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# Association between outdoor air pollution levels and inpatient outcomes in pediatric pneumonia hospitalizations, 2007 to 2008

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## Abstract

**Objective—**Pneumonia is a leading cause of pediatric admissions. While air pollutants are associated with poor outcomes, few national studies have examined associations between pollutant levels and inpatient pediatric pneumonia outcomes. We examined the relationship between ozone ($O_3$) and fine particulate matter with a diameter ≤2.5μm ($PM_{2.5}$) and outcomes related to disease severity.

**Methods—**In this cross-sectional study, we obtained discharge data from the 2007–2008 Nationwide Inpatient Sample and pollution data from the Air Quality System. Patients ≤18 years with a principal diagnosis of pneumonia were included. Discharge data were linked to $O_3$ and $PM_{2.5}$ levels (predictors) from the patient's ZIP Code (not publicly available) from day of admission. Outcomes were mortality, intubation, length of stay (LOS), and total costs. We calculated weighted national estimates and performed multivariable analyses adjusting for sociodemographic and hospital factors.

**Results—**There were a total of 57,972 (278,871 weighted) subjects. Median $PM_{2.5}$ level was 9.5 (interquartile range [IQR] 6.8 to 13.4) μg/m$^3$. Median $O_3$ level was 35.6 (IQR 28.2 to 45.2) parts per billion. Mortality was 0.1%; 0.75% of patients were intubated. Median LOS was 2 (IQR 2 to

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4) days. Median costs were $3,089 (IQR $2,023 to $5,177). Higher levels of $PM_{2.5}$ and $O_3$ were associated with mortality, longer LOS, and higher costs. Higher $O_3$ levels were associated with increased odds of intubation.

**Conclusions—**Higher levels of $O_3$ and $PM_{2.5}$ were associated with more severe presentations of pneumonia. Future work should examine these relationships in more recent years and over a longer time period.

**Keywords**

air pollution; pneumonia; hospitalizations; disease severity; mortality

## Introduction

Pneumonia is one of the most common illnesses of childhood in the United States (US). There are approximately 2 million pediatric ambulatory visits for pneumonia in the US annually.[1] In addition, pneumonia is the most common reason for children under 18 years old to be hospitalized in the US, with hospitalization rates of nearly 170 per 100,000 annually.[2] Annual hospitalization rates for pneumonia are even higher (over 700 per 100,000) for children under 2 years old.[3] It is the second most expensive reason for pediatric admissions in the US.[4]

Several studies have documented the role of outdoor air pollutants as risk factors for pneumonia and other respiratory illnesses and subsequent poor outcomes.[5,6] Several of these pollutants, including particulate matter and ozone ($O_3$) are tracked by the Environmental Protection Agency (EPA) as part of the Air Quality Index (AQI).[7] Exposures to these pollutants cause lung dysfunction and harmful effects on the respiratory tract.[8,9] Fine particulate matter with a diameter ≤2.5μm ($PM_{2.5}$) and $O_3$ have been linked to mortality[10,11] and increased hospitalizations due to respiratory causes in studies mostly focusing on adults.[11,12]

Some pediatric studies have linked $PM_{2.5}$ and $O_3$ to poor outcomes. Higher levels of these and other air pollutants are associated with pediatric emergency department (ED) visits,[13,14] as well as increased rates of hospitalization due to respiratory diagnoses.[15,16] Few studies have examined the association between outdoor air pollutant exposures and subsequent inpatient outcomes for children admitted with pneumonia. In addition, most studies linking these pollutants to poor outcomes have focused on urban populations.[6,11,12] Nationally representative studies have linked long-term air pollution exposure to increased costs in children admitted for bronchiolitis[17] and increased costs and length of stay (LOS) with pediatric asthma hospitalizations.[18] Acute exposure to air pollution can also be harmful; one study showed that young adults subjected to $O_3$ for 6.6 hours had increased neutrophilic airway inflammation and decreased forced expiratory volume over one second.[9] Exposure to higher levels of $PM_{2.5}$ and $O_3$ over a short time frame is associated with increased mortality in adults.[19] Few studies have examined the acute effects of air pollution exposure on mortality, intubation, LOS, and costs for pediatric inpatients with pneumonia on a national level. In addition, few studies have examined the effects of specific recommended air pollutant levels[7] on these outcomes.

The purpose of this hypothesis-generating pilot study was to determine whether acute exposure to levels of $O_3$ and $PM_{2.5}$ in a patient's ZIP Code are associated with inpatient outcomes of mortality, intubation, LOS, and costs in children admitted for pneumonia between 2007 and 2008. This is the first time these relationships are being studied in this way while linking two nationally representative data sets on US hospitalizations and air quality; we aimed to gather preliminary data over this two year period to inform the design of larger future studies.

## Methods

### Study Design/Data Source

In this cross-sectional study, discharge level data were abstracted from the 2007–2008 Nationwide Inpatient Sample (NIS), the largest all-payer publicly available inpatient data set; the data set is part of the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Quality and Research. The NIS contains a stratified sample of about 20% of US hospitals; national estimates can be calculated given the complex sampling design.[20] A special discharge data analysis file was created for this study that included patient ZIP Code, a variable not publicly available but that allowed linkage to pollution data.

Air pollution data were taken from the EPA's Aerometric Information Retrieval System, now known as the Air Quality System (AQS). The data set contains estimated air pollution data collected at national, state, and local levels.[21] Levels are monitored at ~4,000 sites nationwide (43% of US population within 10 kilometers of a site, while some are >300 kilometers from a site) and are collected over a time frame ranging from hourly to every three days; Bayesian modeling is used to estimate air pollution levels within a ZIP Code.[22] Estimated $O_3$ and $PM_{2.5}$ levels for each day from 2007 to 2008 and ZIP Code in the US were then matched to ZIP Code (of the subject's residence)-day combination from the NIS by HCUP (similar linkages performed in other studies[19]) so the estimated admission date outdoor air pollution levels were known for each hospitalization. Given that the NIS and AQS are de-identified and all matching was performed by HCUP, this study was exempt from full review by the New York University School of Medicine Institutional Review Board as it did not meet the definition for human subjects research.

### Subjects

Subjects records were included if they had a principal diagnosis of pneumonia by Clinical Classification Software Code 122 (codes developed by HCUP for *International Classification of Diseases Ninth Revision, Clinical Modification* [ICD-9-CM])[23], were <18 years old, and were able to be linked to air pollution data via patient ZIP Code. There were no additional exclusion criteria.

### Measures

The primary predictor variables were $PM_{2.5}$ and $O_3$. Effect of $PM_{2.5}$ was assessed at a threshold of 12 μg/$m^3$ (the EPA's National Ambient Air Quality Standards [NAAQS] primary standard for $PM_{2.5}$ averaged over one year).[24] $O_3$ cutoffs were set at 60 parts per billion [ppb] (suggested as a possible $O_3$ standard by the Clean Air Scientific Advisory

Committee[25]) and 70 ppb (current primary and secondary standard averaged over eight hours per the NAAQS[24]). We dichotomized pollutant levels at the listed cut points. As part of a sensitivity analysis and in order to determine whether mortality and other outcomes associated with more severe disease were more likely above pollutant standards established by the EPA or were simply a function of increasing pollutant levels in general, we ran separate models in which we assessed each pollutant 1) as a log-transformed continuous variable (given a non-normal distribution) and 2) grouped as quartiles.

Outcome variables included of mortality, intubation (ICD-9-CM procedural codes: 96.04, 96.70, 96.71, 96.72), LOS, and total costs. Estimated total hospitalization costs were calculated by using NIS charge data and converting them to costs using NIS group-weighted Cost-to-Charge data files.[26]

Additional covariates, both patient-related and hospital-level, were included a priori in the analyses due to their association with outcomes for respiratory conditions[27,28] and availability in the NIS.[20] Added patient-related variables were: asthma as a secondary diagnosis (the only other respiratory-related diagnosis coded for in an adequate number of subjects in the data set to allow for analysis); race/ethnicity, combined into a single variable in the NIS; insurance type; median household income quartile by patient ZIP code; sex; and age, grouped as ages 0–1, 2–5, 6–12, and 13–18 years. Hospital-level variables were: region; rural/urban setting; teaching status; bedsize; and hospital admission timing by year, discharge quarter, and weekend vs. weekday admission. A hospital's "bedsize" is categorized as small, medium, or large and varies, per HCUP definitions, based on hospital location and teaching status.[20]

### Analysis

Descriptive statistics were used to assess demographic variables. Unadjusted regression analyses were performed including one pollutant ($O_3$ or $PM_{2.5}$ as categorized by EPA standards[24]) as a predictor in models for the outcomes of mortality and intubation (logistic regression), LOS (Poisson regression) and costs (linear regression). Multivariable regression analyses were then performed, now adjusting for other covariates described above. The same method was used with pollutants levels grouped into quartiles or as log-transformed continuous variables as predictors in the model. To evaluate whether $O_3$ and $PM_{2.5}$ were independently associated with outcomes, we first evaluated the relationship between these pollutants using Spearman correlation. We then included both pollutants as predictors for the above-mentioned outcomes (along with the other covariates) in a two-pollutant model, utilizing pollutant thresholds set by the EPA; we evaluated for possible effect modification between $O_3$ and $PM_{2.5}$ by including the product of these variables dichotomized by levels set by the EPA as an interaction term in the analysis. Missing data for covariates were reassigned to a separate missing data category. Cost data were log-transformed as distributions were skewed. After performing the linear regressions for costs, we applied Duan's method to retransform linear regression results from the log to the original scale.[29] A p value less than 0.05 was considered significant. All analyses respected the complex survey design using sample weighting in Stata SE 12.1 (StataCorp, College Station, TX). Unweighted analyses were also performed given potential bias associated with sample weighting; unweighted regression analyses mirrored results from weighted regressions and are presented in Appendix 1.

## Results

### Descriptive Results

Of the 60,137 discharges representing children ≤18 years old with a primary diagnosis of asthma, 57,972 (96.4%) could be linked to pollution data; this represents a weighted statistical sample of 278,871 discharges. Data related to patient demographics, hospital and hospitalization-level factors, patient outcomes, and air pollution levels are presented in Table 1. Most patients were <6 years old. Slightly more than half were male and had public insurance. A total of 0.1% of patients died; 0.75% were intubated. Median LOS was 2 (interquartile range [IQR] 2 to 4) days. Median total costs (2008 dollars) were $3089 (IQR $2,023 to $5,177).

Median $PM_{2.5}$ level was 9.5 (IQR 6.8 to 13.4, range 0.4 to 86.8) μg/$m^3$. Median $O_3$ level was 35.6 (IQR 28.2 to 45.2, range 0.7 to 115.3) ppb. Spearman correlation between the two pollutants was 0.055 ($p<0.001$).

Results of unadjusted analyses are presented in Appendix 2.

### Multivariable Analyses

**$PM_{2.5}$—**Table 2 represents results of regression models assessing the associations between $PM_{2.5}$ level (>12 μg/$m^3$) and mortality, intubation, LOS, and costs. Results of sensitivity analyses are presented in Appendix 3.

**Mortality:** There was an increased odds of mortality when $PM_{2.5}$ levels were >12 μg/$m^3$ (adjusted odds ratio [aOR] 1.92, 95% confidence interval [CI] 1.25 to 2.94, p=0.003). Associations were also found when $PM_{2.5}$ level was assessed as a log-transformed continuous variable and as an ordinal variable.

**Intubation:** $PM_{2.5}$ was not associated with intubation in adjusted analyses.

**LOS:** LOS was +0.05 (95% CI +0.01 to +0.10) days longer when $PM_{2.5}$ was >12 μg/$m^3$.

Similar results were seen when $PM_{2.5}$ was assessed as a log-transformed continuous variable and at levels higher than 14.2 μg/$m^3$.

**Costs:** Cost of admission was significantly higher at $PM_{2.5}$ levels >12 μg/$m^3$ (increment + $278, 95% CI +$49 to +$588, p=0.01).

**$O_3$—**Associations between $O_3$ levels as a dichotomous variable and study outcomes are presented in Table 3. Sensitivity analyses are presented in Appendix 4.

**Mortality:** When $O_3$ levels were dichotomized, increased odds of mortality were observed with levels >60 ppb (aOR 2.33, 95% CI 1.14 to 4.78, p=0.02) and >70 ppb (aOR 3.11, 1.24 to 7.79, p=0.02).

**Intubation:** Significantly higher odds of intubation were seen for patients subjected to $O_3$ >60 ppb (aOR 1.61, 95% CI 1.19 to 2.17, p=0.002). Similar results were seen when $O_3$ was assessed as a log-transformed continuous variable.

**Length of Stay:** Patients exposed to >70 ppb $O_3$ had a +0.19 (95% CI +0.05 to +0.33, p=0.008) day longer LOS.

**Costs:** Costs of admission were $820 higher at exposures >70 ppb $O_3$ (95% CI +$35 to + $1935, p=0.04).

**Two Pollutant Models—**Table 4 presents results for a 2-pollutant model, using a cutoff of $PM_{2.5}$ >12 μg/m$^3$ and $O_3$ >70 ppb. Higher $PM_{2.5}$ levels were associated with increased odds of mortality, higher costs, and longer LOS. $O_3$ levels of >70 ppb were associated with longer LOS. The interaction term between $O_3$ and $PM_{2.5}$ was not significant for any of the four outcomes.

## Discussion

In this national pilot study of pediatric admissions for pneumonia, significant associations were observed between pollutants ($PM_{2.5}$ and $O_3$) and outcomes of mortality, intubation, LOS, and costs over the two-year study period. To our knowledge, this is the first time that associations between acute exposures to these air pollutants and adverse inpatient outcomes in children admitted with pneumonia has been studied using nationally representative data sets

Mortality was more likely in patients exposed to higher levels of either pollutant. Mortality was almost twice as likely when $PM_{2.5}$ level was >12 μg/m$^3$ (the NAAQS primary yearly average standard).[24] Odds of mortality were more than double for exposures to $O_3$ levels > 60 ppb and more than triple when >70 ppb. Only $PM_{2.5}$ was associated with mortality in a two-pollutant model. The serious health effects of exposure to $PM_{2.5}$ and $O_3$ have been well documented; elevated levels have been linked to mortality in patients with pneumonia.[10,30] Much of this work has been performed in adult patients, in the outpatient setting, and sub-chronic or chronic exposure to these pollutants.[10,30]

Intubation was more likely at higher $O_3$ levels. After adjusting for other variables, odds of intubation were 60% higher when $O_3$ levels were >60 ppb, a clinically meaningful result. Intubation was not statistically more likely for $O_3$ levels >70 ppb (the current standard), although our study may not be powered to detect a difference as only 1.5% of cases were exposed to levels >70 ppb. Intubation was not independently related to $PM_{2.5}$ levels; intubation was not associated with elevated $O_3$ levels when adjusting for $PM_{2.5}$ in two-pollutant models.

Interestingly, elevated $PM_{2.5}$ levels have been associated with intensive care unit admissions,[6] another indicator of severe illness. Few studies have specifically examined the impact of air pollution on intubation, although intubation is more likely in urban areas compared to rural areas;[28] this may be a function of there being more air pollution in urban areas or that rural hospitals may be less well equipped to treat the sickest patients who might require intubation. As our definition of intubation is dependent on accuracy and completeness of coding by the physicians who saw these patients initially, future prospective work is needed to confirm these findings.

$O_3$ and $PM_{2.5}$ were also associated with increased LOS and costs. LOS was 0.19 days longer for children exposed to $O_3$ >70 ppb on their day of admission, which translates to one day added onto the LOS for every five children with this exposure. While $PM_{2.5}$ was significantly associated with LOS, these results are likely less clinically meaningful (increment of only 0.05 days) compared to the impact of $O_3$. In single-pollutant models, costs were higher in the setting of elevated levels of either pollutant, supporting associations found in other studies.[18,31] Hospitalization costs were notably $820 higher for $O_3$ levels >70 ppb; this translates into an additional $700,000 in total hospitalization costs for the 856 children (unweighted) exposed to $O_3$ >70 ppb (and an estimated $3.5 million when accounting for sample weighting). In our two-pollutant model, only $PM_{2.5}$ levels >12 μg/m$^3$ were predictive of higher costs, with an additional increment of more than $250 per hospitalization.

It is also important to examine the results of this study in the context of pollutant standards set by the EPA as part of the NAAQS. The largest impact of $PM_{2.5}$ was found using a cutoff of 12 μg/m$^3$ (primary standard for $PM_{2.5}$ averaged over one year).[24] Mortality was higher, LOS was longer, and costs were greater when $PM_{2.5}$ levels were above this threshold. This supports the results of other studies that have shown the benefits of an annual average threshold of 12 μg/m$^3$ in terms of preventing premature deaths.[32] Our study has shown the potential harm of short-term exposure to $PM_{2.5}$ above 12 μg/m$^3$ (the current annual average threshold).[24] The current EPA short-term $PM_{2.5}$ standard (8 hour average) is 35 μg/m$^3$, nearly triple the level associated with poor outcomes in our study. Future work should explore whether short-term $PM_{2.5}$ exposure above a lower threshold such as 12 μg/m$^3$ is associated with mortality and other adverse outcomes for other diagnoses (e.g., asthma, bronchiolitis) as well as if setting lower short-term thresholds would be cost effective. Analysis of $PM_{2.5}$ levels as a continuous variable also showed effects on mortality and costs, indicating overall that higher levels of this pollutant can incrementally lead to more severe illness, although few significant effects were observed when $PM_{2.5}$ levels were broken up into quartiles, and the largest associations were observed above 12 μg/m$^3$, indicating that utilizing a threshold lower than 12 μg/m$^3$ would likely not be beneficial.

Analysis of $O_3$ according to recommended thresholds provided support for use of 70 ppb as the NAAQS standard.[24] We found higher mortality, LOS, and cost outcomes at this level, providing evidence for continuing this standard, which may be a difficult standard for to achieve consistently.[33] Other work has established the benefits of utilizing 70 ppb and a stricter standard of 60 ppb in decreasing the likelihood of premature deaths.[34] We found that intubation was more likely at a threshold of 60 ppb (and not at 70 ppb, although our study may not have been powered to detect a difference). There appeared to be a dose response for the association of $O_3$ with mortality, which was twice as high above an $O_3$ threshold of 60 ppb but three times as high above 70 ppb. While the benefits of using a cut point of 70 ppb are clear, our results support clinically meaningful outcomes for mortality and intubation using the lower threshold of 60 ppb. Future work could focus on what additional benefits could come from a lower $O_3$ standard.

We also examined associations between the two pollutants in the same model with our study outcomes. While exposure to $O_3$ above 70 ppb was associated with mortality and increased costs in single pollutant models, these associations were no longer present after adding $PM_{2.5}$ to the model. The associations between $PM_{2.5}$ and study outcomes were largely unchanged after adding $O_3$ to the model. The more severe outcomes observed, therefore, are more likely a function of elevated $PM_{2.5}$ rather than $O_3$ levels. In addition, in the two-pollutant models for all four outcomes, an interaction term was not statistically significant, so the impact of these pollutants on the study outcomes are likely independent of each other. Future work should further explore the interrelationships between air pollutants and their impact on child health outcomes.

This study has limitations. These data are from 2007–2008, which were the most recent data available to be linked during our initial data matching and analysis. Future work should examine whether the preliminary associations identified in 2007–2008 are found in more recent years and over a longer time period, especially for uncommon outcomes such as mortality and intubation. We also recognize that utilizing $p<0.05$ as a cutoff for significance may lead to an increased chance of a type I error. This was a hypothesis generating study meant to lay the groundwork for larger future studies covering a larger number of years. Our selection of cases of pneumonia, as well as the ability to account for other relevant diagnoses in our analyses, was dependent on accurate physician diagnosis and documentation in the medical record. Missing data can be a problem in any large retrospective study using administrative data. Only 3.6% of otherwise eligible cases in the NIS were missing pollution data and were therefore excluded. In addition, nearly 25% of cases were missing data for race/ethnicity. Many states did not report race/ethnicity data to the NIS in 2007–2008.[20] While missing race/ethnicity data was not associated with any of the outcome studied (data not shown), it is possible that the presence of any missing data may have implications on the conclusions drawn. It is possible that the sample may not be fully nationally representative despite the large national sample frame. In addition to air pollution, several other factors in our analyses were associated with adverse outcomes (data not shown); for example, mortality was more likely in children who were older, lacked a diagnosis of asthma, and those at larger teaching hospitals. These variables, as well as other factors not controlled for in our study, including presence of other (outdoor or indoor) pollutants, past medical history, or vaccination status, should be examined in future studies. We also appreciate the potential for ecological fallacy in our analysis. Our study examined the effect of $O_3$ and $PM_{2.5}$ on outcomes for children sick enough to be admitted to the hospital for pneumonia and does not reflect pollutants' effect on admission rates, ED visit rates, or other pre-admission outcomes, nor does it assess associations with outcomes for other diagnoses. Finally, while pollution data are linked to patient home ZIP Code, we cannot guarantee that patients were necessarily present in their ZIP Code on the day of admission.

In conclusion, our large, nationally representative study found that among children admitted to the hospital with pneumonia, higher levels of outdoor air pollutants ($PM_{2.5}$ and $O_3$) were associated with inpatient mortality and other indicators of more severe inpatient disease. Worse outcomes were seen with short-term (one day) estimated $PM_{2.5}$ level exposures over 12 μg/$m^3$, the current long-term (annual) average NAAQS standard; a lower short-term standard (currently 35 μg/$m^3$) would likely be beneficial. Future work should also further explore the value of utilizing a lower $O_3$ standard (e.g., 60 ppb compared to the current standard of 70 ppb) given our study's likely clinically meaningful results at the lower threshold; potential harm associated with loosening of $O_3$ standards (a topic of recent discussion[35]) should also be evaluated. The deleterious effects of the air pollutants studied may be even worse in certain subgroups of patients, such as younger children and asthmatics; future studies with a larger data set should explore these interrelationships. Future work should examine if the effects of air pollution observed in our preliminary analysis from 2007–2008 are applicable in more recent years and over a longer time period (especially with improving air pollution levels in recent years[21]) and should explore whether additional factors not available in this data set affect mortality and measures of more severe disease.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

| | |
|---|---|
| **AQI** | Air Quality Index |
| **aOR** | adjusted odds ratio |
| **AQS** | Air Quality System |
| **CI** | Confidence interval |
| **ED** | Emergency department |
| **EPA** | Environmental Protection Agency |

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|---|---|
| **HCUP** | Healthcare Cost and Utilization Project |
| **ICD-9-CM** | International Classification of Diseases Ninth Revision, Clinical Modification |
| **IQR** | Interquartile range |
| **LOS** | Length of stay |
| **NAAQS** | National Ambient Air Quality Standards |
| **$O_3$** | Ozone |
| **$PM_{2.5}$** | Fine particulate matter with a diameter ≤2.5μm |
| **ppb** | parts per billion |
| **US** | United States |

## References


1. Kronman MP, Hersh AL, Feng R, Huang Y- S, Lee GE, Shah SS. Ambulatory visit rates and antibiotic prescribing for children with pneumonia, 1994–2007. Pediatrics. 2011;127(3):411–418. doi:10.1542/peds.2010-2008. [PubMed: 21321038]
2. Witt WP, Weiss AJ, Elixhauser A. Overview of hospital stays for children in the United States, 2012: Statistical brief #187. Healthc Cost Util Proj Stat Briefs. 2014.
3. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. N Engl J Med. 2013;369(2):155–163. doi: 10.1056/NEJMoal209165. [PubMed: 23841730]
4. Keren R Prioritization of comparative effectiveness research topics in hospital pediatrics. Arch Pediatr Adolesc Med. 2012;166(12):1155–1164. doi: 10.1001/archpediatrics.2012.1266. [PubMed: 23027409]
5. Malley CS, Henze DK, Kuylenstierna JCI, et al. Updated global estimates of respiratory mortality in adults >30 years of age attributable to long-term ozone exposure. Environ Health Perspect. 2017;125(8):087021. doi:10.1289/EHP1390. [PubMed: 28858826]
6. Zhang Z, Hong Y, Liu N. Association of ambient particulate matter 2.5 with intensive care unit admission due to pneumonia: A distributed lag non-linear model. Sci Rep. 2017;7( 1):8679. doi: 10.1038/s41598-017-08984-x. [PubMed: 28819316]
7. Environmental Protection Agency. AirNow. https://www.airnow.gov/ Published 2017 Accessed October 29, 2017.
8. Chen S, Gu Y, Qiao L, et al. Fine particulate constituents and lung dysfunction: A time-series panel study. Environ Sci Technol. 2017;51(3): 1687–1694. doi:10.1021/acs.est.6b03901. [PubMed: 28056177]
9. Kim CS, Alexis NE, Rappold AG, et al. Lung function and inflammatory responses in healthy young adults exposed to 0.06 ppm ozone for 6.6 hours. Am J Respir Crit Care Med. 2011; 183(9): 1215–1221. doi:10.1164/rccm.201011-1813OC. [PubMed: 21216881]
10. Pun VC, Kazemiparkouhi F, Manjourides J, Suh HH. Long-Term $PM_{2.5}$ exposure and respiratory, cancer, and cardiovascular mortality in older US adults. Am J Epidemiol. 2017;186(8):l–9. doi: 10.1093/aje/kwxl66.
11. Atkinson RW, Kang S, Anderson HR, Mills IC, Walton HA. Epidemiological time series studies of PM 2.5 and daily mortality and hospital admissions: A systematic review and meta-analysis. Thorax. 2014;69(7):660–665. doi:10.1136/thoraxjnl-2013-204492. [PubMed: 24706041]

12. Medina-Ramón M, Zanobetti A, Schwartz J. The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary disease: A national multicity study. Am J Epidemiol. 2006; 163(6): 579–588. doi:10.1093/aje/kwj078. [PubMed: 16443803]
13. Xiao Q, Liu Y, Mulholland JA, et al. Pediatric emergency department visits and ambient air pollution in the U.S. state of Georgia: a case-crossover study. Environ Heal 2016; 15(1): 115. doi: 10.1186/s12940-016-0196-y.
14. Darrow LA, Klein M, Dana Flanders W, Mulholland JA, Tolbert PE, Strickland MJ. Air pollution and acute respiratory infections among children 0–4 years of age: An 18-year time-series study. Am J Epidemiol. 2014;180(10):968–977. doi:10.1093/aje/kwu234. [PubMed: 25324558]
15. Nhung NTT, Amini H, Schindler C, et al. Short-term association between ambient air pollution and pneumonia in children: A systematic review and meta-analysis of time-series and case-crossover studies. Environ Pollut. 2017;230:1000–1008. doi:10.1016/j.envpol.2017.07.063. [PubMed: 28763933]
16. Patto NV, Nascimento LFC, Mantovani KCC, Viera LCPFS, Moreira DS. Exposure to fine particulate matter and hospital admissions due to pneumonia : Effects on the number of hospital admissions and its costs. Rev Assoc Med Bras 2016. 2016;62(4):342–346. doi: 10.1590/1806-9282.62.04.342.
17. Sheffield P, Roy A, Wong K, Trasande L. Fine particulate matter pollution linked to respiratory illness in infants and increased hospital costs. Health Aff. 2011;30(5):871–878. doi: 10.1377/hlthaff.2010.1279.
18. Roy A, Sheffield P, Wong K, Trasande L. The effects of outdoor air pollutants on the costs of pediatric asthma hospitalizations in the United States, 1999 to 2007. *Med Care* 2011 ;49(9): 810–817. doi: 10.1097/MLR.0b013e31820fbd9b.
19. Di Q, Dai L, Wang Y, et al. Association of short-term exposure to air pollution with mortality in older adults. JAMA. 2017;318(24):2446. doi: 10.lOOl/jama.2017.17923. [PubMed: 29279932]
20. Agency for Healthcare Research and Quality. Overview of the National (Nationwide) Inpatient Sample (NIS). https://www.hcup-us.ahrq.gov/nisoverview.jsp Published 2017 Accessed November 19, 2017.
21. Environmental Protection Agency. Air Quality System (AQS). https://www.epa.gov/aqs Published 2016 Accessed November 15, 2017.
22. United States Environmental Protection Agency. Bayesian space-time downscaling fusion model (downscaler) - derived estimates of air quality for 2009. 2009 doi:EPA-454/S-15-001.
23. Agency for Healthcare Research and Quality. Clinical Classifications Software (CCS) for ICD-9-CM. https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp Published 2017 Accessed November 29, 2017.
24. US Environmental Protection Agency. NAAQS Table, https://www.epa.gov/criteria-air-pollutants/naaqs-table Published 2017 Accessed November 15, 2017.
25. McCarthy JE, Lattanzio RK. EPA's 2015 Ozone Air Quality Standards. https://fas.org/sgp/crs/misc/R43092.pdf Published 2017 Accessed November 19, 2017.
26. HCUP Cost-to-Charge Ratio Files (CCR). Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality, Rockville, MD 2007-2011 https://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp Accessed March 2, 2015.
27. Sonego M, Pellegrin MC, Becker G, Lazzerini M. Risk factors for mortality from acute lower respiratory infections (ALRI) in children under five years of age in low and middle-income countries: A systematic review and meta-analysis of observational studies. PLoS One. 2015;10(1): 1–18. doi:10.1371/journal.pone.0116380.
28. Glick AF, Tomopoulos S, Fierman AH, Trasande L. Disparities in mortality and morbidity in pediatric asthma hospitalizations, 2007 to 2011. Acad Pediatr. 2016;16(5):430–437. doi:10.1016/j.acap.2015.12.014. [PubMed: 26768727]
29. Duan N Smearing estimate: a nonparametric retransformation method. JAm Stat Assoc. 1983;78:605–610. doi:10.1080/01621459.1983.10478017.
30. Hoek G, Brunekreef B, Verhoeff A, van Wijnen J, Fischer P. Daily mortality and air pollution in the Netherlands. J Air Waste Manage Assoc. 2000;50(8):1380–1389. doi: 10.1080/10473289.2000.10464182.

31. Carpenter BH, Chromy JR, Bach WD, LeSourd DA, Gillette DG. Health costs of air pollution: A study of hospitalization costs. Am J Public Health. 1979;69(12):1232–1241. [PubMed: 315722]
32. Davidson K, Hallberg A, McCubbin D, Hubbell B. Analysis of $PM_{2.5}$ using the environmental benefits mapping and analysis program (BenMAP). J Toxicol Environ Heal - Part A Curr Issues. 2007;70(3-4):332–346. doi:10.1080/15287390600884982.
33. Sather ME, Cavender K. Trends analysis of ambient 8 hour ozone and precursor monitoring data in the south central U.S. J Environ Monit. 2007;9(2):143–150. doi:10.1039/b617603h. [PubMed: 17285156]
34. Berman JD, Fann N, Hollingsworth JW, et al. Health benefits from large-scale ozone reduction in the United States. Environ Health Perspect. 2012;120(10):1404–1410. doi: 10.1289/ehp.1104851. [PubMed: 22809899]
35. Associated Press EPA moving forward with review of standard for ozone The Tribune. http://www.tribtown.com/2018/06/25/us-epa-ozone/ Published 2018 Accessed July 15, 2018.

### What's New

Higher levels of ozone and fine particulate matter with a diameter <2.5μm are associated with more severe disease in children admitted with pneumonia. More severe cases of pneumonia were seen when air pollution levels were above standards set by the Environmental Protection Agency.

**Table 1.**

Patient/hospital characteristics (n=57,972)

| Variable | N (%) |
|---|---|
| Particle Pollution <2.5μm (μg/m$^3$) | |
| <12 | 39,300 (67.8) |
| ≥12 | 18,672 (32.2) |
| Ozone(ppb) | |
| <60 | 54,602 (94.2) |
| 60 to <70 | 2,514 (4.3) |
| ≥70 | 856 (1.5) |
| Race/Ethnicity | |
| White | 21,773 (37.6) |
| Black | 7,603 (13.1) |
| Hispanic | 10,096 (17.4) |
| Asian/Pacific Islander | 1,009 (1.7) |
| Native American | 729 (1.3) |
| Other | 2,559 (4.4) |
| Missing | 14,203 (24.5) |
| Insurance | |
| Public | 30,198 (52.1) |
| Private | 23,524 (40.6) |
| Other | 4,116 (7.1) |
| Missing | 134 (0.2) |
| Median income by ZIP Code | |
| $1 to $38,999 | 21,471 (37.0) |
| $39,999 to $47,999 | 15,372 (26.5) |
| $48,000 to $62,999 | 11,247 (19.4) |
| $63,000+ | 8,778 (15.1) |
| Missing | 1,104 (1.9) |
| Age, years | |
| 0 to 1 | 23,585 (40.7) |
| 2 to 5 | 19,269 (33.2) |
| 6 to 12 | 10,792 (18.6) |
| 13 to 18 | 4,326 (7.5) |
| Asthma diagnosis | 18,402 (31.7) |
| Sex | |
| Female | 25,746 (44.4) |
| Male | 31,947 (54.9) |
| Missing | 379 (0.7) |
| Region | |
| Northeast | 7,539 (13.0) |
| Midwest | 13,104 (22.6) |

| Variable | N (%) |
|---|---|
| South | 27,569 (47.6) |
| West | 9,760 (16.8) |
| Location/teaching status | |
| Rural | 12,337 (21.3) |
| Urban/non-teaching | 21,278 (36.7) |
| Urban/teaching | 24,357 (42.0) |
| Bedsize‡ | |
| Small | 9,237 (15.9) |
| Medium | 13,963 (24.1) |
| Large | 34,772 (60.0) |
| Weekend admission | 13,416 (22.1) |
| Year | |
| 2007 | 29,375 (50.7) |
| 2008 | 28,597 (49.3) |
| Quarter | |
| January to March | 19,862 (34.3) |
| April to June | 10,106 (17.4) |
| July to September | 6,727 (11.6) |
| October to December | 15,188 (26.2) |
| Missing | 6,089 (10.5) |
| Outcomes | |
| Mortality | 82 (0.1) |
| Intubated | 433 (0.75) |
| Median LOS (IQR), days | 2 (2 to 4) |
| Median Total Costs (IQR) | $3089 ($2023 to $5177) |

IQR = Interquartile Range; LOS = Length of Stay

‡Definition differs depending on hospital location and teaching status[18]

**Table 2.**

Association of $PM_{2.5}$ with inpatient mortality, intubation, LOS, and cost†

| $PM_{2.5}$ level ($\mu g/m^3$) | Mortality aOR(95% CI) | Intubation aOR (95% CI) | LOS Increment, days (95% CI) | Costs Increment (95% CI) |
|---|---|---|---|---|
| >12 (reference ≤12) | 1.92 (1.25 to 2.94)** | 1.15 (0.96 to 1.37) | +0.05 (+0.01 to +0.10)** | +$278 (+$49 to +$588)* |

$PM_{2.5}$= fine particulate with a diameter ≤2.5 μm, aOR=adjusted odds ratio, CI=confidence interval, LOS= length of stay

*p<0.05

**p<0.01

†Models were adjusted for the following variables (chosen a priori based on review of the literature[27,28] and availability in the NIS[20]): diagnosis of asthma, race/ethnicity, median income by ZIP Code, age group, sex, region, hospital bedsize, and timing of admission (by quarter of year, weekend vs. weekday, and year)

**Table 3.**

Association of O**3** with inpatient mortality, intubation, LOS, and costs

| $O_3$ level (ppb) | Mortality aOR(95% CI) | Intubation aOR (95% CI) | LOS Increment, days (95% CI) | Costs Increment (95% CI) |
|---|---|---|---|---|
| >60 (reference ≤60) | 2.33 (1.14 to 4.78)* | 1.61 (1.19 to 2.17)** | +0.04 (−0.02 to +0.10) | −$98 (−$421 to $363) |
| >70 (reference ≤70) | 3.11 (1.24 to 7.79)* | 1.50 (0.94 to 2.38) | +0.19 (+0.05 to +0.33)** | +$820 (+$35 to +$1935)* |

$O_3$=ozone, aOR=adjusted odds ratio, CI=confidence interval, LOS= length of stay

*p<0.05

**p<0.01

†Models were adjusted for the following variables (chosen a priori based on review of the literature[27,28] and availability in the NIS[20]): diagnosis of asthma, race/ethnicity, median income by ZIP Code, age group, sex, region, hospital bedsize, and timing of admission (by quarter of year, weekend vs. weekday, and year)

**Table 4.**

Two pollutant model assessing pollutant associations with inpatient mortality, intubation, LOS, and costs

| Pollutant | Mortality aOR(95% CI) | Intubation aOR (95% CI) | LOS Increment, days (95% CI) | Costs Increment (95% CI) |
|---|---|---|---|---|
| $PM_{2.5}$ >12 μg/$m^3$ (reference ≤12) | 1.81 (1.18 to 2.80) ** | 1.13 (0.94 to 1.36) | +0.05 (+0.01 to +0.09) * | +$252 (+$31 to +$551 * |
| $O_3$ >70 ppb (reference ≤70 ppb) | 2.36 (0.97 to 5.77) | 1.41 (0.87 to 2.29) | +0.16 (+0.03 to +0.30) * | +$662 (−$72 to +$1716) |

$PM_{2.5}$= fine particulate with a diameter ≤2.5μm , $O_3$=ozone, aOR=adjusted odds ratio, CI=confidence interval, LOS= length of stay

* p<0.05

** p<0.01

† Model was adjusted for the following variables (chosen a priori based on review of the literature[27,28] and availability in the NIS[20]): diagnosis of asthma, race/ethnicity, median income by ZIP Code, age group, sex, region, hospital bedsize, and timing of admission (by quarter of year, weekend vs. weekday, and year)