

Health Effects of Ozone and Other Environmental Measures on Children's Respiratory Health in the Indianapolis Metropolitan Area, 1997-1999

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Abstract

This study examines the effects of low to moderate air pollution and meteorology on the number of children who sought medical treatment for asthma and other respiratory diseases and were admitted to one of 20 Indianapolis, Indiana metropolitan area hospitals (inpatient data). Emergency room and hospital clinic visits that did not result in a hospital admission are not included in this analysis. Using Multivariate Logit Analysis, the study demonstrates a statistically significant negative association for asthma and ozone, dew point, temperature, and relative humidity and a statistically significant positive association for asthma and nitrogen dioxide and sulfur dioxide. The association was not significant between other respiratory diseases and the air pollution and meteorology measures.

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INTRODUCTION

It is estimated that the prevalence of asthma has increased approximately 50 percent over the last 10 to 15 years on a global basis (NIH 1998). Children are especially vulnerable to asthma, and the asthma rate in children has been increasing more than for adults. On a global basis, asthma is the single most common chronic disease reason that children miss school (NIH 1998), and 35 percent of children with asthma experience significant pain or discomfort from this disease.

In the past two decades, the rate and number of asthmatic cases among American children has grown at a dramatic pace (CDC 1999; NIH 1999), and the increase in asthma is expected to continue (Pew 2000). Asthma results in extensive utilization of health care and asthmatic children utilize health care services more extensively and at a higher rate than do asthmatic adults for outpatient visits, emergency department visits, and hospitalizations (CDC 2001). Poor children are at greater risk, and among children, unlike adults, boys (males) are more likely to have asthma than girls (females) (NIH 1999).

In Indiana, the estimated self-reported asthma prevalence is

estimated to be 6.7 percent of the general population (NIH 1999). During the period 1990-1995, blacks in Indiana experienced a death rate slightly more than two times that of whites for asthma as the underlying cause (Mannino et al. 1998). Asthma has been identified as the number one cause of avoidable hospital admissions for children less than 18 years of age in the Indianapolis metropolitan area (Bowen Research Center 1996).

The Indianapolis Metropolitan Asthma Study focuses on outdoor air pollutant, meteorological, and social factors that may be associated with hospital admissions of children for asthma and other respiratory disease in the Indianapolis metropolitan area of Indiana.

LITERATURE REVIEW

Since the 1980s, there have been hundreds of human exposure and epidemiological studies to evaluate the role that specific air pollutants, singly or in combination, play in the causation and exacerbation of respiratory disease. Human laboratory exposure studies have demonstrated that ozone produces three types of response in human lungs: 1) irritative cough and substernal pain on inspiration, 2) decrements in forced vital capacity and forced expiratory volume, and 3) neutrophilic inflammation of the airway submucosa accompanied by biochemical changes (American Thoracic Society 1996). Field studies have also produced

evidence that spirometric decrements are related to ozone exposure in “naturally” exposed children and adults engaging in outdoor activities (American Thoracic Society, 1996). Some studies report that symptoms and medication use also increase with exposure to air pollution in general, and ozone appears to be a key pollutant in these field studies (American Thoracic Society 1996).

The relationship between asthma and other pollutants (in children and adults) and medical treatment has also been studied in epidemiological health care studies (in which patients are examined and/or tested) and in studies that utilize administrative records of admission to hospitals, emergency rooms, or home visits by physicians. The results of these studies for children and adults are mixed. Some studies demonstrate that ozone and other pollutants are important, but others do not (Balmes 1993; American Thoracic Society 1996). Of the 25 epidemiological studies of childhood emergency room visits, hospital admissions, and house calls for asthma that are included in this literature review, 12 studies report a statistically significant positive relationship, 11 report non-significant relationships, and three report statistically significant negative relationships between ozone concentrations and respiratory health in children.

Of the 12 studies reporting positive effects between ozone and respiratory health, 11 demonstrate that children living in cities around the world (Atlanta, Helsinki, London, Mexico City, southern Ontario, Paris, and Singapore) sought more medical treatment for asthma as ozone levels increase (Anderson et al. 1998; Buchdahl et al. 1996; Burnett et al. 1994; Chew et al. 1999; Fauroux et al. 2000; Medina et al. 1997; Pönkä 1991; Pönkä and Virtanen 1996; Romieu et al. 1995; Tolbert et al. 2000; White et al. 1994). One study found a relationship between ozone and other respiratory conditions (Bates et al. 1990). Four of these studies report a positive relationship for asthma during the summer months (Anderson et al. 1998; Romieu et al. 1995; Tolbert et al. 2000; White et al. 1994) and one for ozone and other respiratory conditions (Bates et al. 1990).

No statistically significant effect for ozone and asthma or other respiratory conditions is reported in studies undertaken in Hong Kong, London, Melbourne, Mexico, southern Ontario, Seattle, Sidney, St. John (New Brunswick), and Vancouver (Atkinson et al. 1999; Bates et al. 1990; Bates and Sizto 1983, 1987; Burnett et al. 1995; Morgan et al. 1998; Rennick and Jarman 1992; Rosas et al. 1998;

Schwartz et al. 1993; Stieb et al. 1996; Sunyer et al. 1997; Tseng et al. 1992). One of these studies is a meta analysis of data from Barcelona, Helsinki, London, and Paris (Sunyer et al. 1997). Ozone is not significant for asthma in five studies that included summer season data (Bates et al. 1990; Bates and Sizto 1983, 1987; Rosas et al. 1998; Stieb et al. 1996). Three studies report a negative but statistically significant effect for ozone (Atkinson et al. 1998; Garty et al. 1998; Holmén et al. 1997).

The findings are also mixed for other pollutants and the meteorological variables. Sulfur dioxide and nitrogen dioxide, however, emerge as two additional important air pollution variables related to childhood respiratory health. Eight of 21 studies that include sulfur dioxide demonstrate a positive and statistically significant relationship between medical treatment by children for sulfur dioxide and the outcomes measures. Seven of these studies report a positive relationship for sulfur dioxide and asthma (Anderson et al. 1998; Atkinson et al. 1999; Buchdahl et al. 1996; Chew et al. 1999; Garty et al. 1998; Medina et al. 1997; Romieu et al. 1995; Sunyer et al. 1997), and Bates et al. (1990) report a significant positive relationship for sulfur dioxide and other respiratory conditions in winter. One study reports a significant negative relationship for sulfur dioxide (Tseng et al. 1992).

Nine of 21 studies that include some measure of the oxides of nitrogen report a statistically significant positive relationship between medical treatment visits by children for asthma in children (Anderson et al. 1998; Atkinson et al. 1999; Chew et al. 1999; Garty et al. 1998; Holmén et al. 1997; Medina et al. 1997; Morgan et al. 1998; Pönkä 1991; Sunyer et al. 1997). Bates and Sizto (1987) report a negative relationship in winter but a not significant relationship during the summer.

Of the meteorological variables included in the reviewed studies, only temperature is included in enough studies to allow a summary of findings. The findings for temperature are difficult to interpret because a large proportion of the studies (6 of 16 studies) that include temperature in the analysis of the age group 0-14 years do not provide enough information to discern the role of temperature. Three of the remaining 10 studies report a positive association between the outcome measures and temperature (Bates and Sizto 1987; Rosas et al. 1998; Tolbert et al. 2000), two report a negative association (Buchdahl et al. 1996, Pönkä and Virtanen 1996), and five report that temperature was not

significant (Bates et al. 1990; Bates and Sizto 1987; Pönkä 1991, Romieu et al. 1995; White et al. 1994). There are five studies that include relative humidity in the statistical analysis, and in four, the relationship for relative humidity is not significant, and one does not provide enough information to discern the relationship.

METHODS

STUDY AREA AND POPULATION

The study area is the Indianapolis Metropolitan Statistical Area (MSA), which consists of nine counties in central Indiana. The study population includes all children, ages 1 to 17 years, having ZIP codes in the Indianapolis metropolitan area during the period of May 1, 1997 through September 30, 1999, who are admitted to a hospital. Infants younger than one year of age are excluded because of the difficulty of making an asthma diagnosis in this age group. The study population excludes children who experienced asthma or other respiratory symptoms but were not admitted to a metropolitan area hospital. Although the Indianapolis Metropolitan Asthma Study sought to include outpatient data—including visits to the emergency rooms—practical limitations on the availability of or access to these data, study resources, and time constraints allowed only for the analysis of data from this more restricted study population (in-patient data). The Indiana Hospital and Health Association (IHHA) provided the hospital admissions data used in this study with permission of 20 member hospitals in the nine-county Indianapolis metropolitan area.

AIR QUALITY MEASUREMENTS

The Indiana Department of Environmental Management (IDEM) provided air quality data from its monitoring network, which includes sites that are located in industrial, agricultural, commercial, and residential environments in rural, suburban, and urban settings. All of the data provided by IDEM, which are a part of the EPA's Aerometric Information Retrieval System (AIRS) database, are quality assured. During the period of study, data were collected from nine ozone stations (ultraviolet (UV) photometry), one nitrogen dioxide station (chemiluminescent), and four sulfur dioxide stations (pulsed fluorescent monitors at three stations for all years; one station with a pulsed fluorescent monitor for 1997 and a UV stimulated fluorescent monitor for 1998-99).

Overall, the air quality in the study area can be described as good to moderate based on comparisons with the National

Ambient Air Quality Standards (NAAQS) and the EPA's Air Quality Standards Index (AQI) (U.S. EPA 2001a, b). During the period of study, the mean concentrations are 0.038 ± 0.011 ppm for ozone, 0.016 ± 0.007 ppm for nitrogen dioxide, and 0.005 ± 0.003 ppm for sulfur dioxide. There are 12 days in 1997 that had unhealthy ozone as defined by the EPA's AQI for ozone, 19 days in 1998, and 21 days in 1999 (U.S. EPA 2001c, 221). In comparison to 94 other metropolitan statistical areas in the United States, Indianapolis' ranking worsened over the 3-year period, moving from 59th in 1997 to 61st in 1998 and to 68th in 1999 (U.S. EPA 2001c, Table A-18, pp 221-222). The daily mean nitrogen dioxide and sulfur dioxide levels are about four to five times, respectively, below the EPA annual arithmetic standards for these pollutants (U.S. EPA 2001 a).

METEOROLOGICAL MEASUREMENTS

The meteorological measurements (temperature, relative humidity, and dew point) were obtained from the National Weather Service Indianapolis International Airport weather station (NWS 2001). Additional monitoring stations were available for the meteorological variables; however, they are excluded from the study because of the high percentage of missing data. Temperatures are lower in the summer season of 1997 than in 1998 and 1999; precipitation is higher in 1998 than in 1997 and 1999.

DEPENDENT VARIABLE

The dependent variable DIAG3 (diagnosis) classifies the diagnosis of each child's hospital admission record into one of three categories—Asthma, Other Respiratory, and Other Diagnosis—based on the ICD-9-CM code (ICD 2001) reported in each record. Each patient record contains a primary diagnosis field (DIAG01) and 10 or more secondary diagnoses (DIAG02 through DIAGnn). For the purposes of this study, a patient is categorized, as an Asthma case, if any one of the ICD-9 codes in the patient record for the first 11 fields is 493 (including any fourth and fifth digit extension). The remaining records in the database are then classified as Other Respiratory cases based on the occurrence of one or more ICD-9 codes in the first 11 fields for respiratory infections; conditions for the upper or middle respiratory tract, conditions of the lower respiratory tract, respiratory symptoms, and/or other respiratory classifications. The ICD-9-CM codes in these categories include selected codes from 460-466, 470-478, 480-487, 490-496, 510-519, 748, 786, 011-012, 079, 277. The remaining records, which contain all other diagnostic codes, comprise the Other

Diagnosis category.

for the 48 hours prior to the hospital admission)

EXPLANATORY VARIABLES

The explanatory variables are grouped into three groups: environmental measures (air quality and meteorological variables), social effects measures, and confounding measures.

- 3-day mean (a moving average of the daily mean for the 72 hours prior to the hospital admission)

The analysis strategy includes four measures of ozone, nitrogen dioxide, and sulfur dioxide:

A daily mean was considered to be missing for the air quality and meteorological data if the number of hourly observations was less than 20.

- daily maximum value (highest one-hour mean for each day at each site),
- daily mean (24-hour mean of the individual one-hour means for each day at each site)
- 2-day mean (a moving average of the mean daily ozone concentrations for the 48 hours prior to the hospital admission)
- 3-day mean (a moving average of the mean daily ozone concentrations for the 72 hours prior to the hospital admission)

The social effects variables are Age, Race/Ethnicity, Sex, and Income. Race/Ethnicity is classified as white and nonwhite in this study. Variations in the coding of race and/or ethnicity among the 20 hospitals allowed for this level of detail only. Income is measured by the estimated Median Household Income in 1999 that is associated with the patient's ZIP code.

For ozone, it is assumed that the concentration that is most representative of the child's exposure is the ozone monitoring location that is nearest to the child's home address, calculated as the centroid of the ZIP code coordinates using Geographical Information System (GIS) technology. Nitrogen dioxide exposures are determined by matching each patient's date of admission to a single monitoring site located in Indianapolis. Sulfur dioxide exposures are determined by matching each patient's date of admission to the mean sulfur dioxide level calculated from the four monitoring locations used in the study.

Confounding variables, Day of Week and Admission Source, are included in this analysis to adjust for the self-selection effects inherent in this type of study design. Admission source is a dichotomous variable indicating whether patients were admitted after first using the emergency room or visiting the hospital as an outpatient. Routine admissions and transfers are grouped into the category, Other. This variable does not contain information on children who used the emergency room or were outpatients, but were not admitted to the hospital. For additional information on the use of confounding variables in epidemiological studies, see Kleinbaum et al. (1982, 242-265).

For meteorological measures, the analysis is based on five measures of temperature, relative humidity, and dew point from a single monitoring site:

- daily maximum (highest one-hour observation for each day)
- daily minimum (lowest one-hour observation for each day)
- daily mean (24-hour mean of the individual one-hour observations for each day)
- 2-day mean (a moving average of the daily mean

STATISTICAL METHODOLOGY

The analysis used to explain the diagnosis (DIAG3) is a Multinomial Logit Model, as described by Agresti (1990, pp. 306-346). Each model estimates two logit functions representing the logit of the Asthma versus the Other Diagnosis categories and the logit of the Other Respiratory Disease versus the Other Diagnosis. The third category of the variable DIAG3, Other Diagnosis, is used throughout the analysis as the base category.

The results presented in this report are the estimated probabilities of an asthma diagnosis and other respiratory disease diagnosis for each level of the explanatory variable. These estimated probabilities are calculated from the logit estimates in the final model using the CATMOD procedure in the SAS software (Stokes et al. 2000).

A number of simple statistical models using the individual

explanatory variables are fitted to the data, but only those models that meet the Goodness of Fit (GOF) and explanatory variables criteria are reported below. Acceptable models have a p-value for the GOF test greater than 0.05 and a p-value less than 0.05 for the explanatory variable. For the ozone, nitrogen dioxide, and sulfur dioxide variables, 10 models are fitted for each pollutant, consisting of five different measures and two model assumptions—that the explanatory categories were ordered and unordered. The ordered category assumption tests whether the response variable (DIAG3) levels change in a positive or negative fashion, whereas the unordered assumption only tests whether one or more of the levels of the explanatory variable differ from each other. For the temperature, relative humidity, and dew point variables, there are six measures and two model forms (ordered and unordered) for a total of 12 models for each of the three variables.

The evaluation of the effects of the social variables Race/Ethnicity, Sex, Age, and Median Household Income include fitting simple models for each variable, in the case of Age and Income, for ordered and unordered categories (six models), and all two and three variable combinations. The confounding variables, Day of the Week Admitted and Admission Source, are each evaluated as simple models and a multivariate model.

RESULTS

ENVIRONMENTAL EFFECTS

Table 1 summarizes the findings for the six environmental measures, and the findings from this study are compared with the trend, if any, reported in the literature review.

Figure 1

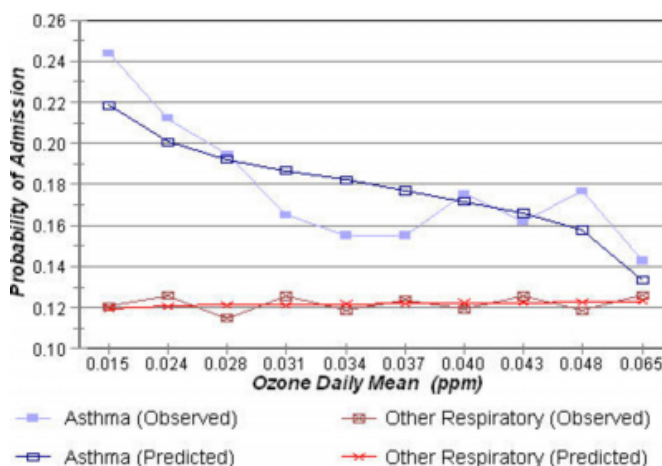
Table 1: Choice of Best Environmental Measure and Summary of Statistical Tests

Environmental Measure	Best Measure	Research Hypothesis	Research Hypothesis Supported?
Ozone	Daily mean ordered categories	a positive relationship between ozone and asthma	a statistically significant negative association for asthma; no relationship for other respiratory diseases
Nitrogen Dioxide	3-day Mean unordered categories	a positive relationship between nitrogen dioxide and asthma	a statistically significant positive association for asthma; no relationship for other respiratory diseases
Sulfur Dioxide	2-day Mean Unordered categories	a positive relationship between sulfur dioxide and asthma	a statistically significant positive association for asthma; no relationship for other respiratory diseases
Dew Point	2-day Mean ordered categories	insufficient research findings; no hypothesis	a statistically significant negative association for other respiratory diseases
Temperature	Daily Minimum ordered categories	a positive relationship between temperature and asthma	a statistically significant negative relationship for asthma; no relationship for other respiratory diseases
Relative Humidity	Daily Minimum ordered categories	insufficient research findings; no hypothesis	a statistically significant negative association for asthma; no relationship for other respiratory diseases

The Ozone Daily Mean provides a statistically significant, but negative association for asthma hospital admissions, but no statistically significant association on other respiratory diseases (Figure 1).

Figure 2

Figure 1: Ozone Daily Mean Effects on Admissions for Respiratory Illness



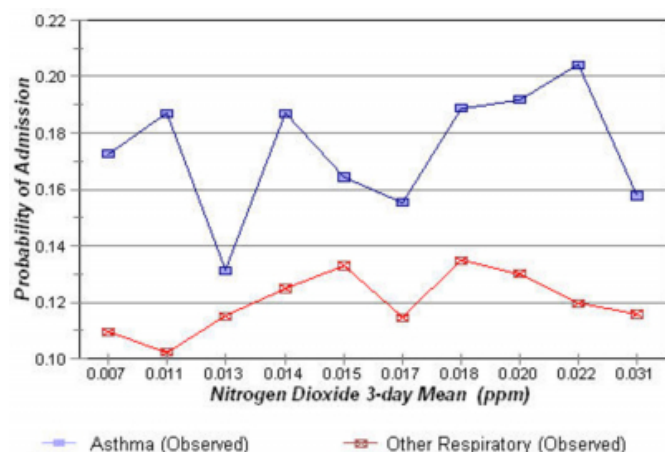
For ozone, the data support a finding namely, that hospital admissions for asthma decrease as ozone levels increase—that is contrary to the hypothesis. The final model estimates that as ozone concentrations increase from about 0.015 ppm to 0.065 ppm, the estimated probability of an

asthma admission declines from about 0.22 (22 percent) to 0.13 (13 percent).

The literature review, which reports that elevated concentrations of nitrogen dioxide increase the likelihood of children's hospital admissions, is generally confirmed by the 3-day Mean Nitrogen Dioxide model fitted to the Indianapolis data. Figure 2 shows a generally increasing probability of asthma admission, ranging from a low of about 0.013 for 3-day Mean concentrations of 0.013 ppm to a high of over 0.20 for concentrations of 0.020 ppm. The final model does not test the order of the categories; rather, confirms only that the levels of nitrogen dioxide show statistically significant different probabilities of admission for asthma. The finding for the Other Respiratory Disease category is not statistically significant, meaning that variations in nitrogen dioxide are not associated with admissions for other respiratory diseases.

Figure 3

Figure 2: Nitrogen Dioxide 3-day Mean Effects on Admissions for Respiratory Illness



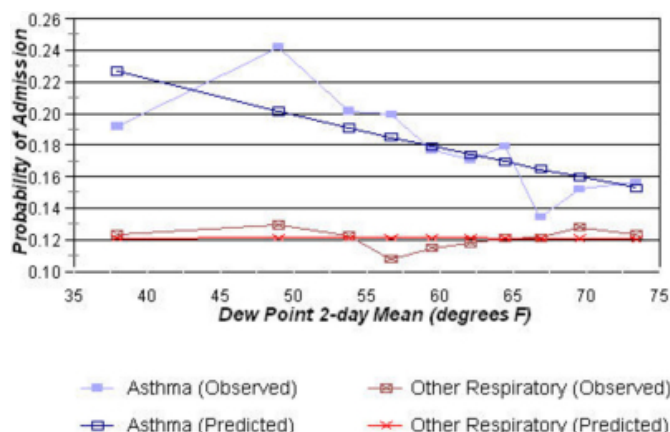
The findings for sulfur dioxide are similar to those reported for nitrogen dioxide. The final model shows a statistically significant association between 2-day Mean Sulfur Dioxide concentrations and admissions for asthma, but no association between it and admissions for other respiratory illnesses. The test of model effects is for unordered categories, and the estimated probabilities show a slight increase in admission probabilities with increased concentrations.

Figure 3 displays the effects of the Dew Point 2-day Mean measure on admissions to a hospital for asthma and other respiratory illness. The figure demonstrates that the probability of admission decreases for asthma as the Dew Point 2-day Mean increases. The model estimates that the

probability of admission is about 0.23 when the dew point is about 38 degrees and drops to less than 0.16 at about 74 degrees. The effect of dew point on asthma admissions is statistically significant; the effect of the Dew Point 2-day Mean on other respiratory illness admissions is not statistically significant. In summary, there is a statistically significant negative (inverse) relationship for dew point on asthma.

Figure 4

Figure 3: Dew Point 2-day Mean Effects on Admissions for Respiratory Illness



For temperature (Daily Minimum) and relative humidity (Daily Minimum), the findings follow a pattern consistent with dew point. All three measures show a statistically significant, negative (inverse) relationship between the measure and asthma admissions. In other words, higher dew point levels, higher daily minimum temperatures, and higher daily minimum relative humidity are associated with lower levels of hospital admissions for asthma. The literature review provides little information for the effects of temperature on asthma, and there are an insufficient number of studies on dew point and relative humidity to form research hypotheses. The data also provide no support for the research hypotheses that admissions for other respiratory illnesses also change as dew point, temperature, or relative humidity rise.

SOCIAL EFFECTS

The effects of four social conditions Race/Ethnicity, Sex, Age (in years), and Income are first examined in a simple, two variable model to determine whether there is an association with admissions. Then, the best social variable predictors are combined into a final multivariate model.

The data support the research hypothesis that as children

age, the probability of admission to a hospital for asthma or other respiratory diseases declines. Children ages 1 to 3 years are most at risk for being admitted for asthma, followed next by children in the 4 through 8 year group, children in the 9 to 14 years group, and lastly, the group 15 to 17 years. Similarly, the probability of admissions for the Other Respiratory diseases category declines, as children grow older.

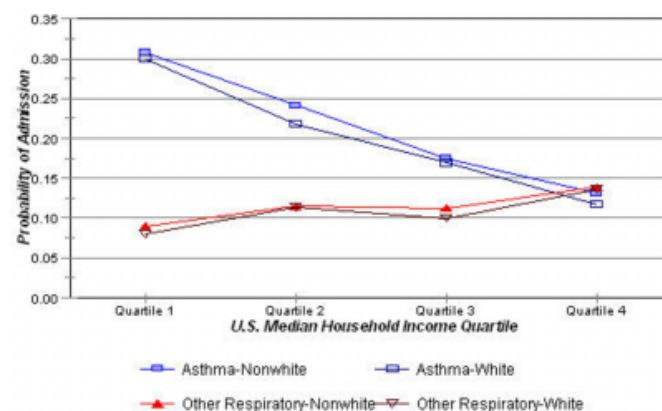
There is a statistically significant difference for the effects of Race/Ethnicity on asthma. Nonwhite children are more likely to be admitted for asthma than white children, a finding consistent with the research literature. Households with incomes in the fourth (upper) quartile of the United States are less likely to be admitted for asthma than lower income groups. It appears that Race/Ethnicity, a stronger measure, is confounded with Income, since nonwhites on average have lower median household incomes than whites. There is a small, statistically significant difference in hospital admissions for girls and boys—boys are more likely than girls to be admitted for asthma and for other respiratory diseases.

The only multivariate model that met the GOF test criterion ($p < 0.05$) is Race and Median Household Income Percentile (unordered categories). Other multivariate models tested suggest the presence of interaction effects, which involve more complex relationships between different levels of the predictor variables.

Figure 4 reports the predicted probabilities of admission for asthma and other respiratory diseases by Race/Ethnicity and U.S. Median Household Income Quartile, 1999. There are distinct race and income effects on hospital admissions for asthma. Nonwhites are more likely than whites to be admitted for asthma, regardless of income level, and children from lower income households are most likely to be admitted for asthma than those children from the higher income households.

Figure 5

Figure 4: Predicted Probabilities of Admission for Asthma and Other Respiratory Diseases by Race/Ethnicity and U.S. Median Household Income Quartile



Combining these two social effects, one finds that nonwhite children from households with the lowest incomes are most likely to be admitted to a metropolitan area hospital for asthma. Conversely, white children from the highest income households are least likely to be admitted for asthma. The estimated admission probability (percent) for asthma for nonwhite children from households in the 1st income quartile is 0.31 compared to 0.30 for white children. For households in the 4th income quartile, nonwhites have an estimated probability of 0.14 compared to 0.12 for whites. The estimated probabilities for other respiratory diagnoses also show statistically significant race and income effects. For these diagnoses, nonwhites have a higher probability than whites to be admitted to an area hospital, but unlike the asthma diagnosis, children from higher income households are more likely to be admitted than those from lower ones. Thus, nonwhite children from the highest income quartile households are most likely to be admitted ($p = 0.14$), whereas white children from the lowest income quartile are least likely ($p = 0.08$) to be admitted.

CONFOUNDING EFFECTS

This section examines the effects of two confounding variables, the Day of the Week When Admitted and the Admission Source, both of which are statistically related to the diagnoses. The Admission Source variable is classified into whether the patient first visited the emergency room or was an outpatient before being admitted (ER/Outpatient) or was routinely admitted or transferred to the hospital (Other). The simple models show that both confounding variables explained a statistically significant amount of variation. The weekend days Saturday and Sunday as well as Mondays had

higher probabilities for admission for asthma than the remaining days of the week. Admissions for other respiratory illnesses varied little during the week, but Fridays had a higher probability than the remaining days of the week. In sum, a more pronounced day effect is observed for asthma admissions than for other respiratory conditions. The Admission Source variable shows that the ER/Outpatient category had higher probabilities of admission for both asthma and other respiratory diseases than the Other admission category.

The multivariate model combining the effects of Admission Source (ER/Outpatient, Other) and Day of Admission reveals a complex relationship between the two confounding variables and diagnosis. Children admitted to the hospital via the ER/Outpatient route have the highest probabilities of admission for asthma, regardless of the day of the week. The probabilities of admission for asthma are highest on Saturday (0.27), Sunday (0.25), and Mondays (0.25), Thursdays (0.24), and Fridays (0.23). Tuesdays and Wednesdays have the lowest probabilities of admission for asthma (0.21). Asthma admissions via the Other (no ER or outpatient visit) category do not follow the pattern found for the ER/Outpatient category. Rather, the probability of admission for asthma is highest on Wednesdays (0.16) and lowest on Saturdays and Sundays (0.12).

The same pattern of the highest admission probabilities on Wednesday and the lowest on the weekends is confirmed for the other respiratory disease diagnosis; the probabilities of admission are higher for children who visited the emergency room or were outpatients than for those who were admitted routinely (Other category).

DISCUSSION

The Metropolitan Indianapolis Asthma Study adds to the picture of childhood asthma from both a methodological and substantive perspectives.

METHODOLOGY

This study uses some methodologies that differ in important ways from the epidemiological studies reviewed for this research. With one exception, these studies use a combination of adjusted time-series and regression methodologies on aggregated daily counts of asthma and daily measures of environmental variables to determine the association of environmental conditions and asthma. This study uses the Multinomial Logit Analysis approach, which permits the examination of how variation among individuals'

characteristics—exposure to environmental conditions, social characteristics, and confounding variables—affects hospital admissions. Each variable is evaluated alone and in combination with others, and the form of the relationship (linear, non-linear) and relative strength of association are examined.

Another methodological innovation was the use of GIS methodology to improve the estimates of ozone exposure to individuals. The reviewed studies generally compute a mean exposure across a wide area (entire city or larger); in the Indianapolis study, individuals are assigned ozone exposure values based on the closest of nine monitors using a line-of-sight distance calculation between the monitor and the patients ZIP code centroid. Tolbert et al. (2000) also use a GIS procedure to interpolate ozone concentrations and link these data to a zip code centroid for each case.

Previous studies use various measures of the environmental variables, ranging from single point daily measures, such as minimum or maximum daily temperature, to longer term measures, such as daily mean ozone (24-hour mean) or the 1-, 2-, or 3-day moving averages. This study examined a range of measures used by others and evaluated their utility by two criteria—whether the model fit the data (GOF test), and if so, whether the measure explained a statistically significant level of variation ($p < 0.05$).

Other strengths of the study include a large number of hospitals, multiple years of data, multiple pollutants and meteorological variables, and inclusion of social characteristics other than age.

The limitations of the study are primarily related to the patient and environmental databases, and these limitations are mirrored in other studies. Over-counting may have occurred because children with repeat admissions for the same asthmatic episode are not excluded. Over-counting might also be because of the coding methodology, which considers a case to be asthma if one of the diagnostic codes was asthma. The extent to which over-counting is a problem is not known. Under-counting may also be a problem, either to missed diagnoses or differences in coding policies from institution to institution (Bieler 2000).

A major assumption in this and other studies is that each child's primary exposure location is the home address (zip code area) given at the time of admission. It is not known to what extent this assumption may over- or under-estimate exposure. The use of area means to characterize exposure

over a broad geographical area is also problematic for this and other studies. The use of GIS methodology counters this limitation for ozone.

SUBSTANTIVE FINDINGS

The Metropolitan Indianapolis Asthma Study supports some of the findings reported in the literature, contradicts others, and provides new findings in areas not fully researched. The study generally supports previous findings on the positive association between nitrogen dioxide and sulfur dioxide, but the Multinomial Analysis suggests that the relationship is curvi-linear, and that the concentration levels may affect the form of the relationship. The nitrogen dioxide and sulfur dioxide concentrations in the Indianapolis study are uniformly low and lower than most of the studies that have reported positive associations between asthma and sulfur dioxide or nitrogen dioxide, suggesting that concentrations below the current EPA air quality standards may affect asthma. However, differences in the monitoring methodology and number of sites points to the need for more work in this area.

The study also confirms the importance of the social variables Race/Ethnicity, Income, Age, and Sex. The model of the combined effects of Race/Ethnicity and Income shows a consistent difference between nonwhite and white children and a non-linear effect associated with income. It also suggests that these variables summarize general life-style differences involving choice of housing, access to medical care, and health-related behaviors, such as smoking. Since these characteristics could not be measured directly, the analysis of these surrogate variables suggests that children from non-white, low-income homes are most likely to be admitted to the hospital for asthma because of these life-style differences.

The main finding that is counter to the prevailing science is the finding of a negative relationship between ozone and hospital admissions for asthma or other respiratory conditions. Twelve of the studies reporting a statistically significant relationship found a positive relationship and three reported a negative relationship. The ozone concentrations in the Indianapolis study are generally higher than concentrations in the reviewed studies; however, the lack of variability in the Indianapolis data may be important. That is, children may be reacting to fluctuations in ozone (or other pollutant) levels, suggesting a need to explore a dataset with more variable pollutant concentrations and more complex models involving interactions among variables. The

literature review also suggests the need to include additional environmental variables such as inhalable particulate matter and pollen to explore these relationships more fully.

The other finding that is somewhat inconsistent with the literature is the negative association between temperature and asthma admissions. Of ten studies that provide enough information to discern the relationship, two report a positive association between the outcome measures and temperature, two report a negative association, and five report that temperature is not significant. Based on the limited data, the role of temperature in this and other studies of asthma is still unclear. This analysis suggests that dew point, which incorporates both temperature and relative humidity, may be the best measure.

The analysis of two confounding variables Admission Source and Day of the Week also contributes some knowledge about how non-experimental designs require adjustments for self-selection errors. Clearly, administrative processes, such as admission scheduling, and other factors, possibly unrelated to asthma, may affect the relationships among the theoretically relevant variables, such as the social and environmental measures. Admission Source gives some insight into how asthmatic children are treated by the health care system. The finding that children who had previously visited the hospital via the emergency room or as an outpatient are more likely to be hospitalized for asthma suggests that future studies need to incorporate other types of administrative records, such as outpatient visits and contacts with clinics and physicians. The outpatient data are especially important because the use of the hospital admission data limits the study mostly to children with severe illness, as demonstrated by the need for hospitalization.

This study also examines whether other types of respiratory disease are affected by the environmental and social variables. Few statistically significant associations are demonstrated in these data. A post-review of the classification system of the ICD-9 codes included in the Other Respiratory Disease category suggests that the category is too inclusive, since it combines infectious and non-infectious respiratory diseases, and diseases of the upper, middle, and lower respiratory track. This classification scheme is now under review and may be revised for further analysis

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References

- r-0. American Thoracic Society. 1996. Health Effects of Outdoor Air Pollution. Part 1. *Am J Respir Crit Care Med* 153: 3-50.
- r-1. Anderson HR, Ponce de Leon A, Bland JM, Bower JS, Emberlin J, Strachan DP. 1998. Air pollution, pollens, and daily admissions for asthma in London 1987-92. *Thorax* 53: 842-848.
- r-2. Atkinson RW, Anderson HR, Strachan DP, Bland JM, Bremner SA, Ponce de Leon A. 1999. Short-term associations between outdoor air pollution and visits to accident and emergency departments in London for respiratory complaints. *Eur Respir J* 13: 257-265.
- r-3. Agresti A. 1990. *Categorical Data Analysis*. New York: John Wiley & Sons.
- r-4. Balmes JR. 1993. The role of ozone exposure in the epidemiology of asthma. *Environ Health Perspect* 101, Suppl. 4: 219-224.
- r-5. Bates DV, Baker-Anderson M, Sizto R. 1990. Asthma attack periodicity: A study of hospital emergency visits in Vancouver. *Environ Res* 51: 51-70.
- r-6. Bates DV, Sizto R. 1983. Relationship between air pollution levels and hospital admissions in southern Ontario. *Can J Public Health* 74: 117-122.
- r-7. ———. 1987. Air pollution and hospital admissions in Southern Ontario: The acid summer haze effect. *Environ Res* 43: 317-331.
- r-8. Bieler, Harvey, M.D. 2000. Personal Communication. Indianapolis, IN.
- r-9. Bowen Research Center. 1996. Marion County Community Health Assessment. Indianapolis, IN: Bowen Research Center.
- r-10. Buchdahl R, Parker A, Stebbings T, Babiker A. 1996. Association between air pollution and acute childhood wheezy episodes: prospective observational study. *Brit Med J* 312: 661-665.
- r-11. Burnett RT, Dales R, Krewski D, Vincent R, Dann T, Brook JR. 1995. Associations between ambient particulate sulfate and admissions to Ontario hospitals for cardiac and respiratory diseases. *Am J Epidemiol* 142: 15-22.
- r-12. Burnett RT, Dales RE, Raizenne ME, Krewski D, Summers PW, Roberts GR, et al. 1994. Effects of low ambient levels of ozone and sulfates on the frequency of respiratory admissions to Ontario hospitals. *Environ Res* 65:172-194.
- r-13. CDC, National Center for Environmental Health. 1999. Asthma Prevention Program of the National Center for Environmental Health. NCEH Pub. No. 98-0367. Available at: http://www.cdc.gov/nceh/programs/asthma/ataglance/asthma_ag2.htm [accessed 20 October 1999].
- r-14. CDC, National Center for Health Statistics. 2001. New asthma estimates: Tracking prevalence, health care, and mortality. Available at: <http://www.cdc.gov/nchs/products/pubs/pubd/hestats/asthma/asthma.htm> [accessed 11 October 2001].
- r-15. Chew FT, Goh DYT, Ooi BC, Saharom R, Hui JKS, Lee BW. 1999. Association of ambient air-pollution levels with acute asthma exacerbation among children in Singapore. *Allergy*. 54: 320-329.
- r-16. Fauroux B, Sampil M, Quénel P, Lemoullec Y. 2000. Ozone: A trigger for hospital pediatric asthma emergency room visits. *Pediatr Pulmonol* 30: 41-46.
- r-17. Garty BZ, Kosman, E, Ganor E, Berger V, Garty L, Wietzen T, et al. 1998. Emergency room visits of asthmatic children, relation to air pollution, weather, and airborne allergens. *Ann Allergy Asthma Immunol* 81: 563-570.
- r-18. Holmén A, Blomqvist J, Frindberg H, Johnelius Y, Eriksson NE, Hendricson KA, et al. 1997. Frequency of patients with acute asthma in relation to ozone, nitrogen dioxide, other pollutants of ambient air and meteorological observations. *Int Arch Occup Environ Health* 69: 317-322.
- r-19. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). 2001. Available at: <http://www.mcis.duke.edu/standards/termcode/icd9> [accessed 15 February 2001].
- r-20. Kleinbaum DG, Kupper LL, Morgenstern H. 1982. *Epidemiologic Research: Principles and Quantitative Methods*. New York: John Wiley & Sons.
- r-21. Mannino DM, Homa DM, Pertowski CA, Ashizwa A, Nixon LL, Johnson CA, et al. 1998. Surveillance for asthma—United States, 1960-1995. *MMWR Surveillance Summaries*. 24 April 1998/47(SS-1); 1-28. Available at: <http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00052262.htm> [accessed 18 May 2000].
- r-22. Medina S, Tertre AL, Quénel P, Le Moullec Y, Lameloise P, Guzzo JC, et al. 1997. Air pollution and doctors' house calls: Results from the ERPURS system for monitoring the effects of air pollution on public health in Greater Paris, France, 1991-1995. *Environ Res* 75: 73-84.
- r-23. Morgan G, Corbett S, Wlodarczyk J. 1998. Air Pollution and hospital admissions in Sydney, Australia, 1990 to 1994. *Am J Public Health* 88(12): 1761-1766.
- r-24. NIH. 1998. Global plan launched to cut childhood asthma deaths by 50%. Available at: <http://www.nhlbi.nih.gov/new/press/asthma1.htm>. [accessed 20 May 2001].
- r-25. NIH, National Heart, Lung, and Blood Institute. 1999. Data Fact Sheet, Asthma Statistics. U.S. Department of Health and Human Services: Bethesda, MD. Available at: <http://www.nhlbi.nih.gov>. [accessed 20 May 2001].
- r-26. National Weather Service. 2001. NWS Climate Table. Available at <http://www.nws.noaa.gov/climatex.html>. [accessed 27 October 2001].
- r-27. Pew Environmental Health Commission. 2000. *Attack Asthma: Why America Needs a Public Health Defense System to Battle Environmental Threats*. Available at <http://pewenvirohealth.jhsph.edu/html/reports/menu.html>. [accessed 5 February 2001].
- r-28. Pönkä, A. 1991. Asthma and low level air pollution in Helsinki. *Arch Environ Health* 46(5): 262-269.
- r-29. Pönkä, A, Virtanen M. 1996. Asthma and ambient air pollution in Helsinki. *J Epid Community Health* 50(Supp 1):S69-S62.
- r-30. Rennick, GJ, Jarman FC. 1992. Are children with asthma affected by smog. *Med J Australia*. 156: 837-841.
- r-31. Romieu I, Meneses F, Sienna-Monge JLL, Huerta J, Velasco SR, White MC, et al. 1995. Effects of urban air pollutants on emergency visits for childhood asthma in Mexico City. *Am J Epidemiol* 141(6): 546-553.
- r-32. Rosas I, McCartney HA, Payne RW, Calderon C, Lacey J, Chapela R, et al. 1998. Analysis of the relationships between environmental factors (aeroallergens, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. *Allergy* 53: 394-401.

- r-33. Schwartz J, Slater D, Larson TV, Peirson WE, Koenig JQ. 1993. Particulate air pollution and hospital emergency room visits for asthma in Seattle. *Am Rev Respir Dis* 147: 826-831.
- r-34. Stieb, DM, Burnett RT, Beveridge RC, Brook JR. 1996. Association between ozone and asthma emergency department visits in Saint John, New Brunswick, Canada. *Environ Health Perspect* 104(12): 1354-1360.
- r-35. Stokes ME, Davis CS, Koch GG. 2000. *Categorical Data Analysis Using the SAS System*, 2nd Edition. Cary, NC: The SAS Institute Inc.
- r-36. Sunyer J, Spix C, Quénel P, Ponce-de-León A, Pönkä A, Barumandzadeh T, et al. 1997. Urban air pollution and emergency admissions for asthma in four European cities: the AHEA Project. *Thorax* 52: 760-765.
- r-37. Tolbert PE, Mulholland JA, MacIntosh DL, Xu F, Daniels D, Devine OJ, et al. 2000. Air quality and pediatric emergency room visits for asthma in Atlanta, Georgia. *Am J Epidemiol* 151(8): 798-810.
- r-38. Tseng RYM, Li CK, Spinks JA. 1992. Particulate air pollution and hospitalization for asthma. *Ann Allergy* 68: 425-432.
- r-39. U.S. EPA. 2001a. National Ambient Air Quality Standards (NAAQS). Available at: <http://www.epa.gov/air/oaqps/greenbk/criteria.html> .[accessed 30 May 2001].
- r-40. ———. 2001b. Pollutant Standards Index and Air Quality Index. Available at: <http://www.epa.gov/oaqps/psiaqui.html> . [accessed 9 July 2001].
- r-41. ———. 2001c. Ozone and Carbon Monoxide 1997-99 Air Quality Data Update. Available at: <http://www.epa.gov/oar/aqrend99/carboz99.html> . [accessed 17 October 2001].
- r-42. White MC, Etzel RA, Wilcox WD, Lloyd C. 1994. Exacerbations of childhood asthma and ozone pollution in Atlanta. *Environ Res* 65: 56-68.

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