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A Case-Crossover Analysis of Out-of-Hospital Cardiac Arrest and Air Pollution

Running title: *Ensor et al.; Out-of-hospital cardiac arrest and pollution*

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Abstract:

Background—Evidence of association between exposure to air pollution and overall cardiovascular morbidity and mortality is increasingly found in the literature. However, results from studies of the association between acute air pollution exposure and risk of out-of-hospital cardiac arrest (OHCA) are inconsistent for fine particulate matter ($PM_{2.5}$), and while pathophysiological evidence indicates a plausible link between OHCA and ozone, none has been reported. Approximately 300,000 persons in the U.S. experience an OHCA each year of which over 90% die. Understanding the association provides important information to protect public health.

Methods and Results—The association between OHCA and air pollution concentrations hours/days before onset was assessed using time-stratified case-crossover design using 11,677 emergency medical service logged OHCA events between 2004-2011 in Houston, Texas. Air pollution concentrations were obtained from an extensive area monitor network.

An average increase of 6 $\mu g/m^3$ in $PM_{2.5}$ 2 days before onset was associated with an increased risk of OHCA (1.046; 95% CI 1.012 to 1.082). A 20 ppb ozone increase for the eight-hour average daily maximum was associated with an increased risk of OHCA on the day of the event (1.039; 95% CI 1.005 to 1.073). Each 20 ppb increase in ozone in the previous 1 to 3 hours was associated with an increased risk of OHCA (1.044; 95% CI 1.004 to 1.085). Relative risk estimates were higher for men, African Americans or those aged over 65.

Conclusions—The findings confirm the link between OHCA and $PM_{2.5}$ and introduce evidence of a similar link with ozone.

Key words: sudden death, heart arrest, epidemiology, pollution, ozone, particulates

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Introduction

Out-of-hospital cardiac arrest (OHCA) is defined as a condition characterized by an unexpected cardiovascular collapse due to an underlying cardiac cause occurring out of the hospital. It is of significant concern given that approximately 300,000 persons in the United States experience an OHCA each year and over 90% of those persons who experience an OHCA die.[1] Understanding the role of air pollution in increasing the risk of OHCA is important to protect public health. Evidence that short term exposure to air pollution is associated with cardiovascular morbidity and mortality is increasingly found in the literature, especially with respect to fine particulate matter of aerodynamic diameter smaller than 2.5 μm ($PM_{2.5}$), and to a lesser extent ozone (O_3).[2,3,4,5,6] A handful of case-crossover studies have specifically examined the association between $PM_{2.5}$ and ozone air pollution with a focus on OHCA or out-of-hospital cardiac death.[7,8,9,10,11] However, in these studies, results of an association between OHCA and $PM_{2.5}$ have been inconsistent and no association was found between OHCA and ozone (e.g. studies reported a range of -6.0% to 11.0% increase in risk of OHCA per 10 $\mu g/m^3$ increase in $PM_{2.5}$ and -5.5% to 22.8% increase in risk of OHCA per 20ppb increase in O_3).

In an effort to better understand the association of air pollution and OHCA, we used an extensive air monitoring network and a large Emergency Medical Service (EMS) call database spanning eight years. We focused on two pollutants, $PM_{2.5}$ and ozone, both with epidemiological evidence supported by pathophysiologic arguments that link them to cardiac endpoints.[4,12,13,14,15,16,17,18] We also examined the association between nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and carbon monoxide (CO) with cardiac arrest. Our studies were conducted on both a daily and hourly time scale.

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Methods

Out-of-Hospital Cardiac Arrest Data

The Rice University and Baylor College of Medicine Institutional Review Board approved all data-collecting procedures for human subjects. All cases where EMS performs chest compressions are considered OHCA cases. The OHCA study data included non-dead-on-arrival adults aged 18 or older cases from Houston Fire Department EMS calls over the eight year period from 2004 to 2011. The database consisted of 11,677 cases of OHCA events. In addition to recording the time and location of the event, other relevant information necessary for age, sex, race, and pre-existing condition stratification were also available. This additional information was collected by EMS using Utstein guidelines.[19]

Ambient Air Quality and Meteorological Data

Ambient pollution concentration data were obtained from the Texas Commission of Environmental Quality (TCEQ) for the eight-year study period of 2004 through 2011. In this analysis, hourly data from 47 monitors measuring O_3, 12 measuring $PM_{2.5}$, 22 measuring NO_2, 13 measuring SO_2 and 12 measuring CO were used. The hourly and daily average values of $PM_{2.5}$, ozone, NO_2, SO_2, and CO were calculated across monitors. For ozone, we calculated the daily maximum 8 hour running mean. The number of air monitors measuring a specific pollutant changed through the study years as monitors went on and off line. However, less than 1% of the time all monitors were simultaneously down. All air pollution data were collected using Environmental Protection Agency federal reference methods[20] and validated by the TCEQ.

In order to control for potential confounding meteorological events, one-hour ambient meteorological (temperature, relative humidity and wind speed) data were obtained from the TCEQ for the study years. These data were used to estimate the average hourly and daily

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ambient apparent temperature level during the study period. The apparent temperature was calculated with the method used by O'Neill et al.[21] originally described by Steadman[22] and Kalkstein and Valimont.[23]

Statistical Methodology

The OHCA event, pollution and meteorological databases were analyzed using a time-stratified case-crossover design coupled with conditional logistic regression. Case-crossover design was first introduced by Maclure[24] and is used increasingly in the literature to assess episodic events following short-term exposure to air pollution.[3,4,7,8,9,10,25] In the case-crossover design, each individual experiencing a health event serves as his or her own reference, in other words individuals act as their own control. Ambient air pollution is used as a proxy for personal exposure. The ambient air pollution concentrations at times when the study individual is not experiencing the OHCA health event are the reference concentrations. The reference concentrations are statistically compared with the concentrations during or around the time the study individual experienced the OHCA health event. Conditional logistic regression is applied to estimate the association of pollution and increased relative risk of the health event while controlling for confounding factors.

In our application of the case-crossover design, we conducted an exploratory sensitivity analysis with single lag models to examine the association of air pollution and OHCA on two time scales: hour and day. The hour or day of the individual OHCA event (depending on the time scale being studied) was the initial exposure period (lag 0) considered for that case. For the hourly time scale analysis, we examined the association at the hour of onset (lag 0 hour) and one to eight hours prior to onset (lag 1,2,3,4,5,6,7,8). For the daily time scale analysis, we examined the association at the day of onset (lag 0 day) and the one to five days prior to onset (lag

1,2,3,4,5).

We then implemented constrained distributed lag models to estimate the cumulative effect over two hour average or two day average increments (lag 0-1, lag 1-2, lag 2-3) for those pollutants where associations were indicated in our exploratory analysis.

Referent exposures, selected by time stratified sampling, were the exposures in the day (and hour for the hourly analysis) of the event on all days falling within the same month and on the same day of the week as the event. This reference period design has been shown to limit bias present due to patterns in air pollution.[26] A conditional logistic regression was used to estimate the relative risk associated with each pollutant. We included apparent temperature in our conditional logistic regression model using a nonparametric smoothing spline of degree three with four knots optimally chosen.[27,28,29,30,31]

The EMS data, in which the call time acts as the time of the OHCA, provided the ability for an analysis on the hourly as opposed to the daily scale typically assessed. However, since both cardiac arrest and pollutant data may have diurnal patterns, temporal confounding must be considered.[10] For our analysis of the hourly relationship, we explored the impact of the cardiac arrest temporal pattern in confounding our understanding of the relationship between OHCA and hourly air pollution (when an effect was found) by comparing the OHCA/air pollution relationship when the temporal OHCA pattern was constant to the finding from the full data set.

When a significant association between individual pollutants and OHCA was found, we investigated potential confounding between pollutants. We estimated correlations between pollutants on the daily and hourly scale and also included pollutants as a covariate in the model. The main concern was potential confounding between $PM_{2.5}$ and ozone as indicated by previous researchers.[32] When a relationship was found between OHCA and an air pollutant, we stratified

the analyses by age, sex, race and season to examine effects by subgroup. The case-crossover logistic regression was conducted in SAS version 9.3.[33]

Results

Figure 1 identifies the location of OHCA events for the eight-year period (geo-masked for privacy). Characteristics of the OHCA study group are shown in **Table 1**. Of the 11,677 qualified cases of OHCA during the study period, the largest percent of cases were individuals between the age of 35 and 64, more of the cases were male (59%) than female (41%), and most of the cases were of African American individuals (46%), followed by Caucasian individuals (35%) and Hispanic individuals (16%). The data indicate that 79% of the cases presented with a pre-existing condition, not necessarily cardiac related. Because of the stressful conditions during the EMS call, the designation of pre-existing conditions by the victim or relatives is considered less reliable by the Houston EMS than the other data. For this reason, stratification by pre-existing condition was not explored in this study. To evaluate the impact of the season, we broke the year into cold (November to March) and warm season (April to October). During the study period 55% of the cases were in the warm season and 45% were in the cold season.

Statistics of the average hourly and daily pollutant levels during the study period are listed in **Table 2**. Pearson correlation coefficients between pollutants and apparent temperature on both time scales (hourly and daily) and each season (all, warm and cold) were calculated (**Table 3**). Note, correlations vary between daily and hourly time scales due to different diurnal pollutant patterns. On the daily scale, the strongest correlation was between CO and NO_2 at 0.75, 0.72, 0.79 for all year, warm and cold season. Ozone is most correlated with $PM_{2.5}$ on the day scale during the warm season (0.40, 0.37, 0.26 for all year, warm, and cold season). On the

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hourly scale there is little to no correlation between ozone and $PM_{2.5}$ during warm season (0.01, 0.07 and -0.21 for all year, warm, and cold season).

Conditional logistic regression results for each pollutant on the hourly and daily time frame are summarized on **Table 4** and **Figure 2**. The plots and the table offer different information. The plots graphically show the change in effect estimates with increasing lags for ozone and $PM_{2.5}$ while the table shows more limited ozone and $PM_{2.5}$ lags information and includes other pollutants.

$PM_{2.5}$ Results

The lag model results for $PM_{2.5}$ on the daily analysis scale indicate that a daily average increase of 6 $\mu g/m^3$ in $PM_{2.5}$ in the 2 days before onset (average of one and two days) was associated with an increase of OHCA risk (1.046; 95% CI 1.012 to 1.082). This was the strongest effect found. There was no effect after three days (1.021; 95% CI 0.991 to 1.051).

Ozone Results

The lag model results for ozone on the hourly analysis scale indicate that each 20 ppb ozone increase in the average of the previous 1 to 3 hours was associated with an increase OHCA risk (1.044; 95% CI 1.004 to 1.085). This was the strongest effect found in the distributed lag model. No effect was found after three hours.

Also included in **Figure 2** are the results for the single lag model for lag 0 day. The results indicate an increase of 20 ppb ozone for the eight-hour average daily maximum on the day of the event was associated with an increased risk of OHCA (1.038; 95% CI 1.004 to 1.072). The finding of a significant association between OHCA and ozone on lag 0 day indicates that this association found on the hourly scale within the day of onset is not simply reflecting the temporal cardiac pattern. To further investigate confounding from the cardiac temporal pattern,

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we compared the results of the same analysis limited to a time of day when the cardiac temporal pattern was constant and found no change in the risk.

Stratification and Sensitivity

Analysis of stratification of the cases by the demographic characteristics of the data (age, sex and race) found that the risk from exposure to ozone or $PM_{2.5}$ is highest for men (1.051; 95% CI 1.006 to 1.097), those of African American ethnicity (1.053; 95% CI 1.003 to 1.105), and over 65 years of age (1.049; 95% CI 1.000 to 1.100) (**Figure 3**). The apparent temperature is most correlated with ozone on the hourly scale during the cold season (0.20, 0.03, and 0.39 for all year, warm, and cold season). Apparent temperature itself was not a significant predictor for OHCA nor did inclusion of apparent temperature change our conclusions related to the pollutants.

Discussion and Conclusions

We find consistent evidence of an association between OHCA and exposure to ozone in Houston, Texas at short time scales up to three hours in duration and also at the daily level on the day of the event. For exposure to $PM_{2.5}$ an association is found for two-days prior to the event. Other pollutants were not found to impact the occurrence of OHCA.

Our findings add to the significant literature relating OHCA with $PM_{2.5}$, where findings across studies are inconsistent. Further we add to the small but growing scientific conversation relating OHCA and ozone. Finally, we bring the most comprehensive data set to date to this literature, in terms of duration of the study, number of pollution monitors included and the number of OHCA events studied. The implications of this work are improved health policy and action with the objective of reducing the number of annual OHCA currently at approximately

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300,000 in the nation and 1,460 in Houston.

Association between $PM_{2.5}$ and OHCA

The association between $PM_{2.5}$ and OHCA varies across studies, and is due in large part to the variation in study design. A detailed synthesis of recent studies is provided in Raun and Ensor (2012)[34] for both $PM_{2.5}$ and ozone. Some of the key features that varied across studies included number of monitors used, area covered, sample size of cases, designation of health endpoint, co-morbidities studied, method of pollution measurement, composition of particulates and level of ambient concentration. The early studies, which did not find an association, had fewer OHCA events, and lower $PM_{2.5}$ concentrations and/or different $PM_{2.5}$ composition than the later studies that did find an association.[3,7,8,9,10,11]

Association between Ozone and OHCA

While few studies have examined the link between ozone and OHCA, there is growing evidence of a pathophysiological link. As well as effects seen in animal toxicology studies after human ozone exposure, researchers have found reduction in serum tocopherol (free radical scavenger),[35] increase in gradient of alveolar-to-arterial PO2 potentially due to alveolar-arterial oxygen impairment,[36] and most recently changes in several proinflammatory cytokines in blood.[12] The lack of investigation of the association between ozone and OHCA may stem from practical considerations such as data limitations. In some locations ozone is only monitored periodically. When the association is investigated, the lack of significant findings may be a product of the additional complexity of controlling accurately for the impact from temperature. Clearly, ozone is more often found at higher temperatures and an increased risk of OHCA is closely tied to the combined effect. Finally, our results indicate the association may be more readily found at the hourly level over the daily, with the latter the more often studied time frame.

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Examining three recent large studies in comparison to our findings, we find differences in two of the studies[3,7] regarding number of cases, number of monitors, the specific health-endpoint considered, and magnitude and variation in pollution levels studied.[34] The third study, Silverman et al.[10], of New York City (n=8,216) found an increase risk (1.045; 95% CI .991 to 1.1) for a daily average increase of 20 ppb. Our study design is most similar to Silverman et al. (2010), with both studies having a large number of cases extracted from an EMS 911 database, limited exposure concentration uncertainty, and similar ozone IQR. The results found in New York City and Houston are consistent with findings from an important case-crossover study with a more encompassing health endpoint. Stafoggia et al.[30] examined susceptibility factors to ozone mortality. Of interest to our objective is their examination of ozone-related mortality in those with pre-existing cardiovascular conditions. The researchers estimated an increase risk (1.093; 95% CI 1.044 to 1.145) in mortality for a 20 ppb increase in the daily eight-hour ozone running maximum average.

Given the comparability between the study of Houston and New York City and the corroborating study by Stafoggia et al.,[30] current results of the comparable studies support the likelihood that there is an increased risk of OHCA with exposure to ozone.

Limitations

A potential limitation of this study is selection bias from exclusion of cases where chest compressions were not initiated because the adults were considered dead on arrival. Resuscitation was withheld if the individual was dead-on-arrival as defined by decapitation, rigor mortis, dependent lividity, decomposition, incineration or obvious mortal wounds, absence of any signs of life (pulse, respirations, or any spontaneous movement) on EMS arrival associated with a penetrating head injury (gunshot wound, stab, etc.), or penetrating extremity injury with

obvious exsanguination, absence of any signs of life (pulse, respirations or any spontaneous movement) for greater than five minutes associated with a penetrating injury to the chest or abdomen and a greater than 10 minute transport time to a Trauma Center, or absence of any signs of life (pulse, respirations or any spontaneous movement) associated with blunt trauma. However, the large size of this study minimizes risks from selection bias.

Another limitation of the study is the absence of stratification by pre-existing conditions and/or personal risk factors due to lack of this information. Finally, the exposure concentrations in the study are limited to the use of the average pollutant concentration across the city over use of more local pollutant concentrations. This is especially true when the study area is large and the pollutant varies spatially. We chose to use the average concentration rather than potentially misclassifying the associated reference concentrations if the individual experienced the OHCA in a location not representative of his usual exposure. This limitation is inherent in the case-crossover study design.

Future Research

While this study identifies an association between $PM_{2.5}$ and ozone air pollution and OHCA, future research to better define the exposure time period associated with triggering an OHCA is needed. Epidemiological studies have found the time to trigger a cardiac event from exposure to $PM_{2.5}$ or ozone ranges from the day or previous day of onset to hours before onset.[4,7,9,10] Part of this inconsistent range of time to trigger is due to exposure time misclassification. This could be better handled by addressing uncertainty in combining disparate datasets such as OHCA recorded at the minute and continuous across space and air pollution data recorded hourly at fixed locations.[37]

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Conflict of Interest Disclosures: None.

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Table 1. Study population characteristics of OHCA events in Houston, Texas from 2004-2011.

Total	11,677
Pre-Existing Condition	9,196 (79)
Age	
Mean	64 SD:16.81
18 to <35	576 (5)
35-64	5,153 (44)
65-74	2,244 (19)
75+	3,704 (32)
Sex	
Female	4,776 (41)
Male	6,901 (59)
Race	
Caucasian	4,065 (35)
African American	5,338 (46)
Hispanic	1,875 (16)
Other	399 (3)
Season	
Warm (Apr to Oct)	6,411 (55)
Cold (Nov to Mar)	5,266 (45)

Values are n (%). SD: standard deviation

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Table 2. Description of data.

Variable	No. of Monitors	% of Missing Data	Mean (SD)	Percentile					IQR
				5%	25%	50%	75%	95%	
$PM_{2.5}$ ($\mu g/m^3$) hourly	12	0	11.42 (5.89)	3.87	7.34	10.3	14.37	22.8	7.03
O_3 (ppb) hourly	47	0	25.52 (16.14)	4.3	13.23	22.92	34.61	57.25	21.38
NO_2 (ppb) hourly	22	1	9.16 (5.76)	2.84	4.96	7.52	11.84	21.18	6.87
SO_2 (ppb) hourly	13	1	1.97 (3.23)	0.28	0.75	1.45	2.48	5.18	1.73
CO (ppb) hourly	12	1	281.91 (202.45)	121.23	171.94	225.09	315.75	632.76	143.81
Apparent Temperature daily (°F)	15	0	73.37 (17.39)	42.58	59.70	75.89	88.89	95.53	29.19
$PM_{2.5}$ ($\mu g/m^3$) daily	12	0	11.42 (4.73)	5.50	8.18	10.45	13.71	20.96	5.52
NO_2 (ppb) daily	22	0	9.11 (4.17)	3.51	6.01	8.41	11.66	16.87	5.65
SO_2 (ppb) daily	13	0	1.96 (2.38)	0.44	0.97	1.66	2.55	4.27	1.57
CO (ppb) daily	12	0	279.90 (130.90)	139.89	194.69	249.89	332.36	526.16	137.67

IQR: interquartile range; SD: standard deviation.

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Table 3. Pearson correlation coefficients between pollutants and apparent temperature.

All pollution data

	$PM_{2.5}$, µg/m^3	O_3, ppb	NO_2, ppb	SO_2, ppb	CO, ppb	AT, °F	
$PM_{2.5}$, µg/m^3		0.01	0.24	0.05	0.34	0.22	Hourly
O_3, ppb	0.40		-0.33	0.11	-0.32	0.20	
NO_2, ppb	0.08	0.24		0.11	0.71	-0.49	
SO_2, ppb	0.07	0.08	0.23		0.08	-0.08	
CO, ppb	0.21	0.23	0.75	0.22		-0.24	
AT, °F	0.31	0.14	-0.57	-0.14	-0.25		
			Daily				

AT: Apparent Temperature

Warm/cold season (hour)

	$PM_{2.5}$, µg/m^3	O_3, ppb	NO_2, ppb	SO_2, ppb	CO, ppb	AT, °F	
$PM_{2.5}$, µg/m^3		-0.21	0.44	0.11	0.46	0.07	Cold (Nov to Mar)
O_3, ppb	0.07		-0.49	0.12	-0.46	0.39	
NO_2, ppb	0.27	-0.21		0.21	0.72	-0.32	
SO_2, ppb	0.06	0.12	0.05		0.13	0.00	
CO, ppb	0.34	-0.23	0.72	0.05		-0.20	
AT, °F	0.11	0.03	-0.50	-0.04	-0.28		
			Warm (Apr to Oct)				

Warm/cold season (day)

	$PM_{2.5}$, µg/m^3	O_3, ppb	NO_2, ppb	SO_2, ppb	CO, ppb	AT, °F	
$PM_{2.5}$, µg/m^3		0.26	0.29	0.20	0.33	0.19	Cold (Nov to Mar)
O_3, ppb	0.37		0.19	0.09	0.18	0.15	
NO_2, ppb	0.20	0.61		0.47	0.79	-0.32	
SO_2, ppb	0.09	0.13	0.13		0.43	-0.09	
CO, ppb	0.27	0.42	0.72	0.15		-0.13	
AT, °F	0.15	-0.33	-0.53	-0.10	-0.26		
			Warm (Apr to Oct)				

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Table 4. Percentage change in risk of OHCA for an interquartile increase in air pollutants.

	$PM_{2.5}$ IQR 6 μg/m^3	O_3 IQR 20 ppb	NO_2 IQR 6 ppb	SO_2 IQR 2 ppb	CO IQR 141 ppb
Lag	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Daily Lag					
0	2.7 (-0.3 to 5.8)	3.8 (0.4 to 7.2)	0.9 (-3.0 to 5.0)	-0.2 (-2.1 to 1.7)	1.8 (-0.9 to 4.6)
1	3.5 (0.5 to 6.6)	1.8 (-1.4 to 5.2)	-0.7 (-4.4 to 3.0)	-1.2 (-3.2 to 0.8)	-0.2 (-2.8 to 2.4)
2	3.7 (0.7 to 6.8)	2.7 (-0.6 to 6.1)	-0.4 (-4.1 to 3.4)	-0.7 (-2.9 to 1.5)	0.9 (-1.7 to 3.6)
3	2.1 (-0.9 to 5.1)	-0.6 (-3.8 to 2.7)	0.9 (-2.8 to 4.7)	-1.3 (-3.3 to 0.7)	0.4 (-2.2 to 3.1)
4	0.2 (-2.7 to 3.2)	-1.2 (-4.3 to 2.1)	0.3 (-3.4 to 4.1)	-0.9 (-2.6 to 0.8)	0.3 (-2.4 to 3.0)
0 to 1	3.9 (0.5 to 7.4)	3.6 (0.0 to 7.4)	-0.1 (-4.3 to 4.3)	-0.9 (-3.0 to 1.3)	0.9 (-2.1 to 4.0)
1 to 2	4.6 (1.2 to 8.2)	3.0 (-0.6 to 6.8)	-0.8 (-4.9 to 3.5)	-1.3 (-3.7 to 1.1)	0.4 (-2.5 to 3.4)
Hourly Lag					
0	0.9 (-1.4 to 3.4)	3.7 (-0.1 to 7.7)	-0.1 (-0.6 to 0.4)	0.4 (-0.2 to 1.0)	0.0 (0.0 to 0.0)
1	1.1 (-1.3 to 3.5)	4.2 (0.4 to 8.2)	0.0 (-0.5 to 0.5)	0.0 (-0.7 to 0.8)	0.0 (0.0 to 0.0)
2	1.1 (-1.2 to 3.5)	4.6 (0.8 to 8.7)	0.0 (-0.5 to 0.5)	0.2 (-0.5 to 0.9)	0.0 (0.0 to 0.0)
3	0.3 (-2.0 to 2.7)	4.0 (0.2 to 8.0)	0.1 (-0.3 to 0.6)	0.2 (-0.6 to 0.9)	0.0 (0.0 to 0.0)
4	0.9 (-1.5 to 3.3)	3.4 (-0.5 to 7.4)	0.2 (-0.3 to 0.7)	0.0 (-0.8 to 0.7)	0.0 (0.0 to 0.0)

O_3 was based on 8-hr maximum
Statistics reflect adjustment for apparent temperature

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Figure Legends:

Figure 1. Locations of OHCA events between 2004 and 2011 in Houston, Texas. Subject locations have been randomly shifted to protect confidentiality.

Figure 2. Forest plot of Houston relative risk of OHCA associated with 20 ppb increase in ozone or 6 $\mu g/m^3$ increase in $PM_{2.5}$.

Figure 3. Forest plot of relative risk of OHCA associated per an inter quartile range (IQR) increase in the average of 1 to 3 hour lagged ozone and 1-2 day lagged $PM_{2.5}$ by age, ethnicity, gender, and season.

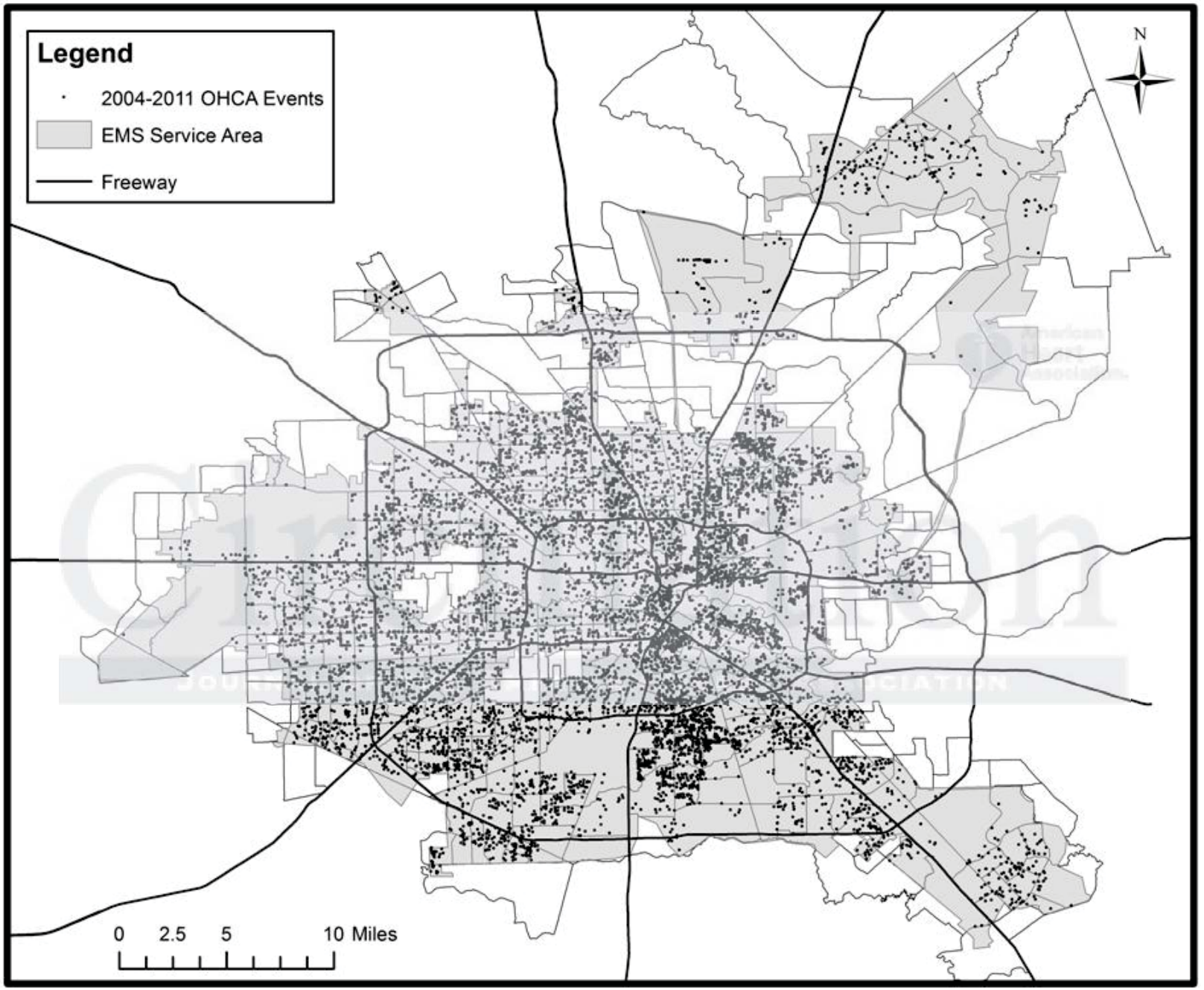

Figure 1

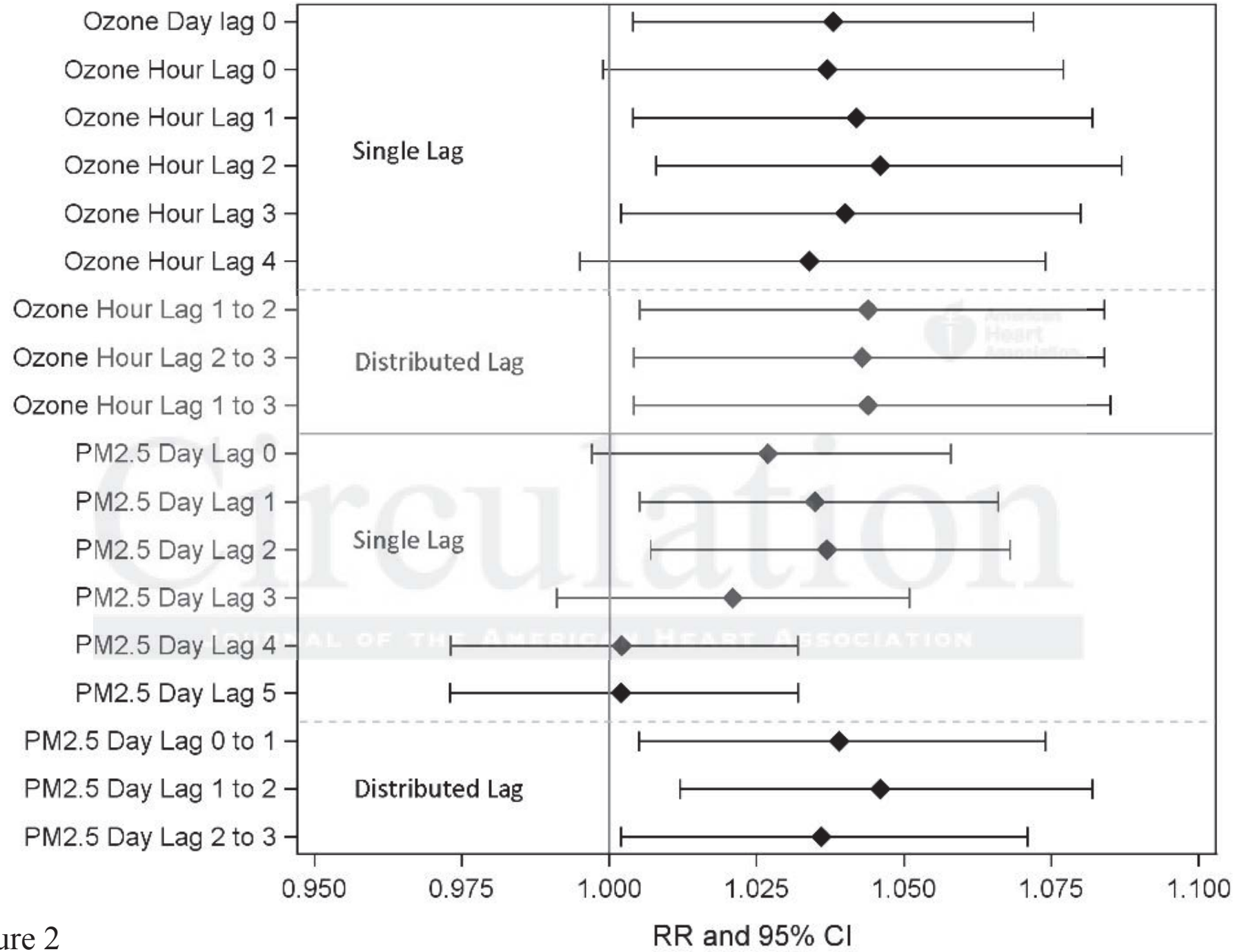

Figure 2

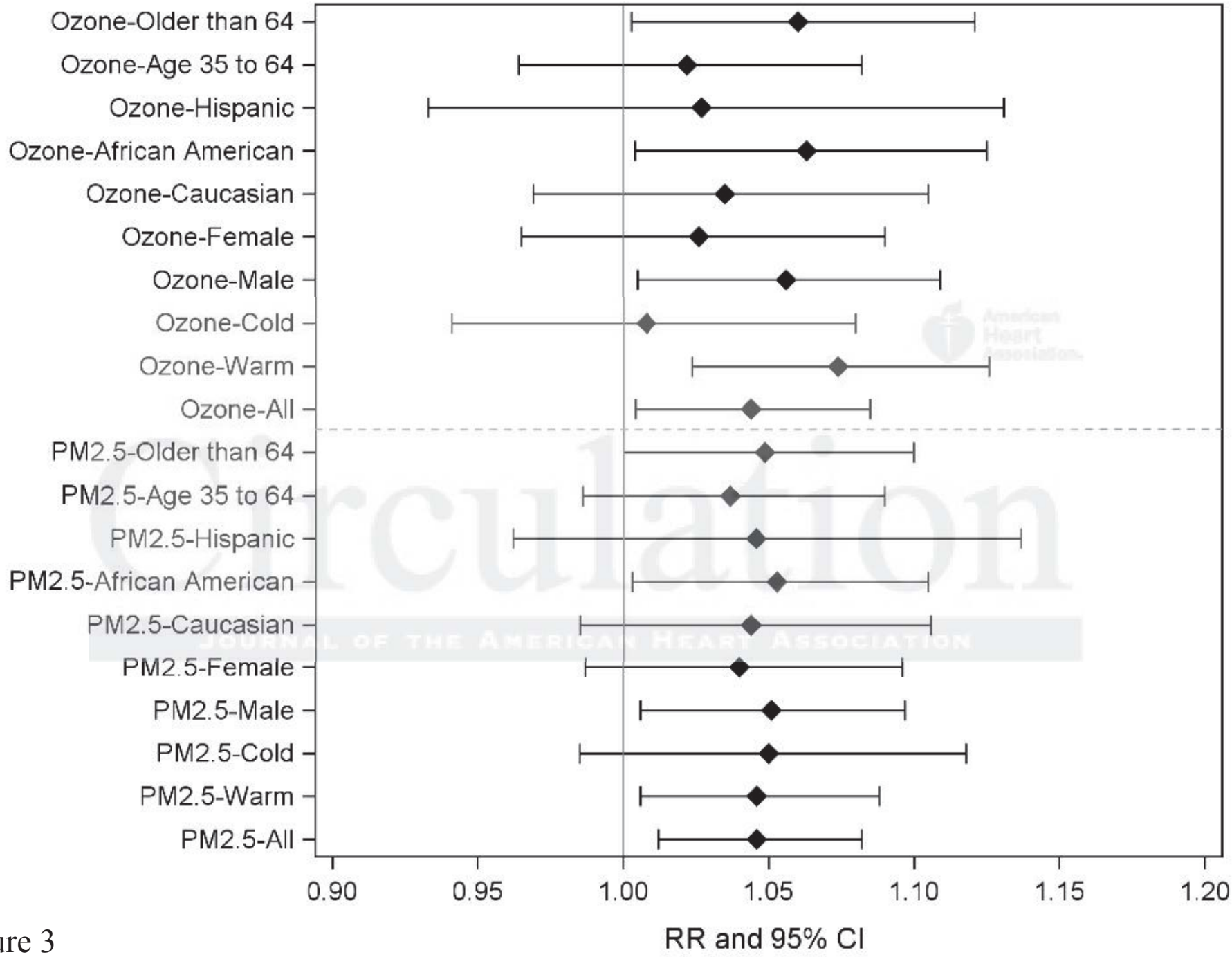

Figure 3

A Case-Crossover Analysis of Out-of-Hospital Cardiac Arrest and Air Pollution

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