

# Ambient Air Pollution and Cardiovascular Emergency Department Visits

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**Background:** Despite evidence supporting an association between ambient air pollutants and cardiovascular disease (CVD), the roles of the physicochemical components of particulate matter (PM) and copollutants are not fully understood. This time-series study examined the relation between ambient air pollution and cardiovascular conditions using ambient air quality data and emergency department visit data in Atlanta, Georgia, from January 1, 1993, to August 31, 2000.

**Methods:** Outcome data on 4,407,535 emergency department visits were compiled from 31 hospitals in Atlanta. The air quality data included measurements of criteria pollutants for the entire study period, as well as detailed measurements of mass concentrations for the fine and coarse fractions of PM and several physical and chemical characteristics of PM for the final 25 months of the study. Emergency department visits for CVD and for cardiovascular subgroups were assessed in relation to daily measures of air pollutants using Poisson generalized linear models controlling for long-term temporal trends and meteorologic conditions with cubic splines.

**Results:** Using an a priori 3-day moving average in single-pollutant models, CVD visits were associated with NO<sub>2</sub>, CO, PM<sub>2.5</sub>, organic

carbon, elemental carbon, and oxygenated hydrocarbons. Secondary analyses suggested that these associations tended to be strongest with same-day pollution levels.

**Conclusions:** These findings provide evidence for an association between CVD visits and several correlated pollutants, including gases, PM<sub>2.5</sub>, and PM<sub>2.5</sub> components.

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Despite evidence supporting an association between ambient air pollution and cardiovascular health, much remains to be understood about the roles of specific pollutants individually and in combination. Most of the information on the association between particulate matter (PM) and cardiovascular morbidity is based on epidemiologic studies using PM mass.<sup>1–13</sup> However, less is known about the specific physical or chemical characteristics of PM that could be responsible for adverse health effects, because these characteristics vary by source, geographic location, season, and concentrations of gaseous copollutants.

To examine the physicochemical components of PM that could be associated with the observed health associations, an innovative air quality monitoring station was installed near downtown Atlanta, Georgia. This monitoring station, operated by the Aerosol Research and Inhalation Epidemiology Study (ARIES), is collecting detailed information on particle composition and physical characteristics.<sup>14</sup> Data from this station are available from August 1, 1998, to August 31, 2000. The present study is one of several on the cardiovascular and respiratory health effects of ambient air pollution in Atlanta being undertaken by this Emory investigative team, collectively referred to as the Study of Particles and Health in Atlanta (SOPHIA). To investigate the association between ambient air pollution and cardiovascular emergency department visits, we studied outcome data compiled from 31 hospitals in relation both to routinely collected criteria pollutant data for the period January 1, 1993, to August 31, 2000, and to ARIES data for the period August 1, 1998, to August 31, 2000.

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## METHODS

### Emergency Department Data

We asked 41 hospitals with emergency departments that serve the 20-county Atlanta metropolitan statistical area (MSA) to provide computerized billing data for all emergency department visits between January 1, 1993, and August 31, 2000. (A map showing hospital locations is available with the electronic version of this article at [www.epidem.com](http://www.epidem.com).) Thirty-seven hospitals agreed to participate. Of these, 31 provided useable electronic data; the remaining 6 either did not maintain electronic records or the data were determined to be of poor quality. The data included the following information: medical record number, date of admission, International Classification of Diseases, 9th Revision (ICD-9) diagnosis codes, date of birth, sex, and residential zip code. Data for visits by individuals residing in any one of 222 zip codes located wholly or partially within the Atlanta MSA were included in the analyses.

Using the primary ICD-9 diagnosis code, we defined several cardiovascular disease (CVD) groups based largely on ICD-9 diagnosis codes used in published studies. The case groups were: ischemic heart disease (410–414), acute myocardial infarction (410), cardiac dysrhythmias (427), cardiac arrest (427.5), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433–437, 440, 443–444, 451–453), atherosclerosis (440), and stroke (436). The combined CVD case group pooled the ICD-9 diagnoses of these case groups. We assessed the adequacy of the a priori model by evaluating emergency department visits for finger wounds (883.0), a condition unlikely to be related to air pollution. Repeat visits within a day were counted as a single visit.

### Ambient Air Quality Data

For the period January 1, 1993, to August 31, 2000, we compiled air quality data for criteria pollutants from existing data sources with monitoring stations located in the Atlanta MSA, including the Aerometric Information Retrieval System (AIRS) and the Metro Atlanta Index (MAI), both operated by the Georgia Department of Natural Resources. (Monitoring stations are shown on the map available with the electronic version of this article.) We chose the pollutants and their metrics for analyses a priori based on hypotheses regarding potentially causal pollutants,<sup>15,16</sup> availability from the monitoring networks, and the form of the national ambient air quality standards: 24-hour average PM<sub>10</sub> mass (PM with an average aerodynamic diameter less than 10  $\mu\text{m}$ ), 8-hour maximum ozone (O<sub>3</sub>), 1-hour maximum nitrogen dioxide (NO<sub>2</sub>), 1-hour maximum carbon monoxide (CO), and 1-hour maximum SO<sub>2</sub> (sulfur dioxide). For each criteria pollutant, data from the most central monitoring site were used in the analyses. On days when measurements were missing at the central site, data for the pollutant were imputed using an algorithm that modeled measurements from at least one

secondary monitoring site in addition to meteorologic and time variables. Because ozone levels were not measured during the winter months, data for ozone were imputed only during the scheduled monitoring period (1896 days).

For the period August 1, 1998, to August 31, 2000, multiple physicochemical characteristics of PM were measured at the ARIES monitoring station. After considering the prevailing hypotheses regarding potentially causal pollutants and components,<sup>15,16</sup> 14 analytes were chosen a priori for analysis. The a priori metrics for all PM measurements were 24-hour averages. PM<sub>2.5</sub> mass (PM with an average aerodynamic diameter less than 2.5  $\mu\text{m}$ ) was measured using the Federal Reference Method (FRM); for days that these were missing, scaled measurements from a collocated Particle Composition Monitor were used. Coarse PM mass (PM with an average aerodynamic diameter between 2.5 and 10  $\mu\text{m}$ ) was measured directly. Daily PM<sub>10</sub> mass was reconstructed by adding the coarse PM mass and PM<sub>2.5</sub> mass. Components of PM<sub>2.5</sub>, including water-soluble metals, sulfates, acidity, organic carbon, and elemental carbon, were also assessed. The count of ultrafine particles with mobility diameter of 10 to 100 nm was measured. Twenty-four-hour concentrations of oxygenated hydrocarbons, a measure of polar volatile organic carbons, were evaluated. The gaseous criteria pollutants (O<sub>3</sub>, NO, CO, and SO<sub>2</sub>) were also measured continuously.

We obtained daily meteorologic data from the National Climatic Data Center at Hartsfield-Atlanta International Airport, including mean temperature and dew point temperature, estimated by averaging the minimum and maximum daily values. Data on relative humidity, wind speed, and wind direction were also obtained.

### Analytic Methods

Based on a priori model specification, we constructed single-pollutant models that controlled for temporal trends in the outcome variable and meteorologic conditions. The analyses involving the criteria pollutants used data for the entire study period; the analyses involving PM<sub>2.5</sub>, coarse PM, 10–100-nm particle count, PM<sub>2.5</sub> components, and oxygenated hydrocarbons included data from August 1, 1998, to August 31, 2000. All analyses were performed using SAS statistical software (SAS Institute, Inc., Cary, NC) unless otherwise indicated. The primary analyses used Poisson generalized linear modeling (GLM).<sup>17</sup> All risk ratios (RR) were calculated for an increase of approximately 1 standard deviation in the pollutant measure. The basic model had the following form:

$$\begin{aligned} \text{Log}[E(Y)] = & \alpha + \beta \text{pollutant} + \sum_k \lambda_k \text{day-of-week}_k \\ & + \sum_m \nu_m \text{hospital}_m + \sum_p \zeta_p \text{holiday}_p \text{g}(\gamma_1, \dots, \gamma_N; \text{time}) \\ & + \text{g}(\delta_1, \dots, \delta_N; \text{temperature}) + \text{g}(\eta_1, \dots, \eta_N; \text{dewpoint}) \end{aligned}$$

Y indicated the count of emergency department visits for a

given day for the outcome of interest. For each air quality variable (*pollutant*), the 3-day moving average of the 0-, 1-, and 2-day lags was used as the a priori lag structure. Models included indicator variables for day-of-week (*day-of-week*). Hospital entry and exit indicator variables (*hospital*) were used to account for the partial availability of data for some hospitals during the study period. An indicator variable for federally observed holidays (*holiday*) was also used. To control for long-term and seasonal variability, cubic splines for temporal trends ( $g(\gamma_1, \dots, \gamma_N; \text{time})$ ) were included using monthly knots ( $\tau_j$ ) on the 21st of each month. Cubic splines were also used to control for average temperature ( $g(\delta_1, \dots, \delta_N; \text{temperature})$ ) and average dew point temperature ( $g(\eta_1, \dots, \eta_N; \text{dew point})$ ), with knots at the 25th and 75th percentiles. Cubic splines were defined such that:

$$g(\gamma_1, \gamma_2, \dots, \gamma_N; x) = \gamma_1 x + \gamma_2 x^2 + \gamma_3 x^3 + \sum_{j=4}^N \gamma_j w_j(x),$$

where  $\gamma_1, \gamma_2, \dots, \gamma_N$  were parameters to be estimated, and where  $w_j(x) = (x - \tau_j)^3$  if  $x \geq \tau_j$ , and  $w_j(x) = 0$  otherwise. The first and second derivatives of  $g(x)$  were continuous, allowing time trends and meteorologic variables to be modeled as smooth functions. To avoid collinearity in the cubic spline terms, we used linear transformations of the original spline terms, obtained by multiplying the design matrix of the data to be transformed by the eigenvectors of its variance-covariance matrix. Variance estimates were scaled to account for Poisson overdispersion.

Other models were run as sensitivity analyses. The frequency of knots for cubic splines was varied in GLM analyses. Alternative GLMs using natural splines with monthly knots were evaluated in S-Plus (Insightful Corp., Seattle, WA). Day-to-day serial correlation was assessed by allowing for a stationary 4-dependent correlation structure in generalized estimating equations (GEE).<sup>18</sup> Generalized additive models (GAM)<sup>19</sup> with nonparametric LOESS smoothers and nonparametric smoothing splines were also assessed in S-Plus (convergence criterion of  $10^{-14}$ ).<sup>20</sup> We did not use standard errors for GAMs because the standard software underestimates the variance of the parameter estimates.<sup>21,22</sup> Methods to obtain correct variance estimates are still in development.<sup>23,24</sup>

Several exploratory analyses were conducted after a priori modeling. Secondary models explored alternative pollutant lag structures, including lag 0 (same-day pollution levels) to lag 7 (pollution levels 1 week prior). Season-specific analyses for warm (April 15–October 14) and cool (October 15–April 14) seasons were conducted. Age-specific analyses for CVD visits were also explored by subsetting visits for adults (age 19 years and older) and the elderly (age 65 years and older). Multipollutant models were evaluated.

## RESULTS

Thirty-one hospitals provided data on 4,407,535 emergency department visits by Atlanta residents for the study period. These 31 hospitals were estimated to receive 79% of emergency department visits in the Atlanta MSA. Five hospitals provided data for the entire 7-year time period of the study; the remaining 26 hospitals provided data for part of the period. The number of total emergency department visits in the study database increased from a mean of 413 (standard deviation = 50) per day in 1993 to 2675 (201) in 2000.

There was an average of 37 CVD visits per day (an average of 55 CVD visits per day for the 25-month ARIES time period); CVD subgroups had between 0.2 visits per day (atherosclerosis) and 11.7 visits per day (ischemic heart disease) (Table 1). Because the mean number of daily visits for cardiac arrest, acute myocardial infarction, atherosclerosis, and stroke were low (<5) and models using these outcomes were therefore unstable, we do not present the results for these CVD subgroups. The proportion of CVD visits contributed by each subgroup was stable over the study period. There was a seasonal pattern in CVD visits, with the highest number of daily visits occurring in the winter months and lowest in the summer months. The number of CVD visits was highest on Monday and lowest on Saturday.

Tables 2 and 3 provide descriptive statistics for the daily concentrations of the air quality analytes and correlations among analytes. Correlations between  $\text{PM}_{2.5}$  mass and its components were generally high ( $r > 0.5$ ), as were correlations between different PM mass size fractions. Measurements of 10 to 100 nm particle count were generally uncorrelated with other pollutant measures. Strong correlations were noted between daily measures of  $\text{PM}_{2.5}$  and  $\text{O}_3$  ( $r = 0.65$ ) and  $\text{NO}_2$  and CO ( $r = 0.68$ ). Measurements of  $\text{O}_3$ ,  $\text{PM}_{10}$ , and  $\text{PM}_{2.5}$  peaked in warmer months.  $\text{PM}_{2.5}$  components such as water-soluble metals, sulfate, and acidity varied temporally with  $\text{PM}_{2.5}$  mass, whereas organic carbon and elemental carbon peaked in colder months.  $\text{SO}_2$  exhibited a bimodal pattern with peaks in both summer and winter. Concentrations of CO tended to peak during winter. The highest concentrations for  $\text{NO}_2$  occurred in spring. Compared with other U.S. cities,  $\text{O}_3$  and  $\text{PM}_{2.5}$  are relatively high (with sulfate and organic carbon comprising relatively high proportions of the fine particle mass) and acidity is relatively low.<sup>25</sup>

In a priori single-pollutant models using 3-day moving averages, CVD visits were associated with  $\text{NO}_2$ , CO,  $\text{PM}_{2.5}$ , organic carbon, elemental carbon, and oxygenated hydrocarbons (Table 4). Of the cardiovascular subgroups, congestive heart failure was positively associated with  $\text{PM}_{2.5}$ , organic carbon, and elemental carbon. Ischemic heart disease was positively associated with  $\text{NO}_2$  and oxygenated hydrocarbons. Peripheral vascular and cerebrovascular disease was positively associated with  $\text{NO}_2$ , CO, and  $\text{PM}_{2.5}$ . No positive

**TABLE 1.** Mean of Daily Counts of Emergency Department Visits at 31 Participating Hospitals for the Period January 1, 1993–August 31, 2000, Study of Particles and Health in Atlanta (SOPHIA)\*

	ICD-9 Codes	Mean
Total emergency department visits per day		1574
All cardiovascular disease	410–414, 427–428, 433–437, 440, 443–444, 451–453	37.0
Dysrhythmia	427	9.8
Cardiac arrest	427.5	3.0
Congestive heart failure	428	7.2
Ischemic heart disease	410–414	11.7
Acute myocardial infarction	410	4.5
Peripheral vascular and cerebrovascular disease	433–437, 440, 443–444, 451–453	8.4
Atherosclerosis	440	0.2
Stroke	436	1.3
Finger wounds	883.0	21.4

\*Standard deviation and selected percentiles available with the electronic version of this article.  
ICD-9, International Classification of Diseases, 9th Revision; SD, standard deviation.

**TABLE 2.** Median and 10% to 90% Range of Daily Ambient Air Quality Measurements for Criteria Pollutants from AIRS/MAI During the Period January 1, 1993–August 31, 2000, and for Other Pollutants From ARIES During the Period August 1, 1998–August 31, 2000\*

	Beginning Year	No. of Days	Median	(10% to 90% range)
24-h PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ ) <sup>†</sup>	1993	2703	26.3	(13.2 to 44.7)
8-h ozone (ppb) <sup>†‡</sup>	1993	1892	53.9	(26.8 to 87.6)
1-h NO <sub>2</sub> (ppb) <sup>†</sup>	1993	2775	44.0	(25.0 to 68.0)
1-h CO (ppm) <sup>†</sup>	1993	2758	1.5	(0.5 to 3.4)
1-h SO <sub>2</sub> (ppb) <sup>†</sup>	1993	2775	11.0	(2.0 to 39.0)
24-h PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	1998	750	17.8	(8.9 to 32.3)
24-h coarse PM ( $\mu\text{g}/\text{m}^3$ )	1998	679	9.1	(4.4 to 16.2)
24-h 10–100 nm particle count (no/cm <sup>3</sup> )	1998	427	25,900	(11,500 to 74,600)
24-h PM <sub>2.5</sub> water-soluble metals ( $\mu\text{g}/\text{m}^3$ )	1998	692	0.021	(0.006 to 0.061)
24-h PM <sub>2.5</sub> sulfates ( $\mu\text{g}/\text{m}^3$ )	1998	687	4.5	(1.9 to 10.7)
24-h PM <sub>2.5</sub> acidity ( $\mu\text{-equ}/\text{m}^3$ ) <sup>§</sup>	1998	646	0.010	(–0.001 to 0.045)
24-h PM <sub>2.5</sub> organic carbon ( $\mu\text{g}/\text{m}^3$ )	1998	715	4.1	(2.2 to 7.1)
24-h PM <sub>2.5</sub> elemental carbon ( $\mu\text{g}/\text{m}^3$ )	1998	714	1.6	(0.8 to 3.7)
24-h oxygenated hydrocarbon (ppb)	1998	594	29.1	(15.0 to 53.1)
Average temperature (°C) <sup>¶</sup>	1993	2800	18.3	(6.1 to 27.2)
Average dew point (°C) <sup>¶</sup>	1993	2800	12.0	(–2.2 to 20.8)

\*Mean, standard deviation, selected additional percentiles, and number of nonmissing days available with the electronic version of this article. www.epidem.com

<sup>†</sup>Data were imputed for 17% (458 of 2703) of PM<sub>10</sub> values, 2% (46 of 1892) of O<sub>3</sub> values, 14% (398 of 2775) of NO<sub>2</sub> values, 6% (161 of 2758) of CO values, and 9% (237 of 2775) of SO<sub>2</sub> values.

<sup>‡</sup>Ozone was measured for 1896 days: 3/1/1993–11/30/1993, 3/1/1994–11/30/1994, 3/1/1995–11/30/1995, 3/1/1996–10/31/1996, 4/1/1997–10/31/1997, 4/1/1998–10/31/1998, 4/1/1999–10/31/1999, 3/1/2000–8/31/2000.

<sup>§</sup>Acidity is reported in units of  $\mu\text{-equ}/\text{m}^3$ , a measure of pH level. If converted into units of nmol/m<sup>3</sup>, the median is 10.

<sup>¶</sup>For temperature and dew point: average of minimum and maximum values recorded at Hartsfield-Atlanta International Airport.

AIRS, Aerometric Information Retrieval System; ARIES, Aerosol Research and Inhalation Epidemiology Study; CO, carbon monoxide; MAI, Metro Atlanta Index; NO<sub>2</sub>, nitrogen dioxide, PM, particulate matter; SO<sub>2</sub>, sulfur dioxide.



**TABLE 3.** Spearman Correlation Coefficients for Daily Ambient Air Quality Measurements

	24-h PM <sub>10</sub>	8-h O <sub>3</sub>	1-h NO <sub>2</sub>	1-h CO	1-h SO <sub>2</sub>	24-h PM <sub>2.5</sub>	24-h Coarse PM	24-h Ultrafine (10–100 nm) Count	24-h PM <sub>2.5</sub> Water- Soluble Metals	24-h PM <sub>2.5</sub> Sulfates	24-h PM <sub>2.5</sub> Acidity	24-h PM <sub>2.5</sub> OC	24-h PM <sub>2.5</sub> EC	24-h OHC	Average Temper- ature
24-h PM <sub>10</sub>	1														
8-h O <sub>3</sub>	0.59	1													
1-h NO <sub>2</sub>	0.49	0.42	1												
1-h CO	0.47	0.20	0.68	1											
1-h SO <sub>2</sub>	0.20	0.19	0.34	0.26	1										
24-h PM <sub>2.5</sub>	0.84	0.65	0.46	0.44	0.17	1									
24-h coarse PM	0.59	0.35	0.46	0.32	0.21	0.43	1								
24-h ultrafine (10–100 nm) PM	–0.13	–0.13	0.26	0.10	0.24	–0.16	0.13	1							
24-h PM <sub>2.5</sub> water- soluble metals	0.74	0.48	0.32	0.28	0.00	0.70	0.47	–0.27	1						
24-h PM <sub>2.5</sub> sulfates	0.74	0.63	0.17	0.13	0.08	0.77	0.26	–0.31	0.71	1					
24-h PM <sub>2.5</sub> acidity	0.68	0.64	0.10	–0.01	–0.03	0.58	0.23	–0.39	0.62	0.82	1				
24-h PM <sub>2.5</sub> organic carbon	0.69	0.59	0.63	0.55	0.18	0.73	0.51	0.08	0.46	0.39	0.30	1			
24-h PM <sub>2.5</sub> elemental carbon	0.56	0.37	0.61	0.63	0.20	0.61	0.48	0.08	0.49	0.29	0.14	0.82	1		
24-h oxygenated hydrocarbon	0.42	0.42	0.30	0.31	0.14	0.40	0.31	0.05	0.33	0.32	0.32	0.46	0.41	1	
Average temperature	0.58	0.58	0.08	0.09	–0.06	0.39	0.20	–0.33	0.56	0.64	0.84	0.15	0.06	0.34	1
Average dew point	0.44	0.26	–0.13	–0.01	–0.15	0.29	0.00	–0.41	0.48	0.57	0.77	–0.01	–0.04	0.25	0.92

associations were observed for any pollutant measure and dysrhythmia. No associations were observed for finger wounds.

The observed associations from the a priori model were robust to model structure and specification. In sensitivity analyses of GLMs using alternative frequencies of knots in cubic splines for control of long-term temporal trends, similar results were observed (table available with the electronic version of this article). Residual serial correlation, assessed by GEE with a stationary 4-dependent correlation structure, was minimal. No negative autocorrelation of the residuals was observed for the a priori model. Point estimates obtained from analyses using GAMs were similar to those from GLMs.

We conducted secondary analyses of GLMs with single-day pollutant lags up to 7 days before the CVD visit. Figure 1 presents results for CVD visits with each air-quality analyte lagged zero to 7 days. For the 6 pollutants with significantly positive associations using the 3-day moving average (PM<sub>2.5</sub>, NO<sub>2</sub>, CO, organic carbon, elemental carbon, and oxygenated hydrocarbons), the associations for pollution levels on the same day as CVD visits tended to be the strongest. Results for the CVD subgroups showed similar patterns, with the strongest associations observed for pollut-

ant concentrations on the same day or days immediately before the emergency department visit.

In age-specific analyses, associations for CVD visits by both adults and the elderly were similar in magnitude to those obtained in analyses, including all ages. Season-specific analyses indicated some seasonal variation in the associations between certain pollutants and CVD visits. Associations tended to be highest during colder months and lowest during warmer months.

Table 5 shows a comparison of results from models for the period August 1, 1998, to August 31, 2000, using data on criteria pollutants from the ARIES and AIRS/MAI monitors. The magnitude of effect estimates from the 2 sources of air quality data was similar.

Multipollutant models were evaluated for CVD visits with the pollutants that were statistically significant in a priori models (Fig. 2). Because organic carbon and elemental carbon were highly correlated ( $r = 0.82$ ), a measure of total carbon was defined by summing them for use in multipollutant models (in single-pollutant models with CVD, per 3  $\mu\text{g}/\text{m}^3$ : RR = 1.026; 95% confidence interval = 1.007–1.045). In a 2-pollutant model for the entire study period (January 1, 1993–August 31, 2000), the estimate for NO<sub>2</sub> was attenuated slightly, whereas the estimate for CO was indis-

**TABLE 4.** Results of a priori Models\* for the Association of Emergency Department Visits for Cardiovascular Disease, Cardiovascular Subgroups, and Finger Wounds With Daily Ambient Air Quality Measurements

Pollutant <sup>†</sup>	Unit <sup>‡</sup>	All CVD		Dysrhythmia		CHF		IHD		PERI		Finger Wounds <sup>§</sup>	
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	
January 1, 1993–August 31, 2000													
24-h PM <sub>10</sub>	10 µg/m <sup>3</sup>	1.009 (0.998–1.019)	1.008 (0.989–1.029)	0.992 (0.968–1.016)	1.011 (0.992–1.030)	1.020 (0.999–1.043)	1.008 (0.995–1.022)						
8-h O <sub>3</sub>	25 ppb	1.008 (0.987–1.030)	1.008 (0.967–1.051)	0.965 (0.918–1.014)	1.019 (0.981–1.059)	1.028 (0.985–1.073)	1.014 (0.987–1.042)						
1-h NO <sub>2</sub>	20 ppb	1.025 (1.012–1.039)	1.019 (0.994–1.044)	1.010 (0.981–1.040)	1.029 (1.005–1.053)	1.041 (1.013–1.069)	1.010 (0.993–1.027)						
1-h CO	1 ppm	1.017 (1.008–1.027)	1.012 (0.993–1.031)	1.010 (0.988–1.032)	1.016 (0.999–1.034)	1.031 (1.010–1.052)	1.008 (0.995–1.021)						
1-h SO <sub>2</sub>	20 ppb	1.007 (0.993–1.022)	1.001 (0.975–1.028)	0.992 (0.961–1.025)	1.007 (0.981–1.033)	1.028 (0.999–1.059)	1.007 (0.988–1.026)						
August 1, 1998–August 31, 2000													
24-h PM <sub>2.5</sub>	10 µg/m <sup>3</sup>	1.033 (1.010–1.056)	1.015 (0.976–1.055)	1.055 (1.006–1.105)	1.023 (0.983–1.064)	1.050 (1.008–1.093)	0.995 (0.968–1.023)						
24-h coarse PM	5 µg/m <sup>3</sup>	1.012 (0.985–1.040)	1.021 (0.974–1.070)	1.020 (0.964–1.079)	0.994 (0.946–1.045)	1.022 (0.972–1.074)	1.000 (0.967–1.035)						
24-h 10–100 nm particle count	30,000 no/cm <sup>3</sup>	0.985 (0.965–1.005)	0.972 (0.937–1.008)	0.983 (0.943–1.025)	0.989 (0.953–1.026)	0.998 (0.960–1.038)	0.999 (0.974–1.024)						
24-h PM <sub>2.5</sub> water-soluble metals	0.03 µg/m <sup>3</sup>	1.027 (0.998–1.056)	1.031 (0.982–1.082)	1.040 (0.981–1.103)	1.000 (0.951–1.051)	1.043 (0.991–1.098)	1.001 (0.968–1.036)						
24-h PM <sub>2.5</sub> sulfates	5 µg/m <sup>3</sup>	1.003 (0.968–1.039)	0.986 (0.926–1.048)	1.009 (0.938–1.085)	0.997 (0.936–1.062)	1.025 (0.964–1.090)	0.983 (0.942–1.025)						
24-h PM <sub>2.5</sub> acidity	0.02 µequ/m <sup>3</sup>	0.994 (0.966–1.022)	0.991 (0.942–1.043)	0.989 (0.930–1.052)	0.992 (0.944–1.043)	1.004 (0.955–1.056)	0.969 (0.935–1.004)						
24-h PM <sub>2.5</sub> organic carbon	2 µg/m <sup>3</sup>	1.026 (1.006–1.046)	1.008 (0.975–1.044)	1.048 (1.007–1.091)	1.028 (0.994–1.064)	1.026 (0.990–1.062)	0.990 (0.966–1.014)						
24-h PM <sub>2.5</sub> elemental carbon	1 µg/m <sup>3</sup>	1.020 (1.005–1.036)	1.011 (0.985–1.037)	1.035 (1.003–1.068)	1.019 (0.992–1.046)	1.021 (0.994–1.049)	1.003 (0.984–1.021)						
24-h oxygenated hydrocarbon	15 ppb	1.029 (1.000–1.059)	1.007 (0.958–1.059)	1.034 (0.972–1.099)	1.066 (1.012–1.122)	1.008 (0.954–1.065)	1.011 (0.973–1.050)						

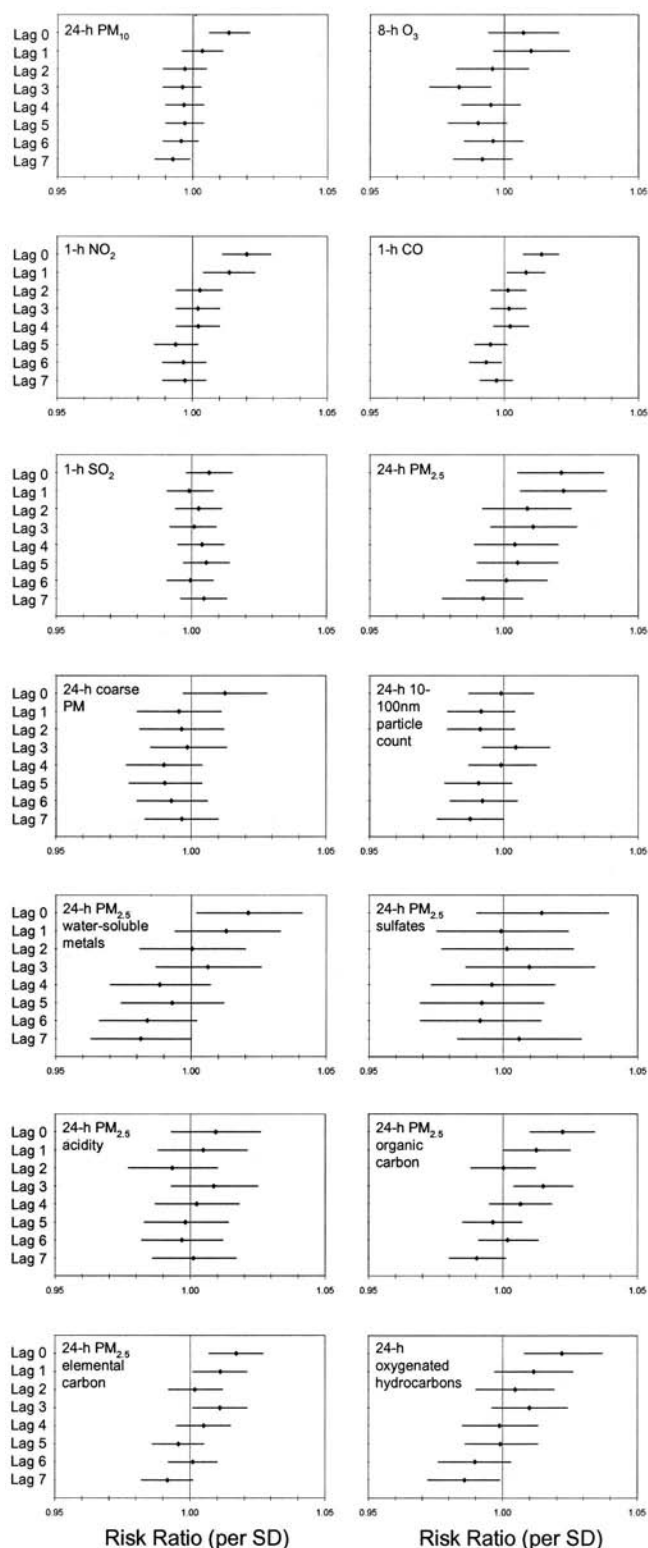
\*Single-pollutant GLM models including indicators for day-of-week, hospital entry, and holidays; cubic splines for time with monthly knots; cubic splines for temperature and dewpoint temperature with knots at the 25th and 75th percentile

<sup>‡</sup>3-day moving average.

<sup>†</sup>Approximately 1 standard deviation.

<sup>§</sup>Emergency department visits for finger wounds were used to assess the adequacy of the a priori model.

CVD, cardiovascular disease; CHF, congestive heart failure; IHD, ischemic heart disease; PERI, peripheral vascular and cerebrovascular disease;



**FIGURE 1.** Risk ratios (diamonds) and 95% confidence intervals (horizontal lines) of single-day lag models for the association of emergency department visits for cardiovascular disease with daily ambient air quality measurements.

tinguishable from the null. In contrast, in the 2-pollutant models for the time period August 1, 1998, to August 31, 2000, the magnitude of the estimates for CO were similar to the magnitude observed in the single-pollutant model in models with PM<sub>2.5</sub>, with NO<sub>2</sub>, and with oxygenated hydrocarbons. The estimates for PM<sub>2.5</sub>, NO<sub>2</sub>, total carbon, and oxygenated hydrocarbons were generally attenuated and indistinguishable from the null in 2-pollutant models. These patterns persisted in 3-, 4-, and 5-pollutant models. All multipollutant models had a reduced number of days available for the analysis, because only days with nonmissing data for all pollutants in the model were included.

**DISCUSSION**

This time-series study of emergency department visits provided a unique opportunity to examine the relationship between cardiovascular conditions and ambient gaseous and particulate pollution levels, including the physicochemical components of PM. In a priori models, CVD visits were associated with several particle measures (PM<sub>2.5</sub> mass, organic carbon, and elemental carbon) and gas measures (CO, NO<sub>2</sub>, and oxygenated hydrocarbons). Visits for peripheral vascular and cerebrovascular disease were associated with PM<sub>2.5</sub> and the gases NO<sub>2</sub> and CO. Congestive heart failure visits were associated with PM<sub>2.5</sub> and two PM<sub>2.5</sub> components, organic carbon, and elemental carbon. The gaseous pollutants NO<sub>2</sub> and oxygenated hydrocarbons were associated with ischemic heart disease. In multipollutant models, the estimates for NO<sub>2</sub> remained elevated during the 7-year period, whereas CO estimates were elevated during the 25-month period; these 2 pollutants are strongly correlated ( $r = 0.68$ ).

Although other time-series studies have used different cardiovascular morbidity measures such as hospital admissions, our results are consistent with previously reported associations for all cardiovascular conditions combined, as well as ischemic heart disease and congestive heart failure, with PM,<sup>4,7-10,12,13</sup> NO<sub>2</sub>,<sup>2,3,5,7,8,10,12,26,27</sup> and CO.<sup>3,4,7,9,11,12,26,28,29</sup> Because two-thirds of emergency department visits for cardiovascular conditions result in hospital admission,<sup>30</sup> these 2 measures of cardiovascular morbidity comprise overlapping populations. Emergency department visits also include some cardiovascular conditions that, although not severe enough to lead to hospitalization, nonetheless require medical attention. The observed associations for CVD visits in the present study contribute to the coherence of evidence supporting the relation between cardiovascular morbidity and ambient air pollution levels.

The biologic mechanisms underlying the relation between ambient air pollution and cardiovascular conditions are unknown, but could involve modulation of the autonomic nervous system or induction of circulating inflammatory parameters. Several small studies indicated that ambient PM<sub>2.5</sub> levels were associated with decreased heart rate variability, reflecting changes in autonomic nervous activity.<sup>31-34</sup>

**TABLE 5.** Comparison of Results of a priori Models\* for the Association of Emergency Department Visits for Cardiovascular Disease With Daily Ambient Air Quality Levels Measurements

Pollutant <sup>†</sup>	Unit <sup>‡</sup>	AIRS/MAI Data	AIRS/MAI Data	ARIES Data
		January 1, 1993–August 31, 2000	August 1, 1998–August 31, 2000	August 1, 1998–August 31, 2000
		RR (95% CI)	RR (95% CI)	RR (95% CI)
24-h PM <sub>10</sub> <sup>§</sup>	10 µg/m <sup>3</sup>	1.009 (0.998–1.019)	1.027 (1.009–1.046)	1.017 (0.997–1.037)
8-h O <sub>3</sub> <sup>§</sup>	25 ppb	1.008 (0.987–1.030)	0.994 (0.957–1.032)	0.994 (0.954–1.035)
1-h NO <sub>2</sub> <sup>§</sup>	20 ppb	1.025 (1.012–1.039)	1.025 (1.004–1.045)	1.037 (1.005–1.070)
1-h CO <sup>§</sup>	1 ppm	1.017 (1.008–1.027)	1.029 (1.012–1.046)	1.044 (1.022–1.067)
1-h SO <sub>2</sub> <sup>§</sup>	20 ppb	1.007 (0.993–1.022)	1.019 (0.996–1.043)	1.016 (0.989–1.044)

\*Single-pollutant GLM models including indicators for day-of-week, hospital entry and holidays; cubic splines for time with monthly knots; cubic splines for temperature and dewpoint temperature with knots at the 25th and 75th percentile.

<sup>†</sup>3-day moving average.

<sup>‡</sup>Approximately 1 standard deviation.

<sup>§</sup>Spearman correlation coefficients for data on the same pollutant from AIRS and ARIES monitors for PM<sub>10</sub>,  $r = 0.88$ ; O<sub>3</sub>,  $r = 0.98$ ; NO<sub>2</sub>,  $r = 0.78$ ; CO,  $r = 0.70$ ; and SO<sub>2</sub>,  $r = 0.81$ .

Several cardiac conditions, including sudden cardiac death and myocardial infarction, are associated with altered autonomic function.<sup>35</sup> Ambient PM<sub>10</sub> has also been associated with increased levels of circulating fibrinogen and markers of inflammation.<sup>36,37</sup> Fibrinogen and acute-phase proinflammatory proteins can increase blood coagulability, leading to ischemia and exacerbating cardiovascular disease.<sup>38</sup>

Major challenges in interpreting studies such as the present one include the likelihood of confounding by correlated pollutants and the possibility that a given pollutant is acting as a surrogate for other unmeasured or poorly measured pollutants. Multipollutant models are often used to address confounding by correlated pollutants, but these results can be as misleading as single-pollutant models. In a situation in which a poorly measured pollutant that is truly associated with the outcome is correlated with another pollutant that is better measured but biologically irrelevant, the latter pollutant could be a predictor both in a single pollutant and a multipollutant model.<sup>39</sup> Moreover, if the pollutants act as surrogates for unmeasured agents that are truly responsible for the association,<sup>40</sup> the strongest predictor in a multipollutant model could simply indicate which measured pollutant is the best surrogate for the unmeasured pollutant of interest. For example, suppose that traffic particles are qualitatively different from other particles and that these are the agents largely responsible for a particular health outcome. We had no direct measurement of traffic particles, and it is possible that a number of the pollutant measurements associated with CVD visits are surrogates for such an agent.

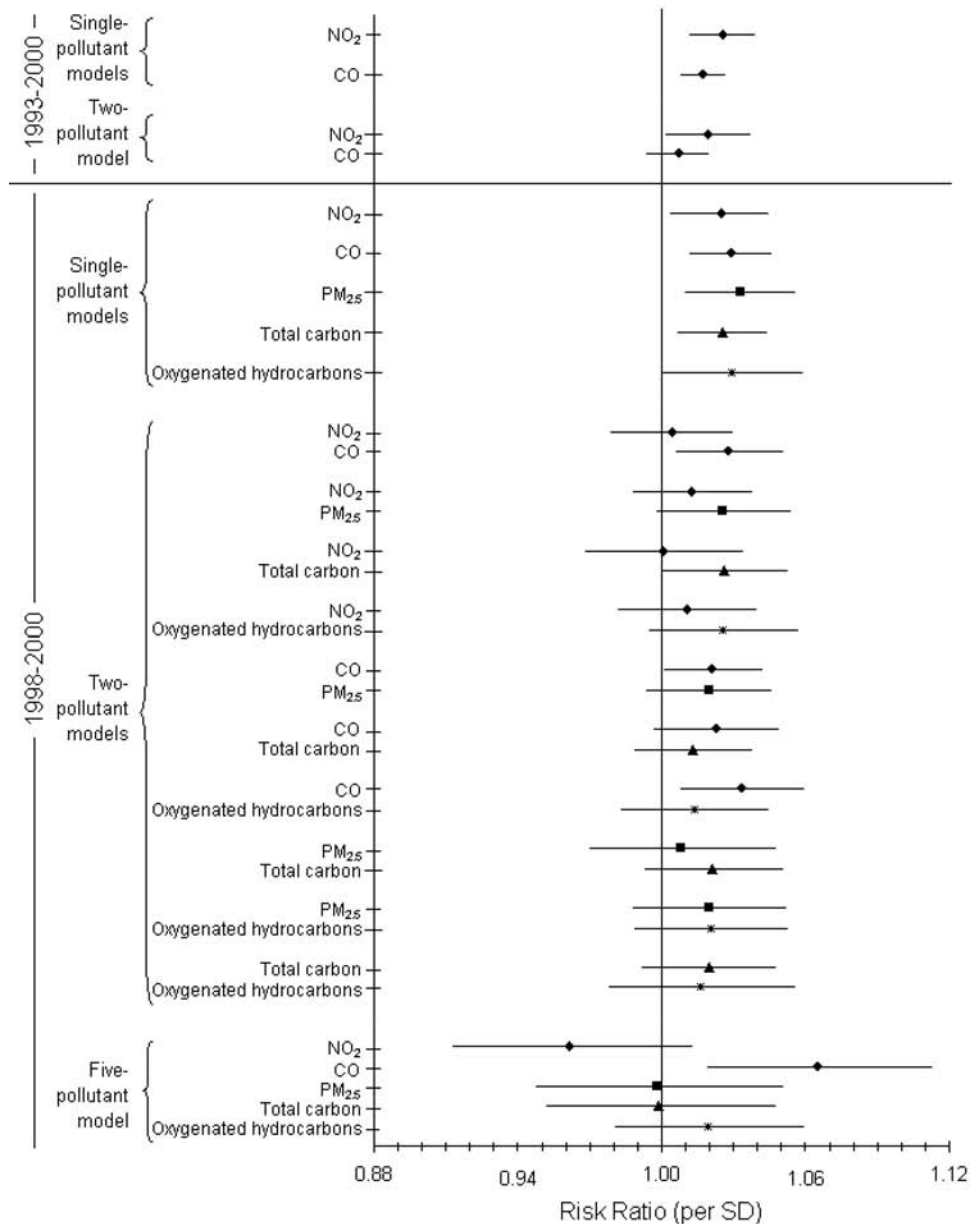
Because the goal of this study was to assess the impact of ambient pollution levels on the cardiovascular health of the population, the error that results from the use of ambient air quality measurements from centrally located monitors must be considered. The measurement error in data from a central

monitor, rather than a weighted average of individual ambient exposures, includes instrument error, error from local sources, and error resulting from regional spatial heterogeneity, all of which would likely lead to attenuation of the effect estimates. These types of measurement error in the exposure could have led to the lack of association observed with some pollutants, but are unlikely to have led to spurious results. Additionally, the present study assessed the relationship between ambient air pollution and cardiovascular conditions in this population, given personal behaviors that could modify exposure levels. In Atlanta, approximately 83% of homes are equipped with central air conditioning,<sup>41</sup> the use of which can reduce personal air pollution exposure during the warm season. Thus, the effect for a given increment in the ambient level of a pollutant in Atlanta during warmer months could be smaller than in some other cities without widespread air conditioning use.<sup>42</sup>

Ultrafine PM data presented problems beyond measurement error. Although the instruments used to measure ultrafine PM were state-of-the-art, they had not been used extensively in the field. Because of instrument malfunctions, the ultrafine PM measurements were frequently missing during the study period, often for long periods of time. The large missing data problem could have led to unreliable effect estimates. Additional discussion of the ultrafine measurements can be found elsewhere.<sup>43,44</sup>

Many of the air quality concentrations measured at the ARIES monitoring site appeared to be spatially representative of the Atlanta MSA. Measurements of criteria pollutants were available from both the ARIES and AIRS/MAI monitoring sites; concentrations measured at the 2 types of sites were highly correlated and not substantially or systematically different. For spatially variable pollutants that vary by distance from mobile sources, such as NO<sub>2</sub> and CO, the measurements





**FIGURE 2.** Risk ratios (symbols) and 95% confidence intervals (horizontal lines) of multipollutant models for the association of emergency department visits for cardiovascular disease with daily ambient air quality measurements.

from the ARIES site appear to reflect what is being measured at the AIRS sites. Epidemiologic analyses using ARIES data for criteria pollutants yielded similar results to a priori analyses using AIRS/MAI data. The spatial distribution of ambient PM<sub>2.5</sub> and several of its constituents, including sulfates, organic carbon, and elemental carbon, appear to be relatively homogenous; measurements from the ARIES monitoring site were similar to those from other monitoring sites in Atlanta.<sup>25</sup> No information was available to assess the spatial variability for 10- to 100-nm particle count or oxygenated hydrocarbons.

To reduce the problems associated with multiple testing and model selection strategies, we used a priori models for our primary analyses, specifying analytes of interest, pollutant lag, and the structure of the model.<sup>45,46</sup> An a priori list of 14 air quality measures was distilled from the large number of pollutant metrics available after taking into account the current hypotheses on potentially causal pollutants and components.<sup>15,16</sup> The choice of a priori pollutant lag structure was based on previously reported associations in time-series studies of cardiovascular morbidity and influenced by biologi-

cally plausible hypotheses. The a priori model was constructed by using information obtained from previously published health effects studies regarding methods of controlling for temporal trends and other confounding factors. Although the periodic frequency of long-term trends in the data might not have necessitated the use of monthly knots, potentially overcontrolling for confounding by time was considered a better alternative to undercontrolling. In comparing the a priori models to GLMs using alternative frequencies of knots, the magnitude of the estimates for CVD visits were similar. Although the satisfaction of statistical criteria (eg, Akaike's Information Criteria, Bartlett test) does not imply successful control of confounding, the application of such criteria yielded results similar to those obtained using the a priori model. Further evidence of the robustness of the a priori model was provided by the similarity of results from analyses using GAMs. Additionally, no associations were observed with finger wounds, providing no indication that the a priori model structure systematically induced spurious results. Simulation studies have demonstrated that selecting an a priori model avoids bias introduced when choosing and reporting results from the best model and lag structure based on the strongest effect estimate.<sup>47,48</sup> Although some of the associations observed are likely to be random, the number and consistency of positive associations seen for CVD and cardiovascular subgroup visits and various pollutant measures is notable.

The study took advantage of a unique source of air quality data in Atlanta to examine the relation between ambient air pollutants, including physicochemical components of PM, and cardiovascular emergency department visits. CVD visits were positively associated with ambient concentrations of CO, NO<sub>2</sub>, PM<sub>2.5</sub>, organic carbon, elemental carbon, and oxygenated hydrocarbons. CVD subgroups such as congestive heart failure, ischemic heart disease, and peripheral and cerebrovascular disease were also associated with several pollutant measures. The relationships observed in this study could represent an association with one or more correlated copollutants such as other characteristics of traffic-related pollution. The effect of ambient pollution on cardiovascular conditions appeared to be rapid, because the strongest associations tended to be observed with pollution levels on the same day as the emergency department visits.

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