: 577-579.

Rotenstein LS, Berwick DM, Cassel CK. **Addressing Well-being Throughout the Health Care Workforce: The Next Imperative.** *JAMA.* 2022 Aug 9;328(6):521-522

# Global Respiratory Health in the Setting of Climate Change

Dwan Vilcins, PhD, MPH

The University of Queensland  
Child Health Research Centre  
Brisbane, Queensland, Australia

## IMPROVED INDOOR AIR QUALITY DURING DESERT DUST STORMS: THE IMPACT OF THE MEDEA EXPOSURE-REDUCTION STRATEGIES

Achilleos S, Michanikou A, Kouis P, Papatheodorou SI, Panayiotou AG, Kinni P, Mihalopoulos N, Kalivitis N, Kouvarakis G, Galanakis E, Michailidi E, Tymvios F, Chrysanthou A, Neophytou M, Mouzourides P, Savvides C, Vasiliadou E, Papasavvas I, Christophides T, Nicolaou R, Avraamides P, Kang CM, Middleton N, Koutrakis P, Yiallourous PK. **Improved indoor air quality during desert dust storms: The impact of the MEDEA exposure-reduction strategies.** *Sci Total Environ.* 2023 Mar 10;863:160973. Doi: 10.1016/j.scitotenv.2022.160973. Epub 2022 Dec 17. PMID: 36539092.

### Summary

Desert dust storms (DDS) are a natural phenomenon that create high levels of particle air pollution, particularly in the area spanning north Africa, the Middle East, and East Asia. Climate change has been linked to DDS. While public health messages exist to reduce exposure, these have not been tested. This paper reports the results of an intervention study aimed at reducing the amount of particulate matter (PM) entering homes and schools. 21 houses and 18 schools were randomized into one of three arms: a control arm (no intervention), interventions to reduce outdoor exposure (reduction in outside time) or interventions to reduce indoor air pollution (HEPA air filters, closing doors/windows, sealing cracks). The results showed no differences between DDS days and non-DDS for total PM, but significant differences for several sub-species. Examining the effect of intervention showed a 43% to 32% reduction of particle infiltration in homes for indoor vs control intervention arms, and indoor vs outdoor intervention arms, respectively. The interventions were less successful in schools. This paper provides important evidence that household level interventions can be useful in reducing exposure to particle pollution from DDS.

### Comments

1. Desert dust storms contribute particle pollution in several regions globally and are expected to increase with climate change.

2. This paper found that public health messages are effective in reducing exposure, with interventions in homes being more effective than reducing outdoor exposure or interventions in schools.
3. Public health messages that are aimed at reducing exposure are largely understudied.
4. The paper highlights a tension between infectious disease and environmental exposure strategies in time of changing climate.

## THE OZONE CLIMATE PENALTY, NAAQS ATTAINMENT, AND HEALTH EQUITY ALONG THE COLORADO FRONT RANGE

Crooks JL, Licker R, Hollis AL, Ekwurzel B. **The ozone climate penalty, NAAQS attainment, and health equity along the Colorado Front Range.** *J Expo Sci Environ Epidemiol.* 2022 Jul;32(4):545-553. doi: 10.1038/s41370-021-00375-9. Epub 2021 Sep 10. PMID: 34504294; PMCID: PMC9349035.

### Summary

Ground level ozone is an air pollutant with a significant impact on respiratory health. Despite the EPA tightening ozone restrictions, and efforts in some areas to reduce ozone precursors, exceedances still occur. This paper reports on a climate penalty of ozone: the amount of additional ozone already being created due to climate change. The authors estimated ozone values for the 1950s, based on current factors influencing ozone development but with 1950s meteorological conditions. They then estimated the 'climate penalty' – the difference between the observed ozone levels experienced in 2010 and the ozone level expected with 1950s meteorological conditions. Daily maximum temperature was around 2°C higher and wind speed was lower in the 2010s, compared with 1950s. The climate penalty was evident across virtually all geographical regions, ranging from 0.5 ppb to 1 ppb. The climate penalty contributes to exceedances of the air quality standards and increases the required intervention time to meet them by two years. Several health and sociodemographic variables are associated with the climate penalty; the most notable being asthma, where higher levels of asthma in a county are associated with having a higher ozone climate penalty (0.010 ppb).

### Comments

1. This novel method of estimating a climate penalty shows that climate change is already impacting on air quality.
2. Activities to reduce precursors of ozone are likely to be less effective as our climate changes.
3. There is a significant association between health equity measures and the climate penalty for ozone, most notably for percentage of population with asthma.
4. Climate change action can reduce ozone through two mechanisms; reducing precursors and through slowing climate change.

### WHEN THE FLOOD PASSES, DOES HEALTH RETURN? A SHORT PANEL EXAMINING WATER AND FOOD INSECURITY, NUTRITION, AND DISEASE AFTER AN EXTREME FLOOD IN LOWLAND BOLIVIA

Rosinger AY, Rosinger K, Barnhart K, Todd M, Hamilton T, Arias Cuellar K, Nate D. **When the flood passes, does health return? A short panel examining water and food insecurity, nutrition, and disease after an extreme flood in lowland Bolivia.** *Am J Hum Biol.* 2023 Jan;35(1):e23806. doi: 10.1002/ajhb.23806. Epub 2022 Sep 27. PMID: 36165503.

### Summary

Flooding is one of the most frequent effects of extreme climatic conditions. This paper reports on a field study conducted with the Tsimane', a population of forager-horticulturalists in Bolivia. The goal of the study was to examine food and nutrition security but just prior to fieldwork a major flood event occurred. This paper reports on water, nutrition and health status in the period immediately following the flood event (end of flood) and two months post-flood. Water insecurity was highest at the end of the flood, while food insecurity remained high at the post-flood period. Blood pressure, used as a marker of stress, was lower in the post-flood period. Adults showed lower values on a range of anthropometric measures post-flood, but children maintained their nutritional status. The probability of diarrhea decreased in the post flood period, however the odds of cough was higher at the post-flood period for both adults and children. Overall, the paper reports the negative effects of floods linger for months after the acute effect. Notably, respiratory health appears to experience a lagged effect, where the flood is associated with a delayed increase in the odds of respiratory impacts.

### Comments

1. Respiratory effects post-flood has a lagged effect and thus persist longer than water insecurity and diarrhea
2. There is a need to focus on respiratory effects in long term studies of natural disasters.
3. Natural disasters represent a compounding of risks, physical safety, declines in air quality, nutrition and water insecurity and mental health effects, and these compounded risks may influence respiratory health.
4. Natural disasters, such as floods, disproportionately affect the most vulnerable populations.

### ASSESSMENT OF THE HEALTH BENEFITS TO CHILDREN OF A TRANSPORTATION CLIMATE POLICY IN NEW YORK CITY

Coomes KE, Buonocore JJ, Levy JJ, Arter C, Arunachalam S, Buckley L, Berberian A, Gunasti J, Perera F.

**Assessment of the health benefits to children of a transportation climate policy in New York City.** *Environ Res.* 2022 Dec;215(Pt 3):114165. doi: 10.1016/j.envres.2022.114165. Epub 2022 Sep 7. PMID: 36087775.

### Summary

The Transportation and Climate Initiative (TCI) was a cap and invest program which aimed to reduce carbon emissions from the transportation sector. The TCI proposed a cap on CO<sub>2</sub> emissions (20%, 22% or 25% reduction) from fuel suppliers. Suppliers could purchase emission allowances with the money invested into one of three clean transportation options: improving public transport, electrifying vehicles and switching to cleaner fuels, or a hybrid model. This paper reports the benefits to children's health measured as the number of cases avoided from the following child outcomes: neonatal outcomes (infant mortality, preterm birth, low birth weight), asthma outcomes (incidence, exacerbations, emergency department presentation and hospital admissions), lower respiratory conditions (infections, symptoms, and acute bronchitis), and autism spectrum disorders. The authors report that in each of the programs, significant reductions in adverse health outcomes were present, with a doubling of the number of cases prevented as the cap on emissions increased. Respiratory conditions saw the most benefits. Under the best model these reductions would lead to a \$USD22 million saving. The best performing model was a 25% reduction in CO<sub>2</sub> and investment in public transport. Further, the benefits were highest in communities with higher levels of disadvantage.

## Comments

1. A reduction in PM<sub>2.5</sub> and NO<sub>2</sub>, as a result of the TCI, was associated with a sizable reduction in cases of respiratory conditions, more so than birth outcomes (except for PTB) and autism spectrum disorders.
2. Each increase in CO<sub>2</sub> emissions cap was associated with an approximate doubling of the health gains.
3. Investments into diversified programs that invest in public transport and active mobility gives best benefit to child health and should be prioritized by policy makers.
4. Estimates of the health and cost savings presented in this paper are likely underestimated, as they do not take into account long term health effects.
5. The most benefit was found in communities that experience higher poverty and have a greater proportion of Black residents, suggesting a role of TCI in improving health equity.

### CLIMATE ADVOCACY AMONG ITALIAN PEDIATRIC PULMONOLOGISTS: A NATIONAL SURVEY ON THE EFFECTS OF CLIMATE CHANGE ON RESPIRATORY ALLERGIES

Lauletta M, Moisé E, La Grutta S, Cilluffo G, Piacentini G, Ferrante G, Peroni DG, Di Cicco M. **Climate advocacy among Italian pediatric pulmonologists: A national survey on the effects of climate change on respiratory allergies.** *Pediatr Pulmonol.* 2022 Apr;57(4):862-870. doi: 10.1002/ppul.25842. Epub 2022 Jan 31. PMID: 35060364; PMCID: PMC9303178.

#### Summary

Climate change represents a risk to children, who are uniquely vulnerable to the effects of a changing climate. This paper reports the findings of a survey of members of the Italian Pediatric Respiratory Society. The 21-question survey consisted of questions relating to climate change knowledge, concerns, clinical presentation changes, and demographics. Those who returned surveys were more likely to be female, academic pediatricians, aged 30-39 years, and concerned about climate change, which may not be representative of the society. 91% of respondents reported an increase in allergic respiratory diseases cases. Latent class analysis divided respondents into good vs poor knowledge of the health impacts of climate change (40% and 60%, respectively). Respondents in the good knowledge category were more likely to be older, have more work experience and report an increase in the number of children with pollen allergy. Only 51% of respondents knew of thunderstorm asthma. Overall, this paper finds that pediatric respiratory physicians are interested in climate change and are seeing some level of increase in

the number of patients receiving care for climate related respiratory health outcomes. There is a need for greater educational opportunities to be provided to pediatric respiratory health providers.

## Comments

1. The proportion of respondents rated as having poor knowledge of climate change, whilst also having a high level of concern, suggests more training and information needs to be made available to respiratory physicians.
2. Pediatric respiratory health providers are overwhelmingly interested in the topic of climate change and view it as a significant health risk.
3. Pediatricians should become engaged in strategies to mitigate climate change and its health effects.

### WILDFIRE SMOKE EXPOSURE IS ASSOCIATED WITH ADVERSE RESPIRATORY EVENTS UNDER GENERAL ANESTHESIA IN AT-RISK PEDIATRIC PATIENTS

Marsh BJ, Kolodzie K, Robinowitz D, Jacobson A, Ferschl M. **Wildfire Smoke Exposure Is Associated with Adverse Respiratory Events under General Anesthesia in At-risk Pediatric Patients.** *Anesthesiology.* 2022 Nov 1;137(5):543-554. doi: 10.1097/ALN.0000000000004344. PMID: 35950818.

#### Summary

Children are susceptible to adverse respiratory events while under general anesthesia. Several risk factors are well characterized, such as age, prematurity, reactive airway disease and obesity, among others. Air pollution from bushfires is toxic and a respiratory irritant, however its role in adverse respiratory events during anesthesia for children has not previously been studied. This paper reports the results of a study of  $n=625$  children undergoing general anesthesia at the University of California. The included children were booked for surgery during one of two time periods: within two weeks of a major wildfire event (exposed  $n=331$ ) or a similar period prior to the wildfire event (control  $n=294$ ). The wildfire event period was defined by the air quality index for particulate matter and/or ozone being greater than 100. There was no significant relationship between wildfire smoke exposure prior to anesthesia and adverse respiratory outcomes in the main analysis. However, when stratifying to children with a history of reactive airway disease an increase in the risk of adverse events was seen. When stratifying by preterm birth status, there was a trend towards higher risk for children born preterm, which did not reach statistical significance.

## Comments

1. Wildfire smoke is toxic, and exposures tend to occur at high level compared with ambient air pollution.
2. Children with a history of reactive airway disease may have a higher risk of adverse respiratory outcomes during general anesthesia following acute exposure to wildfire smoke.
3. Medical professionals should assess this risk and consider whether surgery should be delayed for non-essential elective surgeries.
4. More research with a larger sample is required to further test the potential risk for children born preterm.

## OTHER ARTICLES OF INTEREST

Kouis P, Michanikou A, Galanakis E, Michaelidou E, Dimitriou H, Perez J, Kinni P, Achilleos S, Revvas E, Stamatelatos G, Zacharatos H, Savvides C, Vasiliadou E, Kalivitis N, Chrysanthou A, Tymvios F, Papatheodorou SI, Koutrakis P, Yiallouros PK. **Responses of schoolchildren with asthma to recommendations to reduce desert dust exposure: Results from the LIFE-MEDEA intervention project using wearable technology.** *Sci Total Environ.* 2023 Feb 20;860:160518. doi: 10.1016/j.scitotenv.2022.160518. Epub 2022 Nov 26. PMID: 36573449.

Li J, Cai YS, Kelly FJ, Wooster MJ, Han Y, Zheng Y, Guan T, Li P, Zhu T, Xue T. **Landscape fire smoke enhances the association between fine particulate matter exposure and acute respiratory infection among children under 5 years of age: Findings of a case-crossover study for 48 low- and middle-income countries.** *Environ Int.* 2023 Jan;171:107665. doi: 10.1016/j.envint.2022.107665. Epub 2022 Nov 26. PMID: 36493611.

Landwehr KR, Hillas J, Mead-Hunter R, King A, O'Leary RA, Kicic A, Mullins BJ, Larcombe AN; WAERP. **Biodiesel feedstock determines exhaust toxicity in 20% biodiesel: 80% mineral diesel blends.** *Chemosphere.* 2023 Jan;310:136873. doi: 10.1016/j.chemosphere.2022.136873. Epub 2022 Oct 14. PMID: 36252896.

Oh JW. **Pollen Allergy in a Changing Planetary Environment.** *Allergy Asthma Immunol Res.* 2022 Mar;14(2):168-181. doi: 10.4168/aaair.2022.14.2.168. PMID: 35255535; PMCID: PMC8914612.