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# Association of short-term increases in ambient air pollution and timing of initial asthma diagnosis among medicaid-enrolled children in a metropolitan area ☆

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ABSTRACT

*Objective:* We investigated associations of short-term changes in ambient ozone ($O_3$), fine particulate matter ($PM_{2.5}$) and nitrogen dioxide ($NO_2$) concentrations and the timing of new-onset asthma, using a large, high-risk population in an area with historically high ozone levels.
*Methods:* The study population included 18,289 incident asthma cases identified among Medicaid-enrolled children in Harris County Texas between 2005–2007, using Medicaid Analytic Extract enrollment and claims files. We used a time-stratified case-crossover design and conditional logistic regression to assess the effect of increased short-term pollutant concentrations on the timing of asthma onset.
*Results:* Each 10 ppb increase in ozone was significantly associated with new-onset asthma during the warm season (May–October), with the strongest association seen when a 6-day cumulative average period was used as the exposure metric (odds ratio [OR]=1.05, 95% confidence interval [CI], 1.02–1.08). Similar results were seen for $NO_2$ and $PM_{2.5}$ (OR=1.07, 95% CI, 1.03–1.11 and OR=1.12, 95% CI, 1.03–1.22, respectively), and $PM_{2.5}$ also had significant effects in the cold season (November–April), 5-day cumulative lag (OR=1.11. 95% CI, 1.00–1.22). Significantly increased ORs for $O_3$ and $NO_2$ during the warm season persisted in co-pollutant models including $PM_{2.5}$. Race and age at diagnosis modified associations between ozone and onset of asthma.
*Conclusion:* Our results indicate that among children in this low-income urban population who developed asthma, their initial date of diagnosis was more likely to occur following periods of higher short-term ambient pollutant levels.



## 1. Introduction

Asthma is a disease of multi-factorial origin with a prevalence of nearly 10% among American children (Akinbami et al., 2012; Papadopoulos et al., 2012). It is considered a classic demonstration of gene–environment interaction leading to disease onset, although the development of asthma cannot be attributed to a single gene or environmental exposure (Holgate, 2008; Maddox and Schwartz, 2002). The etiology of asthma is a complex process whereby children with genetically based enhanced susceptibility develop allergen sensitization following exposures which begin *in utero* (Holt et al., 1999; Maddox and Schwartz, 2002). Continued allergen exposure leads to immune-inflammatory reactions, and a series of injury/repair cycles which further damage airway tissue and eventually result in structural changes in the lung with permanent effects on pulmonary function (Holt et al., 1999; Papadopoulos et al., 2012). However, despite widespread exposure to common indoor and outdoor allergens, only a minority of atopic children reach a 'tipping point' after which symptoms of asthma become apparent (Holt et al., 1999).

Recent literature has focused on the defective airway epithelium seen in asthmatic children, and the genetic origin of these abnormalities, which lead to inadequate injury and repair responses (Holgate et al., 2010; Papadopoulos et al., 2012). The airway epithelium is more permeable in asthmatics, and less able to prevent access of inhaled irritants to the underlying airways. This decreased barrier function leaves pre-disposed children less able to defend against

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environmental exposures such as respiratory infections, indoor allergens or ambient pollutants, and may explain in part why some atopic children develop asthma while others with good barrier function do not (Holgate et al., 2010; Papadopoulos et al., 2012). Both respiratory viruses and air pollution target the epithelium as an entry point to airway tissue, and this, combined with inadequate anti-oxidant defense seen in the asthmatic epithelium can explain the sensitivity of asthmatic children to short-term increases in ambient ozone ($O_3$) and particulate matter (Holgate et al., 2010; Papadopoulos et al., 2012).

Elevated levels of ambient air pollutants including $O_3$, fine particulate matter ($PM_{2.5}$) and nitrogen dioxide ($NO_2$) have been associated with worsening lung function and asthma symptoms in children (Akinbami et al., 2010; Babin et al., 2008; Lewis et al., 2005; O'Connor et al., 2008). In this study, we investigated whether short-term increases in ambient $O_3$, $NO_2$ and $PM_{2.5}$ levels were related to the timing of initial diagnosis in children with asthma. Our study population was comprised of Medicaid-enrolled children residing in Harris County, Texas between 2005 and 2007, a large population at high risk for asthma, and living in an area with historically high $O_3$ levels.

## 2. Material and methods

### 2.1. Identification of incident asthma cases

We have previously described methods to identify incident asthma cases among Texas Medicaid-enrolled children using Centers for Medicare and Medicaid Services Medicaid Analytic Extract files (Wendt et al., 2012). We restricted the present analysis to cases residing upon enrollment in Harris County, Texas. Harris County encompasses the greater Houston area, with over 1700 square miles and 4 million residents, including 28% who are under the age of 18 years (United States Census Bureau, 2013). It is the largest county in Texas, and the third largest county in the United States.

Briefly, Medicaid Analytic Extract files are created by the Centers for Medicare and Medicaid Services specifically for research, and contain annual data on Medicaid eligibility and healthcare utilization reported by the states. Eligibility files contain person-level data including age, gender, race, zip code of residence, enrollment dates and scope of Medicaid coverage. Due to privacy concerns, street address is not provided in the files. Claims files contain final adjudicated claims by date of service and have undergone quality checks and corrections (Hennessy et al., 2007). We obtained enrollment, inpatient and outpatient medical claims, and pharmacy claims files from the Centers for Medicare and Medicaid Services for Texas beneficiaries under the age of 18 who were enrolled in Medicaid between 2004 and 2007.

Monthly enrollment and eligibility indictors were used to identify children enrolled for at least 13 continuous months (with allowance for a single 1-month gap) during the 4-year period (Fig. 1). Children were considered ineligible during any year that the annual eligibility file indicated private insurance coverage or only premium (i.e., capitated) payment claims during the year, as this would result in incomplete claims history in the Medicaid files. The 13+ month continuous enrollment span provided a 'wash-out' period to distinguish incident from prevalent asthma cases.

All medical and pharmacy claims for the 4-year period were combined, and asthma cases were defined as children with a primary diagnosis of asthma (International Classification of Diseases, 9th revision code=493.xx) on at least one outpatient or inpatient record, or 4 or more asthma medication (National Committee for Quality Assurance, 2011) dispensing events (30-day supply) during a 365-day period. For each case, the diagnosis date was either the date of service for the child's earliest asthma medical claim, or the date when the first of 4+ asthma medication prescriptions was written.

We then merged records from the enrollment and asthma case files, excluding cases without an enrollment record (i.e., no 13+ month span of continuous enrollment between 2004 and 2007). Cases in the enrollment file but not enrolled continuously during the 12 months prior to diagnosis were also excluded, as we could not distinguish incident from prevalent cases. Enrollment and claims files from 2004 were only used to provide a wash-out period for children in the 2005 files. Using these methods, we identified 18,289 incident asthma cases among Harris County Medicaid-enrolled children ages 1–17 during 2005–2007, with an age-adjusted incidence rate of 3.12/100 person-years.

### 2.2. Ambient air pollutant data

Air monitoring data for $O_3$ (daily maximum 8-h moving average), $NO_2$ (daily 1-h maximum) and $PM_{2.5}$ (daily 24-h mean) were obtained from the U.S. Environmental Protection Agency Air Quality System (United States Environmental Protection Agency, 2010). $O_3$ is monitored continuously 24-h a day, 365 days per year at 22 monitoring stations in the Houston–Galveston–Brazoria metropolitan area. Monitors are concentrated in Harris County ($n=17$), with two monitors in Galveston County, two in Brazoria County, and one in Montgomery County. $NO_2$ is also monitored continuously 24-h a day, 365 days per year at 17 monitoring sites across this metropolitan area: 12 in Harris County, two in Brazoria County, two in Galveston County and one in Montgomery County. For $PM_{2.5}$, seven monitoring sites in Harris County and two sites in neighboring counties performed hourly measurements of $PM_{2.5}$ (local conditions) between 2005 and 2007. Beginning in September 2005, measurements were discontinued at the two sites in adjacent counties, and the number of $PM_{2.5}$ monitoring sites in Harris County decreased from seven to four. Also, two of the four monitors were co-located at a single site, one recording daily samples, and a second monitor collecting samples every six days. For this site, we used only the 24-h mean values from the monitor with daily sampling in our analysis. Daily 24-h mean $PM_{2.5}$ measurements were available for the other area monitors every sixth day. Therefore, we used measurements from 8 $PM_{2.5}$ monitors through September 2005, and from 3 monitors between October 2005 and December 2007. A map of the study area, as well as placement of the $O_3$, $NO_2$, and $PM_{2.5}$ monitors is displayed in Fig. 2.

Since there is no consensus on pertinent exposure metrics for these pollutants and asthma, we constructed several lagged and average cumulative exposure variables (i.e., values averaged over 2-, 3-, 4-, 5- and 6-day periods) for each pollutant on all case and control dates, considering both their irritant nature and the number of symptomatic days before a physician's visit might be scheduled. For each date, we determined same-day pollutant values, single-day values lagged 1 through 5 days, and cumulative values averaged over 2 day (i.e., same day and lag 1) through 6 day (i.e., same day through lag 5) periods. We tested for non-linearity of effect for all three pollutants using restricted cubic splines, with three knots at the 5th, 50th and 95th percentiles (Desquilbet and Mariotti, 2010).

Our primary analyses considered temporal changes in ambient pollutant concentrations, that is, by averaging pollutant levels from monitoring sites across Harris County for each calendar day. Specifically, the average maximum 8-h $O_3$ concentration was estimated for each calendar day, and was the same regardless of where in Harris County the child resided. Likewise, we calculated daily $PM_{2.5}$ and $NO_2$

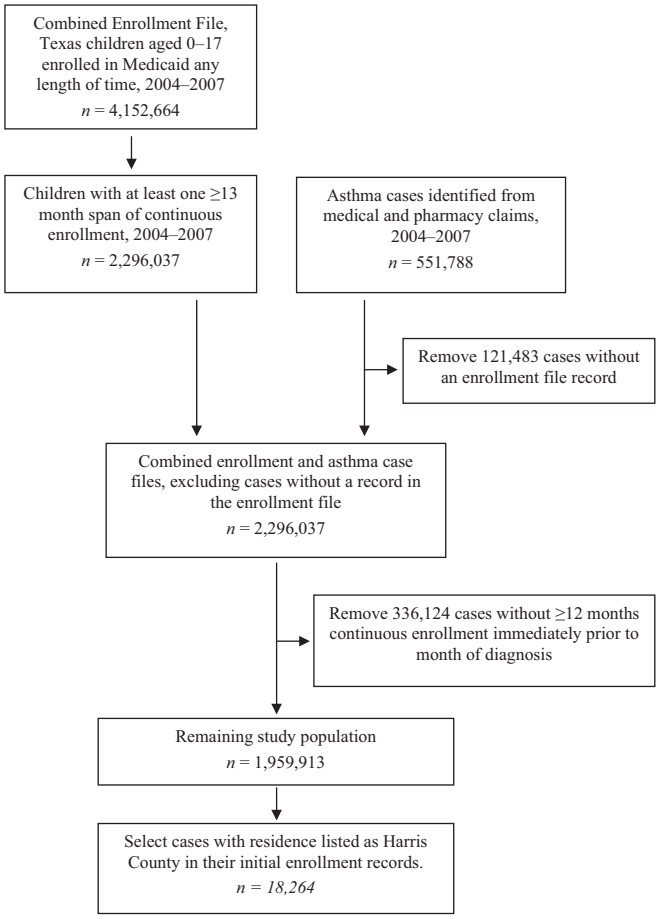


**Fig. 1.** Description of process used to identify study population and cases from the original Medicaid Analytic Extract files containing enrollment and claims records for Texas Medicaid-enrolled children aged 0–17, 2004–2007. The numbers of children with at least 1 ≥ 13 month enrollment span, in the combined enrollment and case file, and in the remaining study population represent the number of ≥ 13 month enrollment spans; a child could have more than 1 enrollment span during the 4-year study period.