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The association between ozone and asthma ED visits by daily air quality alert status

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Abstract

The association between ozone and asthma ED visits by daily air quality alert status

By Kendra Gilbertson

Ambient air pollution levels taken from outdoor monitors may not accurately represent the levels individuals are exposed to if higher pollution levels trigger avoidance behaviors through public health warning systems such as the Air Quality Index (AQI). If this is the case, there may be systematic bias towards the null when estimating the impact of outdoor air pollution on human health. The authors examined the association between ozone concentrations and hospital emergency department (ED) visits in metropolitan Atlanta on days when the AQI is rated 3, “unhealthy for sensitive groups,” or 4, “unhealthy,” versus days when the AQI is rated 1, “good,” or 2, “moderate”. The daily number of pediatric ED visits for asthma and wheezing was merged with daily meteorological, air pollution, and AQI data from 2004 to 2009 and analyzed using a Poisson linear model. The authors observed that controlling for AQI ratings of “unhealthy for sensitive groups” or “unhealthy” led to slightly higher rate ratios for ambient ozone levels and asthma ED visits. However, there was little difference in the association between ozone and emergency department visits on alert and non-alert days.

The association between ozone and asthma ED visits by daily air quality alert status

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Thank you to Dr. Lyndsey Darrow: an inspiring teacher and a patient advisor. For my parents, Barbara and Eric, and my brother Nils. If any of you read this, I'll give you \$50.

Chapter I: Literature Review

A. Asthma

Asthma is an inflammatory chronic lung disease in which the airways narrow, making breathing more difficult, that affects over 25 million people in the United States (1). The inflammation causes airways to swell and become very sensitive and reactive to a range of inhaled substances (1). The muscles surrounding the reactive airways tighten, narrowing the airways, and causing less air to enter the lungs (1). Cells can also produce more mucus, narrowing the airways further, which is part of a chain reaction that can cause asthma symptoms (1). These symptoms vary from mild to severe, and include wheezing, chest tightness and pain, shortness of breath, coughing, and difficulty sleeping (1, 2). Worsening or increase in symptoms is considered an asthma attack, which may necessitate emergency care, and can be fatal (1).

Asthma usually begins in childhood, and approximately 7 million of the asthma sufferers in the United States are children (1). The cause of asthma is still debated, but risk factors include having parents with asthma, a genetic predisposition to allergies, some childhood respiratory infections, and the hygiene hypothesis (1). The hygiene hypothesis posits that children growing up in Western countries have fewer early childhood infections and environmental exposures resulting from a focus on hygiene and sanitation which affects a child's immune system, making them more likely to develop allergies and asthma (1). Risk of asthma increases if a person is overweight, a smoker, exposed to secondhand smoke, had a mother who smoked during pregnancy, air pollution

exposure, or through occupational triggers associated with farming, hairdressing, or manufacturing (2).

The symptoms of asthma have a wide range of potential causes, including allergens from dust, animal fur, cockroaches, molds, and pollens, irritants including smoke, air pollution, and chemicals, non-steroidal anti-inflammatory drugs and non-selective beta-blockers, ingested sulfites, viral upper respiratory infections, and physical activity (1). Triggers also include cold air, GERD (gastroesophageal reflux disease), and the menstrual cycle in some women (2). A runny nose, sinus infection, reflux, stress, and sleep apnea can make managing asthma more difficult (1). Asthma symptoms can interfere with sleep and work, including taking sick days during flare-ups, permanent bronchial tube narrowing, emergency department visits and hospitalizations, as well as side effects from asthma medications (2).

There are several tests that can be used to diagnose asthma (2). The first step is a physical examination to rule out other respiratory diseases (2). After this a common method is measuring lung function, or the amount of air that moves in and out of the lungs during breaths (2). These are often done before and after taking a bronchodilator to see if lung function improves (2). One such test is a spirometry test, which estimates how narrow the bronchial tubes are by measuring the amount and speed of air a person can exhale after taking a deep breath in (2). This involves taking two measures: forced vital capacity (FVC) which is the overall volume exhaled, and forced expiratory volume 1 (FEV1) which is the volume exhaled in one second (3). Another is a peak flow test which measures how forcefully a person can breathe out (2). Additional tests include

administering the asthma trigger methacholine and testing for a reaction, measuring the amount of nitric oxide in the breath, imaging test which show structural irregularities, allergy tests of the skin or blood to determine whether allergen immunotherapy would be beneficial, and sputum eosinophils which tests for specific white blood cells in the saliva and mucus (2).

Asthma treatment can take several approaches. Conditions that interfere with asthma management should be treated, triggers should be avoided, and an asthma action plan should be created with the patient's physician (1). From a medical standpoint there are long-term control medications to reduce inflammation and symptoms, and quick-relief, or 'rescue' medications that address symptoms during flare-ups (1). Long-term medications are used daily, and may need to be monitored via blood test (1). They include:

- i. Corticosteroids: The preferred medication is inhaled corticosteroids, which are also the most successful and work by reducing inflammation and avoiding the chain reaction leading to asthma symptoms (1). Most people who use corticosteroids see a reduction in symptom severity and frequency (1). Side effects of this treatment include thrush, and increased risk of cataracts and osteoporosis (1).
- ii. Cromolyn: Cromolyn is another long-term treatment which works to prevent inflammation by spraying a medicated mist into the lungs (1).
- iii. Omalizumab: Omalizumab is an anti-IgE vaccination that may be useful if other treatments have not worked well (1). It is given monthly or bi-monthly to

prevent a reaction to asthma triggers, and in rare cases can cause anaphylactic shock (1).

- iv. Inhaled long-acting beta2-agonists: Along with inhaled corticosteroids, long-acting beta2-agonists may be prescribed to help open the airways (1).
- v. Leukotriene modifiers: Oral leukotriene modifiers interfere with the chain reaction that increases inflammation of the bronchial tubes (1).
- vi. Theophylline: The oral medication theophylline assists the body in opening the airways (1).

For quick relief treatments during asthma flare-ups many patients use inhaled short-acting beta2-agonists to relax the constricted muscles around their airways (1). In emergency visits for more severe flare-ups doctors will administer oxygen, as well as previously described medications at higher doses than are used at home (1).

Asthma diagnosis and treatment differs when the patient is a child. Risk factors for children developing asthma that lasts longer than the age of six are wheezing, respiratory infections, allergies, eczema, and having parents with asthma (1). Diagnosing asthma in young children may be difficult for a number of reasons. Children may have other childhood illnesses with the same symptoms as asthma, and wheezing can be caused by smaller airways (1). Lung function tests are difficult to administer to children under five years old, so a doctor may choose to put the child on a four to six-week trial course of asthma medication to see if his or her health improves (1).

B. Air Quality Index

The federal Clean Air Act (CAA) of 1970 was passed to regulate air pollution emissions. It gave the Environmental Protection Agency (EPA) the power to determine National Ambient Air Quality Standards (NAAQS) as well as create a nationwide air quality index (4). The original version was the Pollutant Standards Index, which normalized the levels of ground-level ozone, particulate matter, carbon monoxide, sulfur dioxide, and nitrogen dioxide (which has since been dropped) on a scale of 0 to 500, with 500 representing significant harm (5). One hundred is generally considered the standard level for each pollutant in the United States (6). Since the Pollutant Standards Index was implemented there have been several revisions, including changing the 1-hour ozone standard to an 8-hour ozone standard, and adding 24-hour and annual ozone standards for fine particulate matter (6). The name has also been changed to Air Quality Index, or AQI, and the category values have changed. Finally, all Metropolitan Statistical Areas with populations over 350,000 are required to report an AQI value (6).

Concentrations of each pollutant are measured by more than 1,000 monitors around the country, and are each calculated into their own AQI value (7). The AQI is calculated using the equation: $I_p = ((I_{Hi} - I_{Lo}) / (BP_{Hi} - BP_{Lo})) (C_p - BP_{Lo}) + I_{Lo}$ where I_p = the index for pollutant p, C_p = the rounded concentration of pollutant p, BP_{Hi} = the breakpoint that is greater than or equal to C_p , BP_{Lo} = the breakpoint that is less than or equal to C_p , I_{Hi} = the AQI value corresponding to BP_{Hi} , and I_{Lo} = the AQI value corresponding to BP_{Lo} (7). The formula results in a number from 0 to 500, and are color coded from green (good) to maroon (hazardous) (8). Figure 1 shows the complete table of AQI values, along with their colors

and levels of health concern (8). Values above 500 are possible, but are considered past the AQI (8). The highest AQI value among the AQI values calculated for all pollutants must be reported to the public daily (7). If the highest AQI is over 100, the level of health concern must also be reported (7). Many cities also calculate and share a forecast for the next day's AQI rating to help vulnerable individuals take necessary precautions (7).

- i. Ozone: One of the pollutants taken into account when reporting air quality is tropospheric, or ground-level ozone. This differs from stratospheric ozone, which protects the earth from ultraviolet rays (9). Ground-level ozone (referred to simply as 'ozone' from here on out) is not naturally occurring, but is a result of sunlight-driven chemical reactions between nitrogen oxides and volatile organic compounds (VOCs) (9). In other words, when pollution from cars, power plants, and other sources interact in sunlight, chemical reactions produce this form of ozone. Because of this, hot, sunny, urban areas have the highest risk of developing unhealthy ozone levels. People with higher susceptibility to ozone effects include those suffering from asthma, children, the elderly, and those who are active outside (9). They can experience chest pain, coughing, throat irritation, inflame airways, reduce lung function, and damage lung tissue (9). Bronchitis, emphysema, and asthma may all become more severe when a person is exposed to ozone, and people with these conditions can be more seriously affected at lower levels of exposure (9).
- ii. Particle Pollution: Particulate matter, or particle pollution is made up of solid particles and liquid droplets that can be either released directly into the air, or created when other pollutants interact (10). Particulate matter can be either

course (from 2.5 to 10 micrometers in diameter) or fine (2.5 micrometers or less) (10). Course particles include dust from crushing, grinding, or road traffic, while fine particles are created by motor vehicles, power plants, and fires (10). Both course and fine particles are hazardous to human health because they are small enough to enter the lungs (10). Short and long-term exposure to particle pollution puts people with heart and lung disease at risk of deteriorating health, along with the elderly and children (11).

iii. Carbon Monoxide: Carbon monoxide is a gas released when the carbon in fuel is not fully burned off (11). The vast majority of carbon monoxide comes from motor vehicles, which contributes up to 95% of all carbon monoxide in urban areas (11). Unlike ozone, carbon monoxide levels typically peak during cold weather, as the cold causes less of the carbon to burn off and traps pollutants closer to the ground via inversion (11). Carbon monoxide travels through the lungs into the blood stream where it attaches to hemoglobin, which is responsible for carrying oxygen to the cells (11). The binding results in lower oxygenation of the body's tissues (11). Those with cardiovascular disease, impaired cardiovascular and respiratory systems, and possibly newborns and fetuses have, the greatest susceptibility for the health impacts of carbon monoxide (11). Even healthy adults may experience reduced mental capacity and vision at high levels of carbon monoxide exposure (11).

iv. Sulfur Dioxide: Similar to carbon monoxide, sulfur dioxide is a gas released when fuels containing sulfur are burned (11). Industrial facilities are typically large sources of coal and oil burning (11). For most people, exercise that

triggers breathing through the mouth is required to cause health effects, as the nasal passages remove the gas (11). Those with asthma and who are active outdoors are the most susceptible to the adverse effects of sulfur dioxide, which include narrowing airways, wheezing, chest tightness, and shortness of breath (11). Healthy people may also experience these symptoms are very high levels of exposure (11).

C. Asthma and Poverty

In the United States, asthma is an equality issue as well as a medical one. People with low incomes and racial minorities have more severe cases of asthma, more frequent symptoms, and more trips to the emergency department (12). A study examining air pollution and demographic characteristics found that whites had the lowest exposure to air pollution, followed by non-Hispanic blacks, and Hispanics (13). However, the areas with air pollution monitors tended to have more non-Hispanic blacks and lower socioeconomic status than tracts without monitors (13). A large part of this is because these groups are more likely to live in high-traffic areas (12). Traffic increases both the pollution levels people are exposed to, as well as the health effects on children and adults with asthma (12). People of lower socioeconomic status are also less likely to own a car and more likely to rely on public transportation, disproportionately exposing them to air pollution (14).

D. Analysis of the Literature

While the overall message of reducing time outside on high pollution days is clear, there is limited evidence on whether or not public health warning systems, such as

the AQI, motivate people to modify their behavior. One study of the response to air-quality information found that people are unaware of poor air quality, and instead rely on sensory cues such as sight and smell to assess pollution levels (15). This is supported by a literature summary which found that a person's psychological and social perspective affects their perception of air pollution risk (16). Additionally, as little as one third of people surveyed were aware of air quality advisories, and reported taking little action in response to alerts (17).

In contrast, a cross-sectional study across six states with 33,888 participants found that 46% of adults without asthma and 49% of adults with asthma were aware of air quality alerts (18). Of these people, 31% with asthma and 16% without asthma reported that they changed their behavior in response to alerts. Women and people with a disability were more likely to change their behavior according to government health suggestions (18). Another study found that 95% of parents with asthmatic children were aware of air quality ratings, as opposed to 80% of parents whose children did not have asthma (19). On advisory days 64% of parents restricted the outdoor play time of their child with asthma, versus 45% of parents with healthy children (19).

A 2009 paper by Neidell examined the effect of air quality warnings on outdoor events in Southern California. Data on meteorology, air quality, and daily attendance at Los Angeles Zoo and Botanical Gardens and Griffith Park Observatory were combined and analyzed using a semi-experimental regression discontinuity analysis to estimate the impact of air quality warnings on attendance (20). He found a significant 17% decrease in zoo attendance when smog alerts were issued, a significant 7% decline for health

advisories, and a non-significant 1.9% decline in attendance for “unhealthful” air pollution status (20). Observatory attendance only decreased significantly in response to smog alerts (5%) (20). Children, the elderly, and local residents were generally more responsive to air pollution warnings, and there was a greater response to smog alerts versus health advisories (20). The author believed that the behavior change he observed should be accounted for when estimating the association between ozone levels and health outcomes (20).

The study most relevant to the question addressed here was done by Neidell and Kinney (2010) in Southern California, which used air quality information (smog alert indicator and pollutant standards index), meteorological data, and hospital discharge data to assess whether the association between ambient ozone levels and hospitalizations for asthma or wheezing differed when controlling for air quality information. The authors examined this among all ages, age 5-19, age 20- 64, and 65 and over (21). They chose to categorize age because some populations, such as children and the elderly, are more susceptible to the health effects of air pollution (21). For their analysis they used a lag Poisson generalized linear model allowing for over-dispersion, with lags accounting for a possible delay in the onset of symptoms. They combined ambient ozone and ozone alert information into an interaction term representing the amount of time people spent outdoors (21). Carbon monoxide, nitrogen dioxide, daily maximum and minimum temperatures, precipitation, maximum relative humidity, sun cover, resultant wind speed, smog alert status, day of the week, and forecasted air quality were all controlled for in the analysis (21). Their main analysis was running this model with and without an aggregate term for smog alert and pollutant standards index to see if the estimates significantly

changed.

Across all age groups they found a 0.017% increase in asthma hospitalizations from a 0.01 ppm increase in ozone without controlling for air quality information (21). When an indicator variable for alert days was included in the Poisson model, the percent increase rose to 0.027, a significant change in the estimated number of asthma hospitalizations per 0.01 ppm increase in ozone ($p < 0.01$) (21). For the 5-19 year old group, a 0.01 ppm increase in ozone was associated with a 0.016% increase in asthma hospitalizations when not accounting for air quality information, which is significantly lower than the 0.037% increase when including the air quality term (21). The difference between the models for the 20-64 age group was not significant, and the estimates were 0.018 without air quality information and 0.022 with air quality information (21). For people over 64, the increase in hospitalizations associated with the 0.01 ppm increase in ozone is 0.022% without controlling for air quality information, and 0.031% when controlling for air quality information (21). The p-value for this change is 0.07 (21). The authors concluded that the effect of ozone on asthma hospitalization increases when controlling for air quality information across all age strata (21). Choosing to account for air pollution information from smog alerts and pollutant standards index significantly affects the association between ozone and health, possibly resulting from protective behaviors among children and the elderly (21).

Both studies saw a change in outcome consistent with residents modifying their behavior to avoid excess exposure on high pollution days. While these studies motivated the one done here, we will not address the specific question of behavior modification in

our analysis; instead, the main focus will be on how the association between ozone levels and the ED visits changes by accounting for air quality warnings. Behavior change is one possible explanation of such a phenomenon. To do this, a retrospective cohort study was conducted, where information was pulled from hospital records for children in the metropolitan Atlanta area, which has both high levels ozone and high asthma levels. The unit of analysis was days, with ozone level as the exposure, and the number of ED visits for asthma or wheezing for that day were the outcome. Here we use this preexisting dataset to examine this association within the Atlanta area, and compare our findings to the limited amount of previous research into this topic.

Figure 1. Air Quality Index values with corresponding health advisory (8).

Air Quality Index (AQI) Values	Levels of Health Concern	Colors
<i>When the AQI is in this range:</i>	<i>..air quality conditions are:</i>	<i>...as symbolized by this color:</i>
0 to 50	Good	Green
51 to 100	Moderate	Yellow
101 to 150	Unhealthy for Sensitive Groups	Orange
151 to 200	Unhealthy	Red
201 to 300	Very Unhealthy	Purple
301 to 500	Hazardous	Maroon

Chapter II: Manuscript

Title: The association between ozone and asthma ED visits by daily air quality alert status

Authors: Gilbertson K, Darrow L

Abstract

Ambient air pollution levels taken from outdoor monitors may not accurately represent the levels individuals are exposed to if higher pollution levels trigger avoidance behaviors through public health warning systems such as the Air Quality Index (AQI). If this is the case, there may be systematic bias towards the null when estimating the impact of outdoor air pollution on human health. The authors examined the association between ozone concentrations and hospital emergency department (ED) visits in metropolitan Atlanta on days when the AQI is rated 3, “unhealthy for sensitive groups,” or 4, “unhealthy,” versus days when the AQI is rated 1, “good,” or 2, “moderate”. The daily number of pediatric ED visits for asthma and wheezing was merged with daily meteorological, air pollution, and AQI data from 2004 to 2009 and analyzed using a Poisson linear model. The authors observed that controlling for AQI ratings of “unhealthy for sensitive groups” or “unhealthy” led to slightly higher rate ratios for ambient ozone levels and asthma ED visits. However, there was little difference in the association between ozone and emergency department visits on alert and non-alert days.

A. Introduction

Tropospheric ozone is a pollutant created during chemical reactions between

nitrogen oxides and volatile organic compounds (VOCs), meaning hot, sunny, urban areas tend to have higher levels (9). People susceptible to higher ozone exposure include those suffering from asthma, children, the elderly, and those who are active outside (9). Exposure for these groups can have acute health effects including chest pain, coughing, throat irritation, inflamed airways, reduced lung function, and damaged lung tissue (9). Bronchitis, emphysema, and asthma may all become more severe, necessitating medical intervention and even hospitalization (9).

Particulate matter pollution is made up of solid particles and liquid droplets that can be either released directly into the air, or created when other pollutants interact (10). Particulate matter can be either course (from 2.5 to 10 micrometers) or fine (2.5 micrometers or less) (10). Fine particles, or $PM_{2.5}$, are created by combustion from motor vehicles, power plants, and fires (10). Both course and fine particles are hazardous to human health because they are small enough to enter the lungs (10). Short and long-term exposure to particle pollution puts people with heart and lung disease at risk of irritated eyes, nose, and throat, coughing, chest tightness, shortness of breath, reduced lung function, irregular heartbeat, asthma attacks, heart attacks, and death (11).

In 1970 the United States government passed the federal Clean Air Act, which directed the Environmental Protection Agency (EPA) to create a national air quality index to monitor and report levels of air pollutants like ozone (4). The current iteration of the Air Quality Index (AQI) measures ground-level ozone, particulate matter, carbon monoxide, and sulfur dioxide (6). Concentrations of each pollutant are measured by more than 1,000 monitors across the country, with each area calculating its own daily AQI (7).

If the highest AQI among all pollutants is over 100, the level of health concern must also be reported (6). Many cities calculate and share a forecast for the next day's AQI rating to help vulnerable individuals take action to protect themselves (7). Given that the goal of AQI reporting is to allow sensitive individuals to avoid excess exposure to outdoor pollutants, the ozone concentrations detected by outdoor monitors may not accurately represent individual exposure. Many epidemiological investigations into the impact of ozone on human health have used this publically available data as a measure of individual exposure. If individuals avoid exposure to air pollution based on air quality warnings, there may be a systematic bias in the literature underestimating the association between ozone and health effects.

While the overall message of reducing time outside on high pollution days is clear, there is minimal evidence on whether people modify their behavior accordingly. A number of studies suggest that the majority of people are unaware of the air quality, and make subjective assessments of pollution levels based on smog and other sensory cues (15, 16, 17, 22). However, there is also evidence that people who are aware of the alerts limit their outdoor activity, especially those with lifetime asthma (18). Another study found that parents had higher awareness of AQI alerts, and complied with government recommendations some of the time (19).

A 2009 paper by Neidell examined the effect of air quality warnings on outdoor events in Southern California and found significant decreases in attendance when smog alerts and health advisories were issued. Children, the elderly, and local residents were generally more responsive to air pollution warnings, and there was a greater response to

smog alerts versus health advisories (20). The author believed that the behavior change he observed should be accounted for when estimating the association between ozone levels and health outcomes (20).

The study most similar to the question addressed in this paper was done by Neidell and Kinney (2010) in Southern California, and used air quality information (smog alert indicator and pollutant standards index), meteorological data, and hospital discharge data to assess whether the association between ambient ozone levels and hospitalizations for asthma or wheezing differed when controlling for air quality forecasts. The authors examined this among all ages, age 5-19, age 20- 64, and 65 and over (21). They concluded that the effect of ozone on asthma hospitalization increases when controlling for air quality information across all age strata (21). Choosing to account for air pollution information significantly affects the association between ozone and health, possibly resulting from protective behaviors among children and the elderly (21).

Both studies saw a change in outcome consistent with residents modifying their behavior to avoid excess exposure on high pollution days. We will not be addressing the specific question of behavior modification in our analysis; instead, the main focus will be on how the association between ozone levels and ED visits changes when accounting for air quality information. Avoidance behavior is one possible explanation for such a phenomenon. To do this, we used existing data from a retrospective cohort study, where information was pulled from hospital records for children in the metropolitan Atlanta area, which has both high levels of ozone and asthma. The unit of analysis was days, with

ozone level as the exposure, and the number of ED visits for asthma or wheezing for that day was the outcome. This preexisting dataset allowed us to examine the association within the metro Atlanta area, and compare our findings to the limited amount of previous research on this topic.

B. Methods

i. Data sources

Individual level data from computerized billing records from all hospitals in Georgia were obtained from the Georgia Hospital Association for the period 1/1/2002 through 6/30/2010. Information from each visit included patient age, sex, hospital identification number, admission date and International Classification of Diseases, 9th Revision (ICD-9) diagnosis codes. In order to limit the study population to children in the Atlanta area where we could best characterize air quality, we restricted to emergency visits from individuals aged 0-18 with billing zip codes in the 20-county Atlanta metropolitan area who had visited hospitals emergency departments located in the Atlanta area. The counties included in 20-county Atlanta are: Barrow, Bartow, Carroll, Cherokee, Clayton, Cobb, Coweta, DeKalb, Douglas, Fayette, Forsyth, Fulton, Gwinnett, Henry, Newton, Paulding, Pickens, Rockdale, Spaulding, Walton. An emergency department visit was classified as asthma or wheeze if any of the listed ICD-9 diagnosis codes indicated asthma (493) or wheeze (786.07). Counts of ED visits for asthma and wheeze were summed for each day to create a time-series dataset of ED counts for asthma or wheeze among children aged 0-18 in the metropolitan Atlanta area. The population at risk was assumed to be the same across days.

These data were merged by forecast date with AQI forecast data pulled from the AirNOW database, which included both same day and next day predictions of AQI from 1/1/2004 to 10/30/2015. AQI data was shared with us on a one to four scale corresponding to the color coded air quality categories. A score of 1 indicated good air quality, 2 meant moderate air quality, 3 was unhealthy for sensitive groups, and 4 was unhealthy for everyone. There were no ratings of 5 or 6, which equate to very unhealthy and hazardous. An “alert day” was defined as a day where either the same day or next day predictions were a 3 or 4, since either may have affected avoidance behavior. We also controlled for meteorological variables, including dew point and maximum daily temperature, obtained from a weather station at the Atlanta Hartsfield-Jackson International Airport.

After merging the data, the resultant dataset contained values from 5/1/2004 to 9/30/2009. There were no alert days in the colder months of October through April during any year, so these months were excluded from the analysis as no comparison could be made between alert and non-alert days. Days with an observed or predicted AQI value of 3 or 4 were considered “alert” days, and all other days were considered “non-alert” days.

ii. Statistical Analysis

To allow for a possible delayed onset of asthma symptoms in response to ozone exposure, six different lag exposure Poisson linear models were run: same day exposure (lag 0), previous day exposure (lag 1), and three day moving average exposure (average of lag 0-1-2), all controlling and not controlling for $PM_{2.5}$. The outcome was the log of

the number of emergency department visits for asthma or wheezing on a given day. For alert status, this meant taking the alert variable (alert days = AQI of 3 or 4 for same day or next day), and lagging it one day for the “yesterday” models, and creating an indicator for any of the past three days being alerts for the “three day” models. Ozone was a linear term (population weighted average 8 hour maximum) lagged one day for the “yesterday” models, with a three day moving average for the “three day” models. An interaction term between O₃ and alert status allowed the linear effect of ozone to be differ on alert days and non-alert days. Maxtemp was the variable for maximum daily temperature (C), along with its square and cubic version. Average dew point (C) was included in the model as dewpt, along with its square and cubic terms. These values were lagged and averaged as appropriate for the specific model. Indicator variables for year and day of the week were included, as well as hospital terms representing whether or not a given hospital was reporting patients on a specific day. A term for “day of the year” (example: May 1st = 1) was included along with its square and cubic version to account for recurrent seasonal trends in the exposure and outcome within the warm season.

Two different groups of models were run; those excluding interaction terms between alert and ozone, and those including interaction terms. Non-interaction models were run with and without a term for PM_{2.5} (population weighted 24 hour average), and with and without a control for alert status. The models including interaction terms were each run twice, once including a term for PM_{2.5}, and once excluding a term for PM_{2.5}. Estimation of the overall effect of alert status on asthma ED visits was obtained from the no interaction models.

$$\begin{aligned}
\text{Model 1: Log(number of ED visits on day } t) = & O_3 + \text{alert} + (O_3 * \text{alert}) \\
& + \text{maxtemp} + \text{maxtemp}^2 + \text{maxtemp}^3 \\
& + \text{dewpt} + \text{dewpt}^2 + \text{dewpt}^3 \\
& + \text{year}_{2005} + \text{year}_{2006} + \text{year}_{2007} \\
& + \text{year}_{2008} + \text{year}_{2009} \\
& + \text{day}_{\text{tues}} + \text{day}_{\text{wed}} + \text{day}_{\text{thurs}} \\
& + \text{day}_{\text{fri}} + \text{day}_{\text{sat}} + \text{day}_{\text{sun}} \\
& + \text{day_of_year} + \text{day_of_year}^2 \\
& + \text{day_of_year}^3 \\
& + H3 + H8 + H10 + H29 + H30 + H54 \\
& + H59 + H72 + H80 + H81 + H100 + H118 \\
& + H123 + H140 + H143 + H145 + H146 \\
& (+\text{PM}_{2.5})
\end{aligned}$$

The above is an example of a same day model with an interaction and an optional term for $\text{PM}_{2.5}$. The two other sets of models are lagged one day for a “yesterday” models, and use three day moving averages for the “three day” models. Weather is included in the model because it is correlated with ozone levels, and may directly affect both exposure and health. Ozone values included in the model were scaled to 20 parts per billion (ppb) in order to present results for a meaningful change in ozone levels.

C. Results

There were a total of 43,732 ED visits, and an average of 47.6 ED visits per day across all the hospitals included. Descriptive statistics are presented in Table 1. The first

panel shows the counts for alert days overall, and broken down by year, month, day of the week. There is also the average maximum daily temperature, PM_{2.5}, ozone, and dew point. There were 168 alert days, which accounts for 18% of the 918 days included in the analysis. The second panel in Table 1 shows the same measures on non-alert days. There were 750 non-alert days, spread over six years. Even on the hottest months of the year, the percent of non-alert days never dips below 73%. May and September had the lowest proportion of alert to non-alert days. June had the highest percentage of alert days, with a dip in July, and increasing again in August. There is also considerable variability in the number of alert days per year. Two thousand four and 2009 have the fewest alert days, with 16 and 15 respectively. Two thousand eight had the most alert days with 41. The proportion of alert days is very similar on weekends and weekdays. As expected, maximum daily temperature, PM_{2.5}, and ozone levels were all notably higher on alert days. Only average dew point was lower on non-alert days than on alert days.

Table 2 divides ozone and PM_{2.5} into deciles for same day and three day moving average, and tracks the number of alert days that fall into each decile. For example, zero alert days have a same day ozone or PM_{2.5} value that falls within the bottom decile of that air pollutant's overall range. Predictably, the majority of alert days fall within the top five deciles across all categories. Alert days falling within the lower deciles of ozone or PM_{2.5} are explained by a different air pollutant driving the AQI rating on that particular day.

Table 3 contains the regression results from the no interaction models. In model 1 (same day) without a control for alert days, there is a 0.2% increase in ED visits per 20 ppb increase in ozone levels (p=0.9457). Model 1 including an alert term has a change in

estimate of 0.4% ($p=0.8681$), and an 8.5% reduction in the rate of ED visits on alert days versus non-alert days ($RR=0.915$, $p=0.0053$) when including an alert term. Model 2 (same as model 1 without control for $PM_{2.5}$) estimates a 2.4% increase in ED visits ($p=0.2639$) without an alert term, and a 3.5% increase ($p=0.1110$) including an alert term. When model 2 includes an alert term, there is an estimated 6.7% decrease in the rate of asthma ED visits on alert days ($p=0.0228$). The model 3 (previous day exposures, with control for $PM_{2.5}$) estimated increase per 20 ppb ozone without a control for alert days is 3.9% ($p=0.1362$). When this model includes an alert term the estimate for ozone increases to 4.9% ($p=0.0651$), and the estimated decrease in the rate of ED visits for alerts is 8.4% ($p=0.0023$). Model 4 (previous day, without control for $PM_{2.5}$) without an alert term estimates a 4.1% increase in ED visits per 20 ppb increase in ozone ($p=0.0539$). With the alert term the model 4 estimate rises to 6.1% ($p=0.0071$), and the alert estimate is a decrease of 7.9% ($p=0.0033$). The estimated change in asthma and wheezing ED visits in model 5 (3-day moving average, with control for $PM_{2.5}$) excluding an alert term is a 4.8% increase per 20 ppb increase in ozone ($p=0.1988$). When the model includes a term for alert status the increase in ED visits is estimated to be 5.3% ($p=0.1505$), with a 7.4% decrease in ED visits for days with an alert in the previous three days ($p=0.0052$). The final model, model 6 (3-day moving average, without control for $PM_{2.5}$), estimates a 6.2% increase in ED visits ($p=0.0237$) without an alert term, and an 8.3% increase with an alert term. There is an estimated 6.7% decrease in ED visits on alert days in model 6 when an alert term is included ($p=0.0094$) in the model.

The regression results from the models including an interaction term between ozone and alerts are summarized in Table 4. The first two columns contain the estimates

for the “same day” models. Model 1 includes $PM_{2.5}$ as a confounder in the model, while Model 2 does not. Estimates in Model 1 indicate a non-statistically significant 0.3% decrease ($RR=0.997$, $p=0.9522$) in the rate of asthma visits from a 20 ppb increase in ozone for both alert days, and a 0.5% increase on non-alert days ($p=0.8377$). Model 2, the “same day” model showed a 3.2% increase ($p=0.4569$) in asthma visits on alert days, and a 3.5% increase ($p=0.1231$) on non-alert days.

On alert days, the “previous day” exposure models showed a 6.9% increase in ED visits for the model including $PM_{2.5}$, and a 8.2% increase when excluding $PM_{2.5}$ ($p=0.1056$ and $p=0.0362$, respectively). While non-alert days had an increase of 4.4% and 5.5% including and excluding a $PM_{2.5}$ term ($p=0.1082$ and $p=0.0234$).

The “previous day” and “three day moving average” models excluding $PM_{2.5}$ were the only models with a significant association between ozone and asthma ED visits. Model 5 included a term for $PM_{2.5}$, and estimated an increase of 4.0% in the rate of asthma ED visits on alert days, and 5.7% on non-alert days ($p=0.4298$ and $p=0.1364$). Model 6 excluded $PM_{2.5}$ and estimated a 7.6% increase in ED visits per 20 ppb increase in ozone on alert days ($p=0.0741$), and an increase of 8.6% on non-alert days ($p=0.0064$).

D. Discussion

i. Findings

When comparing estimated rate ratios for ozone with and without controls for alert days, the increase in ED visits is higher and the p-values are lower across all the models when air quality was included (Table 3). This suggests that when alert status is

taken into account, the health impact of ozone increases slightly and the estimates are more precise. Overall, while the pattern is consistent, there is only a modest change in estimates and similar confidence intervals with and without a term for alerts. Positive alert status itself was a significant predictor of decreased ED visits on alert days versus non-alert days across all no interaction models, which may indirectly indicate avoidance behaviors and measures being taken by the population to prevent asthma exacerbations on these days.

The associations found in the interaction models are, however, less straight forward. A 20 ppb increase in ozone was associated with more ED visits on alert days than non-alert day in two of our six models, though the change was very slight. When comparing the estimated change on alert and non-alert days we saw little, if any, difference. In fact, in some cases the estimated increase in ED visits for a 20 ppb increase in ozone was higher on non-alert days. Contrary to our hypothesis, alert days did not appear to be associated with a weaker linear association between ozone and asthma ED visits. As shown in Table 4 the ozone-alert interaction term was not significant in any of the models. This supports the conclusion that the estimated effect for ozone is very similar on alert and non-alert days. One explanation is that children in the metropolitan Atlanta area, or their parents, do not modify their behaviors on alert days enough to affect the association examined here. Since asthma is associated with lower SES, those parents may be less aware of the AQI than parents of higher SES. Alternatively, it is possible that the Atlanta population does modify behavior in response to the AQI, but that the effects of ozone on asthma ED visits are nonlinear, with a greater effect for each ppb increase in ozone at the high end of the concentration distribution. Since alert days tend to occur on

days with higher concentrations of ozone than non-alert days, it is difficult to assess this possible nonlinearity of associations in our data. Overall, we observed stronger associations between ozone and asthma ED visits when exposure were lagged. The lack of evidence for an association between same-day ozone and asthma ED visits may be attributable to the diurnal pattern of ozone, with peak concentrations occurring late in the afternoon. If the effects of ozone are delayed even a few hours, any increase in asthma ED visits may not be observable until the following day.

Additional observations in both no interaction and interaction models indicated that $PM_{2.5}$ was a confounder between outdoor ambient ozone levels and ED visits. When looking at the rate ratios for the no interaction models without controls for alert days the models containing $PM_{2.5}$ have consistently lower p-values than the models excluding $PM_{2.5}$. The same pattern holds for the estimates when alert days are included in the model. This indicated that $PM_{2.5}$ confounds the association between ozone levels and ED visits whether or not alert status is taken into account. The regression estimates in the interaction models excluding $PM_{2.5}$ were also higher across the board, suggesting that $PM_{2.5}$ contributes to bias upwards away from the null in most models.

ii. Strengths and Limitations

This study benefits from the use of direct and reliable ambient air pollution measurement from official monitoring stations, as well as hospital records and meteorological data. We did not have to impute any values, preventing additional error in our data. One of the main limitations of the study is the limited power from the relatively low number of alert days. Failure to detect an interaction may reflect this drawback

within our dataset. Additionally, the premise of our analysis requires an assumption that the effect of ozone is linear. It is, however, possible that the association is non-linear, in which case our regressions would not be appropriate for assessing interaction. On a more general note, any result here may not apply to other geographical areas where the air quality index is driven by pollutants other than ozone and PM_{2.5}.

iii. Implications

Given the association between air pollution and asthma, it is important to understand what levels of exposure are safe for vulnerable populations, including children. Part of this is evaluating the association between ozone levels and ED visits for asthma and wheezing, which may differ on alert and non-alert days due to avoidance behaviors. Neidell and Kinney's 2010 examination found a 0.016% increase in asthma hospitalizations when now accounting for air quality forecasts, which was significantly lower than the 0.037% increase when air quality information was included in their model.

In this study of ambient ozone levels and ED visits for asthma, models were run including and excluding terms for alert status, PM_{2.5}, and an interaction term for ozone and alert status. Like the previous study, the association between ozone and the number of ED visits per day differed depending on whether or not air quality information was included in the model, with slightly stronger rate ratios for ozone and asthma ED visits when air quality alerts were controlled. However, there was little difference in the linear association between ozone and asthma ED visits when estimated separately on alert and non-alert days. This suggests that air quality information other than ozone is important to account for when examining the health effects of ozone, but that the associations are not

notably different on alert versus non-alert days. While there appears to be some preliminary agreement between the two studies, further examination is needed. Of particular importance are a studies with larger numbers of alert days, analyses that do not assume a linear association with ozone, and finally looking at this association in areas of the country where AQI is not driven primarily by ozone levels.

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Tables

Table 1. Descriptive statistics, May-September 2004-2009 Atlanta metropolitan area (N=918 days)

	Alert Days		Non-Alert Days	
	No.	%	No.	%
Same day	168	18.30	750	81.70
Past two days	233	25.38	685	74.62
Past three days	292	31.81	626	68.19
Year				
2004	15	9.80	138	90.20
2005	27	17.65	126	82.35
2006	33	21.57	120	78.43
2007	37	24.18	116	75.82
2008	41	26.80	112	73.20
2009	15	9.80	138	90.20
Month				
May	16	8.60	170	91.40
June	53	29.44	127	70.56
July	36	19.35	150	80.65
August	48	25.81	138	74.19
September	15	8.33	165	91.67
Day of the week				
Weekday	120	18.81	518	81.19
Weekend	46	17.56	216	82.44
	Mean	SD	Mean	SD
Maximum daily temperature (C°)	32.74	2.56	28.84	3.30
24hr PM25 (ug/m3) ^a	23.25	8.77	14.32	5.99
8hr maximum O ₃ (ppb) ^a	68.61	12.01	48.89	13.72
Average dew point (C°)	17.19	3.55	17.33	4.13

^a Population weighted average

Table 2. Number of alert days by decile of ozone or PM_{2.5} (single day or 3-day moving average), N=168

Decile of air pollutant	8 hr max O₃ (ppb)^a Same Day	8 hr max O₃ 3 Day Average	24 hr average PM_{2.5} (ug/m³)^a Same day	24 hr average PM_{2.5} 3 Day Average
1	0	0	0	0
2	2	0	2	5
3	1	0	7	3
4	4	3	8	6
5	6	4	8	11
6	10	7	5	17
7	20	12	29	18
8	22	26	24	16
9	37	44	28	30
10	66	72	57	62

^a Population weighted average in study area

Table 3. Modeling results with and without control for alert days (no interaction terms) N=918 days

Rate Ratio	Same Day (lag 0)		Previous Day (lag 1)		Three Day Moving Average (lag 0-1-2)	
	1	2	3	4	5	6
	Including PM _{2.5}	Excluding PM _{2.5}	Including PM _{2.5}	Excluding PM _{2.5}	Including PM _{2.5}	Excluding PM _{2.5}
<u>Model without control for alert days</u>						
Ozone (per 20 ppb)	1.002	1.024	1.039	1.041	1.048	1.062
CI	[0.953, 1.053]	[0.983, 1.067]	[0.988, 1.093]	[0.999, 1.085]	[0.976, 1.125]	[1.008, 1.120]
P-value	[0.9457]	[0.2639]	[0.1362]	[0.0539]	[0.1988]	[0.0237]
<u>Model including control for alert days</u>						
Ozone (per 20 ppb)	1.004	1.035	1.049	1.061	1.053	1.083
CI	[0.956, 1.055]	[0.992, 1.079]	[0.997, 1.103]	[1.016, 1.107]	[0.981, 1.131]	[1.026, 1.143]
P-value	[0.8681]	[0.1110]	[0.0651]	[0.0071]	[0.1505]	[0.0039]
Alert	0.915	0.933	0.916	0.921	0.926	0.933
CI	[0.860, 0.974]	[0.878, 0.990]	[0.866, 0.969]	[0.8719, 0.9729]	[0.878, 0.977]	[0.8853, 0.9831]
P-value	[0.0053]	[0.0228]	[0.0023]	[0.0033]	[0.0052]	[0.0094]

Table 4. Modeling results with control for alert days and interaction term between ozone concentration and alert N=918

Ozone rate ratio (20 ppb)	Same Day (lag 0)		Previous Day (lag 1)		Three Day Moving Average (lag 0-1-2)	
	1	2	3	4	5	6
	Including PM _{2.5}	Excluding PM _{2.5}	Including PM _{2.5}	Excluding PM _{2.5}	Including PM _{2.5}	Excluding PM _{2.5}
Alert Days	0.997	1.032	1.069	1.082	1.040	1.076
CI	[0.913, 1.089]	[0.950, 1.121]	[0.986, 1.158]	[1.005, 1.165]	[0.944, 1.145]	[0.993, 1.165]
P-value	[0.9522]	[0.4569]	[0.1056]	[0.0362]	[0.4298]	[0.0741]
Non-alert Days	1.005	1.035	1.044	1.055	1.057	1.086
CI	[0.955, 1.058]	[0.991, 1.082]	[0.991, 1.100]	[1.007, 1.104]	[0.983, 1.138]	[1.024, 1.153]
P-value	[0.8377]	[0.1231]	[0.1082]	[0.0234]	[0.1364]	[0.0064]
Main Effects (Wald test) Interaction Term O ₃ *Alert						
P-value	[0.8526]	[0.9387]	[0.5561]	[0.5138]	[0.6939]	[0.8172]

Chapter III: Summary

Given the association between air pollution and asthma, it is important to understand what levels of exposure are safe for vulnerable populations, including children. Part of this is evaluating the association between ozone levels and ED visits for asthma and wheezing, which may differ on alert and non-alert days due to avoidance behaviors. Neidell and Kinney's 2010 examination found a 0.016% increase in asthma hospitalizations when now accounting for air quality forecasts, which was significantly lower than the 0.037% increase when air quality information was included in their model.

In this study of ambient ozone levels and ED visits for asthma, models were run including and excluding terms for alert status, $PM_{2.5}$, and an interaction term for ozone and alert status. Like the previous study, the association between ozone and the number of ED visits per day differed depending on whether or not air quality information was included in the model, with slightly stronger rate ratios for ozone and asthma ED visits when air quality alerts were controlled. However, there was little difference in the linear association between ozone and asthma ED visits when estimated separately on alert and non-alert days. This suggests that air quality information other than ozone is important to account for when examining the health effects of ozone, but that the associations are not notably different on alert versus non-alert days. While there appears to be some preliminary agreement between the two studies, further examination is needed. Of particular importance are a studies with larger numbers of alert days, analyses that do not assume a linear association with ozone, and finally looking at this association in areas of the country where AQI is not driven primarily by ozone levels.

Appendix A. Breakpoints for AQI calculations (7)

This Breakpoint...						...equal this AQI		...and this category
O ₃ (ppm) 8-hour	O ₃ (ppm) 1-hour ¹	PM ₁₀ (µg/m ³)	PM _{2.5} (µg/m ³)	CO (ppm)	SO ₂ (ppm)	NO ₂ (ppm)	AQI	
0.000 - 0.064	-	0 - 54	0.0 - 15.4	0.0 - 4.4	0.000 - 0.034	(²)	0 - 50	Good
0.065 - 0.084	-	55 - 154	15.5 - 40.4	4.5 - 9.4	0.035 - 0.144	(²)	51 - 100	Moderate
0.085 - 0.104	0.125 - 0.164	155 - 254	40.5 - 65.4	9.5 - 12.4	0.145 - 0.224	(²)	101 - 150	Unhealthy for Sensitive Groups
0.105 - 0.124	0.165 - 0.204	255 - 354	65.5 - 150.4	12.5 - 15.4	0.225 - 0.304	(²)	151 - 200	Unhealthy
0.125 - 0.374 (0.155 - 0.404) ⁴	0.205 - 0.404	355 - 424	150.5 - 250.4	15.5 - 30.4	0.305 - 0.604	0.65 - 1.24	201 - 300	Very unhealthy
(³)	0.405 - 0.504	425 - 504	250.5 - 350.4	30.5 - 40.4	0.605 - 0.804	1.25 - 1.64	301 - 400	Hazardous
(³)	0.505 - 0.604	505 - 604	350.5 - 500.4	40.5 - 50.4	0.805 - 1.004	1.65 - 2.04	401 - 500	Hazardous

Appendix B. Health guidelines for AQI pollutant levels (11)

AQI Value	Ozone	Particle Pollution	Carbon Monoxide	Sulfur Dioxide
Good (0 - 50)	None	None	None	None
Moderate (51-100*)	Unusually sensitive people should consider reducing prolonged or heavy outdoor exertion.	Unusually sensitive people should consider reducing prolonged or heavy exertion.	None	None
Unhealthy for Sensitive Groups (101-150)	The following groups should reduce prolonged or heavy outdoor exertion: people with lung disease, children and older adults, people who are active outdoors	The following groups should <u>reduce prolonged or heavy</u> outdoor exertion: people with heart or lung disease, children and older adults	People with heart disease, such as angina, should reduce heavy exertion and avoid sources of carbon monoxide, such as heavy traffic.	People with asthma should consider reducing exertion outdoors.
Unhealthy (151-200)	People with lung disease, children and older adults, people who are active outdoors should avoid prolonged or heavy outdoor exertion. Everyone else should limit prolonged outdoor exertion.	The following groups should <u>avoid prolonged or heavy</u> exertion: people with heart or lung disease, children and older adults. Everyone else should reduce prolonged or heavy exertion.	People with heart disease, such as angina, should reduce moderate exertion and avoid sources of carbon monoxide, such as heavy traffic.	Children, asthmatics, and people with heart or lung disease should reduce exertion outdoors.
Very Unhealthy (201-300)	People with lung disease, children and older adults, people who are active outdoors should avoid all outdoor exertion. Everyone else should limit outdoor exertion.	The following groups should <u>avoid all</u> physical activity outdoors: people with heart or lung disease, children and older adults. Everyone else should avoid prolonged or heavy exertion.	People with heart disease, such as angina, should avoid exertion and sources of carbon monoxide, such as heavy traffic.	Children, asthmatics, and people with heart or lung disease should avoid outdoor exertion. Everyone else should reduce exertion outdoors.

* AQI of 100 for ozone corresponds to an ozone level of 0.075 parts per million (averaged over 8 hours). For particles up to 2.5 micrometers: An AQI of 100 corresponds to 35 micrograms per cubic meter (averaged over 24 hours). For particles up to 10 micrometers: An AQI of 100 corresponds to 150 micrograms per cubic meter (averaged over 24 hours). An AQI of 100 for carbon monoxide corresponds to a level of 9 parts per million (averaged over 8 hours). An AQI of 100 for sulfur dioxide corresponds to a level of 75 parts per billion (averaged over one hour).