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Effect of PM2.5 Exposure among Children with Asthma: A Systematic Review

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Abstract
Introduction: Particulate matter (PM), which encompasses tiny particles (PM2.5) and inhalable coarse particles (PM10), is a significant environmental issue that carries potential health consequences, particularly for children, including those who have asthma. This systematic review aims to examine the association between exposure to PM2.5 and the exacerbation of childhood asthma, focusing on publications published between 2018 and 2023. Methods: A comprehensive PubMed search retrieved 147 records, leading to the selection of 11 articles for full-text assessment. Subsequently, four studies meeting the criteria were included in this review, following a meticulous selection process. These studies were rigorously assessed for methodology, study design, and key findings. Results: The chosen studies' findings indicate a negative correlation between short-term PM2.5 exposure and a range of lung function indicators in children diagnosed with asthma. This suggests that prenatal PM2.5 exposure may have enduring effects on respiratory health. Discussion: Childhood asthma, marked by complex pathophysiology involving chronic inflammation and hyperresponsive airways, is indeed influenced by PM2.5 exposure, underlining a multifaceted challenge for public health. Conclusion: This systematic review underscores the importance of addressing environmental PM2.5 as a critical public health concern, particularly for children with asthma. Although the studies in this analysis offer valuable insights, they also underscore the need for additional research to understand the intricate link between exposure to PM2.5 and the worsening of pediatric asthma.

Keywords: PM2.5, Exposure, Children, Asthma, Respiratory

1. Introduction

Particulate matter (PM) encompasses many components, including minuscule solid particles and tiny liquid droplets inside the Earth's atmosphere. The droplets or particles comprise several chemical compositions varying according to the emissions' source (Nevada Department of Environmental Protection, n.d.). Particle pollution is classified into two categories by the United States Environmental Protection Agency (USEPA) (Nevada Department of Environmental Protection, n.d.). “Fine particles,” which include smoke and haze, have a diameter of no more than 2.5 microns. Another name for fine particles is PM2.5. Particles can be emitted into the atmosphere through two primary pathways: direct release from forest fires and indirect release through the atmospheric interactions of gases from industrial facilities, power plants, and vehicles. Because PM2.5 is so tiny, it can travel incredibly long distances while remaining suspended in the atmosphere(Garrett, 2014). Areas with high traffic and dusty industries have been observed to contain inhalable coarse particles with a diameter bigger than 2.5 microns but less than 10 microns. In this context, the inhalable coarse particles are called PM10 (Nevada Department of Environmental Protection, n.d.).

The National Ambient Air Quality Standards (NAAQS) encompass three regulatory standards specifically targeting PM-2.5: (Nevada Department of Environmental Protection, n.d.) leading standard of 12 micrograms per cubic meter annually arithmetic mean (µg/m3), (Garrett, 2014) a supplementary standard of 15 µg/m3 (annual arithmetic mean) and (Meghji et al., 2021) 24-hour average not to exceed 35 µg/m3. PM-10 has a 24-hour average of 150 µg/m3 as the primary and secondary standard (Garrett, 2014). One of the most frequent childhood ailments is asthma. Low- and middle-income nations caused 96 percent of asthma-related fatalities and 84% of disability—adjusted life-years (Meghji et al., 2021). A Japanese study found peak expiratory flow dropped with each ten µg/m3 increase in PM2.5 (PEF, changes: -2.96, 95% CI: -4.55, -1.37) (Zhou et al., 2022). An increase in PM2.5 levels was associated with a significant reduction in forced expiratory volume in 1 second (FEV1) among children diagnosed with asthma, according to the findings of a birth cohort study conducted by the Columbia Center for Children's Environmental Health (CCCEH). This connection's regression coefficient (β) was -0.15, with a 95% confidence interval from -0.29 to -0.01 (Zhou et al., 2022).

The relationship between PM2.5 and pediatric asthma is complex and has multiple dimensions. PM2.5 refers to diminutive particulate matter suspended in the air, characterized by a diameter of 2.5 micrometers or smaller. PM2.5 particles possess a size that enables them to infiltrate the respiratory system profoundly. Upon inhalation, these particles have the potential to incite an inflammatory reaction. The presence of inflammation has the potential to impact the airways, rendering them more susceptible to sensitivity. Consequently, this heightened sensitivity may result in the manifestation of asthma symptoms among youngsters who possess a predisposition to this particular ailment (Sun et al., 2020). This contention is supported by an abundance of scientific research studies that have established a positive correlation between increased PM2.5 exposure and a higher prevalence of asthma in children. The available evidence indicates that extended exposure to PM2.5 is linked to the exacerbation of pre-existing asthma symptoms in pediatric populations (Pothirat et al., 2019).

Examining the correlation between PM2.5 and childhood asthma holds excellent significance due to the widespread prevalence and substantial impact of this public health concern. Gaining a comprehensive understanding of the function of PM2.5 in the development and worsening of asthma will facilitate the formulation of efficacious preventative measures, thereby mitigating the burden of this respiratory condition among children. Research endeavors can facilitate the identification of demographic groups that exhibit heightened susceptibility to the impacts of PM2.5 exposure. Such children possess pre-existing respiratory ailments or individuals residing in regions with elevated pollution levels. This information has the potential to advise and guide targeted actions and healthcare strategies for these specific demographic groups. In conclusion, examining the correlation between PM2.5 and childhood asthma holds significant importance in safeguarding the well-being of children, enhancing air quality, and extending our comprehension of respiratory ailments, yielding advantageous outcomes for public health.

2. Method

2.1 Search Strategy

The systematic review followed the principles outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). The utilization of the “Participants,” “Exposure,” “Comparator”, and “Outcome” (PECO) framework was employed in order to construct a precise study subject. The current systematic review sought to answer the question: "Is exposure to PM2.5 associated with asthma exacerbation in children?". Research investigating the correlation between exposure to PM2.5 and asthma in children has been documented in two prominent English databases, PubMed and Google Scholar. Our search strategy used combinations of air pollution terms ("air pollution, "particulate matter," "air pollutants") and respiratory disease terms ("asthma," "bronchitis," and “bronchiolitis”).

The PubMed search string used turned into as follows:
((children) AND ((particulate matter 2.5) OR (pm2.5))) AND ((((asthma) OR (bronchitis)) OR (bronchiolitis)) OR (lower respiratory infections [MeSH Terms]))

2.2 Eligibility criteria and study selection

The researchers applied the following inclusion criteria in order to identify and choose pertinent papers: (i) original peer-reviewed journals; (ii) published in full-text; (iii) studies published in 2017 until 2023; (iv) studies that identify objective measures of PM2.5; (v) the subject is a child with asthma. Studies were excluded if they met any of the following criteria: (i) not related to PM2.5 exposure; (ii) no quantitative results for the effects; (iii) with insufficient data.

2.3 Data extraction

In the initial search, after deleting duplicates, the first reviewer (CVA) assessed the title and abstract to ensure that the inclusion and exclusion criteria were met. To minimize bias, relevant studies were separately examined by the first and second reviewers (CVA and FNA) using Covidence (an online software for primary screening and data extraction created by the Cochrane Community) to examine the entire text of publications against the inclusion criteria. Before extracting data, CVA and FNA addressed all selected studies and unresolved issues between the two and the third reviewer, PAA. The details are shown in **Figure 1.**

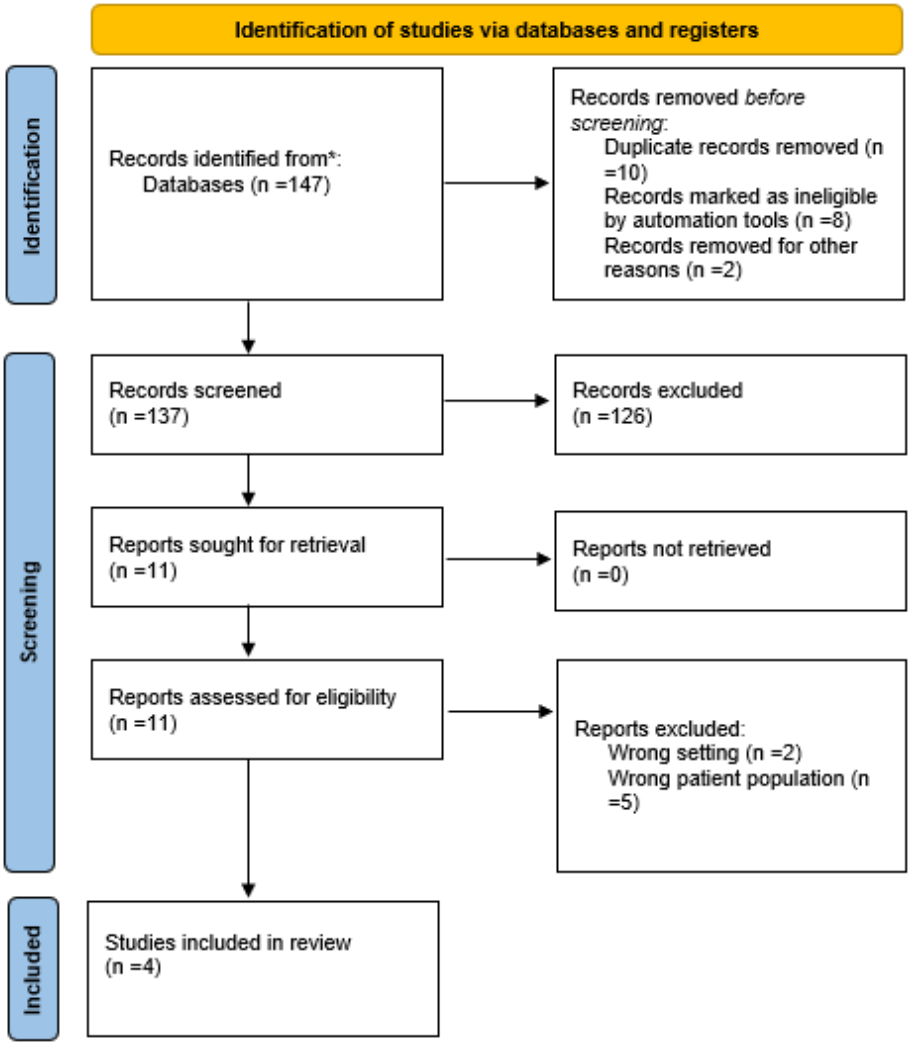

Figure 1: PRISMA flow diagram

2.4 Methodological quality assessment

Due to the absence of a validated scale, it is presently impossible to assess the quality of time-series, panel, and case-crossover study designs. Consequently, the scale proposed by Mustafi et al., derived from the reputable NOS scale, was employed to evaluate the quality of the entities above (Mustafić et al., 2012) and the Cochrane risk of bias tool (Higgins et al., 2011). Mustafi's personalized scale consisted of three items, with the allocation of "0-3" points to the respective factors as follows: The validation of depression assessment, which is classified as either 0 to indicate the absence of valid criteria or 1 to indicate the existence of valid criteria, as well as the assessment of air pollutant measurement quality (0: the measurements were not conducted on a daily basis or there was a data deficiency of more than 25%.; 1: the measurements were conducted on a daily basis, with a 25% occurrence of missing data), and the extent of confounder adjustments (0: long-term trends, season, and air temperature were not accounted for in the analysis; 1: only long-term trends, season, and air temperature were adjusted with a score of 2). A study was deemed of "high quality" if it achieved the maximum score of 5 points across all three categories. Conversely, if the study did not attain the greatest score, it was categorized as "low quality."

2.5 Risk of Bias Assessment

Furthermore, a comprehensive assessment was performed to evaluate the potential risk of bias (ROB) associated with each individual study. The notion being discussed is a relatively recent development within the field of environmental health research, and it is intricately connected to, yet distinct from, the evaluation of methodological rigor. The utilization of the Risk of Bias (ROB) assessment tool developed by the National Institutes of

Environmental Health Sciences National Toxicology Program Office of Health Assessment and Translation (OHAT) was employed to evaluate the potential bias in cohort and cross-sectional studies ("Welcome to the 2015 Annual Meeting," 2015). In light of the lack of a recognized and validated instrument for evaluating the risk of bias (ROB) in time-series and case-crossover studies, we undertook an assessment of their ROB using the OHAT tool and the University of California, San Francisco (UCSF) Navigation Guide (Lam et al., 2016). Critical factors, including confounding bias, exposure assessment, and outcome assessment, were evaluated in the selected studies utilizing the OHAT instrument and the UCSF Navigation Guide. Additional methodological criteria were taken into account, encompassing selection bias, attrition/exclusion bias, selective reporting bias, conflict of interest, and other potential causes of bias. The studies chosen for each of these domains were assessed and categorized as having a level of evidence classified as "low," "probably low," "probably high," or "high." Per the recommendations of the Navigation Guide's OHAT (Office of Health Assessment and Translation) tool, the scholarly journals utilized in our study exhibited a low degree of bias.

3. Results

3.1 Study and participant characteristics

The studies in the analysis were conducted in three countries and employed various research approaches, including cross-sectional, cross-over intervention, and cohort designs. Two studies were undertaken in the People's Republic of China, one in the United States of America, and one in the Republic of Korea. Some studies did not indicate whether they were conducted in rural or urban areas.

The study and participant characteristics were comprehensively documented. The inclusion criteria specified that all participants were children. However, for this review, only data related to children were analyzed. No research reported relationships between religion, disability, or time dependence.

3.2 Literature retrieval

The process of conducting research involves essential elements such as data analysis and reporting of the findings. All research reports need to include accurate, unbiased, thorough, and perceptive reporting of the analytical treatment of data (qualitative or quantitative). Psychologists use numerous ways to analyze data, and no methodology is universally accepted as long as it is suitable for the study questions being asked and the type of data being collected. The techniques employed must yield unambiguous, clear insights into the data and sustain their analytical demands, including robustness against assumptions that are violated.

Table 1: Summary of Selected Study Characteristic

No.	Title	Author, year (Country)	Study design	Aim of the study	Population	Results and Outcomes
1.	Early-life exposure to PM2.5 constituents and childhood asthma and wheezing: Findings from China, Children, Homes, Health Study	Zhang et al., 2022 (China)	Cross-sectional	To examine potential associations of early-life exposures to PM2.5 mass and its major chemical constituents with childhood asthma and wheezing.	30.325 preschool children aged 3-6 years	A total of 1205 children, comprising 4.0% of the sample, self-reported a medical diagnosis of asthma. The mean PM2.5 concentrations across all urban areas during the initial year following birth were recorded as 61.8±10.5 µg/m3. These values exhibited a statistically significant correlation with an

						elevated likelihood of developing asthma.
2.	Personal exposure to PM2.5 oxidative potential in association with pulmonary pathophysiologic outcomes in children with Asthma	He et al., 2021 (China)	Cross-over study	To further examine the associations of health outcomes with personal exposures to PM2.5	43 children aged 5-13 years	The mass concentration of PM2.5 is 55.7 μg/m3. Variability in PM2.5 oxidative potential drives asthmatic children's airway resistance more than PM2.5 mass exposure.
3.	Long-Term Coarse Particulate Matter Exposure Is Associated with Asthma among Children in Medicaid	Keet et al., 2017 (US)	Cohort study	To understand the relationship between long-term fine and coarse PM exposure and asthma prevalence and morbidity among children	Children aged 5 to 20 years old	Asthma diagnosis prevalence increased with coarse PM exposure (RR = 1.006; 95% CI = 1.001-1.011), hospitalizations, and emergency department visits (RR = 1.017; 95% CI = 1.001-1.033), after adjusting for fine PM.
4.	Association between Peak Expiratory Flow Rate and Exposure Level to Indoor PM2.5 in Asthmatic Children, Using Data from the Escort Intervention Study	Kim et al., 2020 (Korea)	Cross-over interventio n study	To evaluate the effects of indoor PM2.5 on children's peak expiratory flow rate (PEFR)	26 children aged between 6–12 years were diagnosed with asthma	They found a 6.5 μg/m3 difference in indoor median PM2.5 levels between control and experiment groups. Asthmatic children with lower PEFR (0.2%, 95% CI = 0.1–0.5%) significantly increased indoor PM2.5 levels, even after controlling for other variables. Our multilevel model included a random intercept for each asthmatic child.

3.3 Increased risk of asthma through exposure to particular matter

There is still a dearth of definitive evidence establishing a conclusive association between exposure to PM2.5 and the manifestation of asthma outcomes in children. In their study, Kim et al. assessed PM2.5 and its impact on asthmatic children, finding a significant association between higher levels of exposure to PM2.5 and decreased peak expiratory flow rate (PEFR) (Kim et al., 2020). However, instead of focusing on asthma, the main focus of the study was on the simultaneous occurrence of acute respiratory symptoms and a mild decrease in lung function. In their study, Zhang et al. discovered a strong correlation between early-life exposures to a combination of primary PM2.5 elements and heightened chances of asthma and wheezing. However, no transparent relationships between specific compositions and wheeze were observed within the first year of life (Zhang et al., 2022). This finding aligns with a study conducted by He et al., which demonstrated that daily personal exposure to PM2.5 is associated with an elevated oxidative potential. This elevated oxidative potential is significantly correlated with increased small, significant, and total airway resistance, heightened airway impedance, reduced lung function, and lower scores indicative of specific asthma symptoms and overall symptom severity (He et al., 2021). According to a separate study conducted by Keet et al., it has been determined that there is a correlation between heightened

asthma prevalence and morbidity among children enrolled in Medicaid and increased exposure to elevated average levels of coarse particulate matter (PM). These findings underscore the necessity for direct monitoring of coarse PM and reevaluating long-term average levels of coarse PM pollution (Keet et al., 2018). Based on the research conducted by Kim et al., a noteworthy correlation has been observed between elevated levels of indoor PM2.5 (particulate matter measuring 2.5 micrometers or smaller in diameter) on a daily or weekly basis and a reduction in peak expiratory flow rate (PEFR) among children diagnosed with asthma. The research study observed a decrease in peak expiratory flow rate (PEFR) by 0.2% (with a 95% confidence interval (CI) of 0.1 to 0.5) or by 1.2% (with a 95% CI of 0.1 to 2.7) for every 1 g/m3 rise in indoor PM2.5 concentrations (Kim et al., 2020).

4. Discussion

Asthma is a multifaceted and diverse medical condition distinguished by persistent inflammation, temporary airflow limitations, and heightened airway sensitivity (Hirose et al., 2017). Around 300 million people globally have asthma (Huo & Zhang, 2018). Exposure to PM2.5 has been linked to impaired lung function and the onset of acute asthma attacks in both children and adults, according to a growing body of epidemiological evidence. The current research conducted in Canada investigated the correlation between exposure to trace metals in PM2.5 and heightened levels of exhaled nitric oxide among a group of school-age children diagnosed with asthma (Godri Pollitt et al., 2016). Duan et al. (Duan et al., 2021) found a negative correlation between short-term exposure to PM2.5 and three respiratory health indicators: forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF). Specifically, for every 10 g/m3 increase in PM2.5 at a lag of three days, FEV1 decreased by 0.012 L, FVC decreased by 0.042 L, and PEF decreased by 0.061 L/s.

Currently, there is a widely held opinion that PM2.5 has a substantial impact on the exacerbation of asthma, particularly in children who are considered to be more vulnerable in comparison to adults (Chi et al., 2019; Fan et al., 2016). According to projections made in 2015, it was estimated that PM2.5 had contributed to a significant number of hospitalizations, ranging from 5 to 10 million, among individuals who have asthma. These hospitalizations accounted for around 4 to 9 percent of the global visits for this medical condition (Anenberg et al., 2018). Research findings have consistently indicated that PM2.5 is the sole chemical compound that has exhibited an independent correlation with emergency room visits among individuals with asthma (Hsu et al., 2020). Furthermore, a research investigation in the South Texas region unveiled a positive correlation between elevated concentrations of PM2.5 particles and an augmented probability of hospital readmissions in pediatric patients diagnosed with asthma (Baek et al., 2020). Research has indicated that individuals may have an elevated vulnerability to asthma development when exposed to small particulate matter measuring 2.5 micrometers or less (PM2.5) during their early childhood. Yan et al. (year) present findings that support the notion that prenatal exposure to PM2.5 may have significant repercussions (Yan et al., 2020), raises the risk of asthma and wheezing in children and is more strongly related to the risk of asthma in children under the age of three. A recent comprehensive study conducted across multiple cities in the United States has provided evidence indicating that exposure to PM2.5 pollution poses a significant risk to fetal lung development during the gestational period from 26 to 36 weeks. Based on the results of their study, an elevation of 2 g/m3 in environmental PM2.5 exposure was associated with a 1.29-fold rise in the likelihood of developing asthma (Hazlehurst et al., 2021).

From a research perspective, there exists a requirement for enhanced exposure assessment methods and precise asthma case definitions. Furthermore, utilizing a broader array of sampling methods for indoor and outdoor pollutants is crucial to fully understand the impact of asthma outcomes across the studies incorporated in the analysis. This is necessary as the findings of these studies were inconsistent and, in certain instances, lacked sufficient clarity in their definitions. Moreover, the existing data is insufficient to determine whether the potential elevation in asthma risk among youngsters varies by gender. Currently, there is limited comprehension of the potential danger associated with the inhalation of each substance. There were significant variations in the substances examined and the methodologies employed for their measurement across different investigations. However, the suitability of conducting a meta-analysis for this review may have been compromised not only by discrepancies in size and definitions but also by the heterogeneity in susceptibility among different individuals within the population and the diverse environmental contexts in which individuals spend their daily lives.

5. Conclusion

Individuals are subjected to a multifaceted amalgamation of biological, chemical, and physical components throughout their lifetimes. Although numerous nations have made advancements in air pollution regulation, the mitigation of environmental PM2.5 continues to be a significant area of focus. This phenomenon is associated with an ongoing increase in morbidity and mortality rates across a range of disorders. Gaining insight into the impact of PM2.5 on commonly occurring chronic respiratory conditions is an essential initial measure in preventing and identifying health issues associated with PM2.5 exposure. Further multi-regional cooperation research is necessary to help mitigate the significant health burden caused by variations in PM2.5 composition and concentration among countries and regions. This review highlights the necessity for more investigation into the impacts of indoor and outdoor air pollution on human health and well-being, employing objective measures. Additionally, it emphasizes the importance of maintaining uniformity in reporting research studies to facilitate comparability.

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References

Anenberg, S. C., Henze, D. K., Tinney, V., Kinney, P. L., Raich, W., Fann, N., Malley, C. S., Roman, H., Lamsal, L., Duncan, B., Martin, R. V., van Donkelaar, A., Brauer, M., Doherty, R., Jonson, J. E., Davila, Y., Sudo, K., & Kuylenstierna, J. C. I. (2018). Estimates of the Global Burden of Ambient PM2.5, Ozone, and NO2 on Asthma Incidence and Emergency Room Visits. *Environmental Health Perspectives*, *126*(10). https://doi.org/10.1289/EHP3766

Baek, J., Kash, B. A., Xu, X., Benden, M., Roberts, J., & Carrillo, G. (2020). Effect of Ambient Air Pollution on Hospital Readmissions among the Pediatric Asthma Patient Population in South Texas: A Case-Crossover Study. *International Journal of Environmental Research and Public Health*, *17*(13), 4846. https://doi.org/10.3390/ijerph17134846

Chi, R., Li, H., Wang, Q., Zhai, Q., Wang, D., Wu, M., Liu, Q., Wu, S., Ma, Q., Deng, F., & Guo, X. (2019). Association of emergency room visits for respiratory diseases with sources of ambient PM2.5. *Journal of Environmental Sciences*, *86*, 154–163. https://doi.org/10.1016/j.jes.2019.05.015

Duan, R., Niu, H., Yu, T., Huang, K., Cui, H., Chen, C., Yang, T., & Wang, C. (2021). Adverse effects of short-term personal exposure to fine particulate matter on the lung function of patients with chronic obstructive pulmonary disease and asthma: a longitudinal panel study in Beijing, China. *Environmental Science and Pollution Research*, *28*(34), 47463–47473. https://doi.org/10.1007/s11356-021-13811-y

Fan, J., Li, S., Fan, C., Bai, Z., & Yang, K. (2016). The impact of PM2.5 on asthma emergency department visits: a systematic review and meta-analysis. *Environmental Science and Pollution Research*, *23*(1), 843–850. https://doi.org/10.1007/s11356-015-5321-x

Garrett, M. (2014). *Encyclopedia of Transportation: Social Science and Policy*. SAGE Publications, Inc. https://doi.org/10.4135/9781483346526

Godri Pollitt, K. J., Maikawa, C. L., Wheeler, A. J., Weichenthal, S., Dobbin, N. A., Liu, L., & Goldberg, M. S. (2016). Trace metal exposure is associated with increased exhaled nitric oxide in asthmatic children. *Environmental Health*, *15*(1), 94. https://doi.org/10.1186/s12940-016-0173-5

Hazlehurst, M. F., Carroll, K. N., Loftus, C. T., Szpiro, A. A., Moore, P. E., Kaufman, J. D., Kirwa, K., LeWinn, K. Z., Bush, N. R., Sathyanarayana, S., Tylavsky, F. A., Barrett, E. S., Nguyen, R. H. N., & Karr, C. J. (2021). Maternal exposure to PM2.5 during pregnancy and asthma risk in early childhood. *Environmental Epidemiology*, *5*(2), e130. https://doi.org/10.1097/EE9.0000000000000130

He, L., Norris, C., Cui, X., Li, Z., Barkjohn, K. K., Brehmer, C., Teng, Y., Fang, L., Lin, L., Wang, Q., Zhou, X., Hong, J., Li, F., Zhang, Y., Schauer, J. J., Black, M., Bergin, M. H., & Zhang, J. J. (2021). Personal Exposure to PM 2.5 Oxidative Potential in Association with Pulmonary Pathophysiologic Outcomes in Children with Asthma. *Environmental Science & Technology*, *55*(5), 3101–3111. https://doi.org/10.1021/acs.est.0c06114

Higgins, J. P. T., Altman, D. G., Gotzsche, P. C., Juni, P., Moher, D., Oxman, A. D., Savovic, J., Schulz, K. F., Weeks, L., & Sterne, J. A. C. (2011). The Cochrane Collaboration's tool for assessing the risk of bias in randomized trials. *BMJ*, *343*(oct18 2), d5928–d5928. https://doi.org/10.1136/bmj.d5928

Hirose, K., Iwata, A., Tamachi, T., & Nakajima, H. (2017). Allergic airway inflammation: key players beyond the Th2 cell pathway. *Immunological Reviews*, *278*(1), 145–161. https://doi.org/10.1111/imr.12540

Hsu, S.-C., Chang, J.-H., Lee, C.-L., Huang, W.-C., Hsu, Y.-P., Liu, C.-T., Jean, S.-S., Huang, S.-K., & Hsu, C.-W. (2020). Differential time-lag effects of ambient PM2.5 and PM2.5-bound PAHs on asthma emergency department visits. *Environmental Science and Pollution Research*, *27*(34), 43117–43124. https://doi.org/10.1007/s11356-020-10243-y

Huo, Y., & Zhang, H.-Y. (2018). Genetic Mechanisms of Asthma and the Implications for Drug Repositioning. *Genes*, *9*(5), 237. https://doi.org/10.3390/genes9050237

Keet, C. A., Keller, J. P., & Peng, R. D. (2018). Long-Term Coarse Particulate Matter Exposure Is Associated with Asthma among Children in Medicaid. *American Journal of Respiratory and Critical Care Medicine*, *197*(6), 737–746. https://doi.org/10.1164/rccm.201706-1267OC

Kim, S., Lee, J., Park, S., Rudasingwa, G., Lee, S., Yu, S., & Lim, D. H. (2020). Association between Peak Expiratory Flow Rate and Exposure Level to Indoor PM2.5 in Asthmatic Children, Using Data from the Escort Intervention Study. *International Journal of Environmental Research and Public Health*, *17*(20), 7667. https://doi.org/10.3390/ijerph17207667

Lam, J., Sutton, P., Kalkbrenner, A., Windham, G., Halladay, A., Koustas, E., Lawler, C., Davidson, L., Daniels, N., Newschaffer, C., & Woodruff, T. (2016). A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLOS ONE*, *11*(9), e0161851. https://doi.org/10.1371/journal.pone.0161851

Meghji, J., Mortimer, K., Agusti, A., Allwood, B. W., Asher, I., Bateman, E. D., Bissell, K., Bolton, C. E., Bush, A., Celli, B., Chiang, C.-Y., Cruz, A. A., Dinh-Xuan, A.-T., El Sony, A., Fong, K. M., Fujiwara, P. I., Gaga, M., Garcia-Marcos, L., Halpin, D. M. G., … Marks, G. B. (2021). Improving lung health in low-income and middle-income countries: from challenges to solutions. *The Lancet*, *397*(10277), 928–940. https://doi.org/10.1016/S0140-6736(21)00458-X

Mustafić, H., Jabre, P., Caussin, C., Murad, M. H., Escolano, S., Tafflet, M., Périer, M.-C., Marijon, E., Vernerey, D., Empana, J.-P., & Jouven, X. (2012). Main Air Pollutants and Myocardial Infarction. *JAMA*, *307*(7), 713. https://doi.org/10.1001/jama.2012.126

Nevada Department of Environmental Protection. (n.d.). *Particulate Matter Pollution Fact Sheet*. 1–4. https://ndep.nv.gov/baqp/monitoring/docs/particulate_matter.pdf

Pothirat, C., Chaiwong, W., Liwsrisakun, C., Bumroongkit, C., Deesomchok, A., Theerakittikul, T., Limsukon, A., Tajarernmuang, P., & Phetsuk, N. (2019). Acute effects of air pollutants on daily mortality and hospitalizations due to cardiovascular and respiratory diseases. *Journal of Thoracic Disease*, *11*(7), 3070–3083. https://doi.org/10.21037/jtd.2019.07.37

Sun, L., Fu, J., Lin, S.-H., Sun, J.-L., Xia, L., Lin, C.-H., Liu, L., Zhang, C., Yang, L., Xue, P., Wang, X., Huang, S., Han, X., Chen, H.-L., Huang, M.-S., Zhang, X., Huang, S.-K., & Zhou, Y. (2020). Particulate matter of 2.5 μm or less in diameter disturbs the balance of TH17/regulatory T cells by targeting glutamate oxaloacetate transaminase 1 and hypoxia-inducible factor 1α in an asthma model. *Journal of Allergy and Clinical Immunology*, *145*(1), 402–414. https://doi.org/10.1016/j.jaci.2019.10.008

Welcome to the 2015 Annual Meeting. (2015). *Academic Emergency Medicine*, *22*(S1). https://doi.org/10.1111/acem.12656

Yan, W., Wang, X., Dong, T., Sun, M., Zhang, M., Fang, K., Chen, Y., Chen, R., Sun, Z., & Xia, Y. (2020). The impact of prenatal exposure to PM2.5 on childhood asthma and wheezing: a meta-analysis of observational studies. *Environmental Science and Pollution Research*, *27*(23), 29280–29290. https://doi.org/10.1007/s11356-020-09014-6

Zhang, Y., Yin, Z., Zhou, P., Zhang, L., Zhao, Z., Norbäck, D., Zhang, X., Lu, C., Yu, W., Wang, T., Zheng, X., Zhang, L., & Zhang, Y. (2022). Early-life exposure to PM2.5 constituents and childhood asthma and wheezing: Findings from China, Children, Homes, Health study. *Environment International*, *165*, 107297. https://doi.org/10.1016/j.envint.2022.107297

Zhou, J., Lei, R., Xu, J., Peng, L., Ye, X., Yang, D., Yang, S., Yin, Y., & Zhang, R. (2022). The Effects of Short-Term PM2.5 Exposure on Pulmonary Function among Children with Asthma—A Panel Study in Shanghai, China. *International Journal of Environmental Research and Public Health*, *19*(18), 11385. https://doi.org/10.3390/ijerph191811385