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Original Contribution

Ambient Air Pollution and Cardiovascular Emergency Department Visits in Potentially Sensitive Groups

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Limited evidence suggests that persons with conditions such as diabetes, hypertension, congestive heart failure, and respiratory conditions may be at increased risk of adverse cardiovascular morbidity and mortality associated with ambient air pollution. The authors collected data on over 4 million emergency department visits from 31 hospitals in Atlanta, Georgia, between January 1993 and August 2000. Visits for cardiovascular disease were examined in relation to levels of ambient pollutants by use of a case-crossover framework. Heterogeneity of risk was examined for several comorbid conditions. The results included evidence of stronger associations of dysrhythmia and congestive heart failure visits with comorbid hypertension in relation to increased air pollution levels compared with visits without comorbid hypertension; similar evidence of effect modification by diabetes and chronic obstructive pulmonary disease (COPD) was observed for dysrhythmia and peripheral and cerebrovascular disease visits, respectively. Evidence of effect modification by comorbid hypertension and diabetes was observed in relation to particulate matter less than 10 μm in aerodynamic diameter, nitrogen dioxide, and carbon monoxide, while evidence of effect modification by comorbid COPD was also observed in response to ozone levels. These findings provide further evidence of increased susceptibility to adverse cardiovascular events associated with ambient air pollution among persons with hypertension, diabetes, and COPD.

air pollution; arrhythmia; cardiovascular diseases; cerebrovascular disorders; diabetes mellitus; emergency service, hospital; lung diseases, obstructive; peripheral vascular diseases

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICD-9, *International Classification of Diseases*, Ninth Revision; OR, odds ratio; PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.

Limited but growing evidence from recent epidemiologic studies suggests that persons with comorbid conditions, including diabetes, hypertension, congestive heart failure, recent myocardial infarction, and respiratory conditions, may be at increased risk of cardiovascular morbidity and mortality in relation to ambient air pollution levels (1–12). However, considerable uncertainty is included in these risk estimates for susceptible populations (13). The most recent report by the National Research Council emphasized the need for continued examination of the most susceptible subgroups, including persons with underlying cardiovascular and respiratory disease (14).

This case-crossover analysis examined the association of ambient air pollution levels and cardiovascular morbidity in visits with and without specific secondary conditions, that is, diabetes, hypertension, dysrhythmia, congestive heart

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failure, atherosclerosis, chronic obstructive pulmonary disease (COPD), pneumonia, upper respiratory infections, and asthma, by use of a large database of emergency department visits compiled for the Study of Particles and Health in Atlanta (referred to as "SOPHIA").

MATERIALS AND METHODS

Ambient air quality data

For the period January 1, 1993, through August 31, 2000, we obtained ambient air quality data for 24-hour particulate matter with an average aerodynamic diameter of less than 10 μm (PM_{10}), 8-hour maximum ozone, and 1-hour maximum nitrogen dioxide, sulfur dioxide, and carbon monoxide from several existing monitoring networks, including the Air Quality System, the Georgia Department of Natural Resources, and the Metro Atlanta Index. Ozone levels were not monitored during the winter months when ozone levels in Atlanta are low; the remaining pollutants were measured daily throughout the year. These air quality data have been described previously (15, 16). For gaseous pollutants, hourly data were used; for PM_{10} mass, daily gravimetric data were used. For each pollutant, data from the most central monitoring site were used. On days when measurements were missing at the central site, data were imputed by use of measurements from at least one other monitoring site in the Atlanta metropolitan statistical area, as well as meteorologic and time variables (values imputed for 17 percent, 2 percent, 14 percent, 6 percent, and 9 percent of PM_{10}, ozone, nitrogen dioxide, carbon monoxide, and sulfur dioxide measurements, respectively).

The average temperature and dew point temperature (average of the daily minimum and maximum), as well as additional meteorologic data measured at the Hartsfield-Atlanta International Airport, were obtained from the National Climatic Data Center network.

Emergency department data

Of the 41 hospitals in the 20-county Atlanta metropolitan statistical area, 37 agreed to participate, and 31 provided usable computerized billing records for at least part of the study period. Computerized billing records for all emergency department visits between January 1, 1993, and August 31, 2000, were collected, including primary *International Classification of Diseases*, Ninth Revision (ICD-9), diagnostic codes, secondary ICD-9 diagnostic codes, age, date of birth, sex, race, and residential ZIP code. The study was approved and was granted a waiver of consent by the Emory University Institutional Review Board. Residents of the Atlanta metropolitan statistical area, determined by residential ZIP code at the time of the visit, were included in the analyses. Repeat visits within a day were counted as a single visit.

Using the primary ICD-9 diagnosis code, we defined several primary cardiovascular disease groups: ischemic heart disease (codes 410–414), dysrhythmia (code 427), congestive heart failure (code 428), and peripheral vascular and cerebrovascular disease (codes 433–437, 440, 443, 444, 451–453). The combined cardiovascular disease case group pooled the ICD-9 diagnoses of the preceding case groups.

The comorbid health conditions for each visit were defined by use of all secondary ICD-9 diagnosis codes listed for the same visit as the primary diagnosis code. The comorbid health conditions that we examined were defined as follows: hypertension (codes 401–405), diabetes (code 250), dysrhythmia (code 427), congestive heart failure (code 428), atherosclerosis (code 440), COPD (codes 491, 492, 496), pneumonia (codes 480–486), upper respiratory infections (codes 460–465, 466.0), and asthma (codes 493, 786.09).

Statistical analysis

All analyses were performed using SAS, version 9.1, statistical software (SAS Institute, Inc., Cary, North Carolina). All odds ratios and confidence intervals were calculated for an increase of approximately 1 standard deviation in the pollutant measure.

Using a case-crossover framework, we modeled the association between air pollution and cardiovascular visits. We used a time-stratified approach to select referent days (17–20); referent days were selected on the same day of week and within the same calendar month as the cardiovascular visit of interest. For example, if the visit occurred on a Tuesday in March (the case day), we selected all other Tuesdays in March as the control days. A subject could have an emergency department visit for the outcome of interest on a selected control day; because this situation occurred so infrequently (0.7 percent of the strata), these days were retained as control days (and were also counted as a case day in another stratum).

For each air quality variable, the moving average of the 0-, 1-, and 2-day lags was used as the a priori lag structure. We used conditional logistic regression for the analysis (PROC PHREG procedure in SAS, version 9.1, software); each stratum consisted of the case day and all selected control days. Cubic splines for average daily temperature and dew point temperature (average of values lagged 0, 1, and 2 days) with knots at the 25th and 75th percentiles were also included in the models.

We compared the results from the case-crossover analysis with those from our previous time-series analysis, which used Poisson generalized linear modeling (15). Then, we examined potentially susceptible subgroups of the primary cardiovascular disease visits with comorbid health conditions as defined by the secondary ICD-9 diagnosis codes as described above. For example, the association of air pollution and emergency visits for dysrhythmia was examined separately in visits with and without a secondary diagnosis of hypertension. We calculated chi-squared statistics and corresponding two-sided p values to assess the heterogeneity of the pollution regression coefficients from the two strata.

RESULTS

Table 1 provides descriptive statistics for the daily concentrations of the air quality measures, as well as for the absolute difference between air pollution levels on event

TABLE 1. Mean, standard deviation, and selected percentiles of daily ambient air quality levels and of the absolute differences between daily levels on event days and the average concentrations on the control days, Atlanta, Georgia, 1993–2000

	Mean	Standard deviation	Percentile	
			10th	90th
Daily levels				
24-hour PM_{10}* ($\mu g/m^3$)†	27.9	12.3	13.2	44.7
8-hour ozone (ppb)†,‡	55.6	23.8	26.8	87.6
1-hour nitrogen dioxide (ppb)†	45.9	17.3	25.0	68.0
1-hour carbon monoxide (ppm)†	1.8	1.2	0.5	3.4
1-hour sulfur dioxide (ppb)†	16.5	17.1	2.0	39.0
Average temperature (°C)	17.5	8.3	6.1	27.2
Average dew point (°C)	10.5	8.9	−2.2	20.8
Absolute differences between the average level on case days and the average level on control days				
24-hour PM_{10} ($\mu g/m^3$)	9.1	7.5	1.4	19.1
8-hour ozone (ppb)	17.5	13.9	2.7	39.2
1-hour nitrogen dioxide (ppb)	16.3	12.7	2.8	32.8
1-hour carbon monoxide (ppm)	1.0	0.8	0.2	2.1
1-hour sulfur dioxide (ppb)	12.6	12.6	1.7	25.8
Average temperature (°C)	7.2	6.0	1.0	15.2
Average dew point (°C)	9.3	7.8	1.0	20.2

* PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.

† Data were imputed for 17 percent (458 of 2,703) of PM_{10} values, 2 percent (46 of 1,892) of ozone values, 14 percent (398 of 2,775) of nitrogen dioxide values, 6 percent (161 of 2,758) of carbon monoxide values, and 9 percent (237 of 2,775) of sulfur dioxide values.

‡ Ozone was measured from March through October only.

days and the average concentrations on the controls days. More detailed descriptions of the emergency department and air quality data for this time period have been presented elsewhere (15, 16).

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 percent of emergency department visits in the Atlanta metropolitan statistical area. Five hospitals provided data for the entire study period; the mean length of time the hospitals provided data was 4.5 years (range: 2–7.5 years). There was an average of 37 cardiovascular disease visits per day; subgroups had between 7.2 visits per day (congestive heart failure) and 11.7 visits per day (ischemic heart disease). Table 2 presents the number and percentage of the secondary diagnoses for each of the primary outcome groups. Hypertension was the largest of the secondary diagnosis groups, with over 30 percent of visits for cardiovascular disease having a secondary diagnosis of hypertension (table 2).

We observed 2–3 percent increases in cardiovascular visits, including the subgroups ischemic heart disease, peripheral and cerebrovascular disease, and congestive heart failure, associated with standard deviation increases of nitrogen dioxide and carbon monoxide in single-pollutant models using 3-day moving averages (pollution lagged 0, 1, and 2 days) (table 3). Associations of peripheral and cerebrovascular disease visits with PM_{10} and sulfur dioxide were also elevated but not significant, as was the association of dysrhythmia and nitrogen dioxide. Results from the case-crossover analysis were largely similar to results from the previous time-series analysis (15) (table 3). The greatest inconsistencies were observed for congestive heart failure, the smallest of the subgroups, and for ozone across the outcome groups.

Results from analyses examining visits for cardiovascular disease with comorbid diagnoses are presented in tables 4–8. There were low numbers of visits with comorbid atherosclerosis, asthma, pneumonia, and upper respiratory infection, resulting in unstable models; therefore, the results for these comorbid conditions are not presented. The estimated associations of cardiovascular disease, specifically visits for congestive heart failure and dysrhythmia, in relation to nitrogen dioxide, carbon monoxide, and PM_{10} were substantially higher among patients with a secondary diagnosis of hypertension than for patients without comorbid hypertension (table 4). The strongest associations among hypertensive patients were observed for dysrhythmia visits in relation to nitrogen dioxide (per 20 ppb: odds ratio (OR) = 1.095, 95 percent confidence interval (CI): 1.030, 1.165) and in relation to carbon monoxide (per 1 ppm: OR = 1.065, 95 percent CI: 1.015, 1.118). Generally, the estimated associations were stronger in patients with hypertension compared with patients without hypertension. A similar, although weaker, pattern was observed for comorbid diabetes (table 5); the association of dysrhythmia visits in relation

TABLE 2. Number and percentage of cardiovascular emergency department visits with the comorbid conditions listed at the same visit, Atlanta, Georgia, 1993–2000

Comorbid condition	Primary diagnosis									
	All cardiovascular disease ($n = 103,551$)		Ischemic heart disease ($n = 32,731$)		Dysrhythmia ($n = 27,342$)		Peripheral and cerebrovascular disease ($n = 23,411$)		Congestive heart failure ($n = 20,073$)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Hypertension	30,658	30	11,592	35	4,218	15	8,574	37	6,227	31
Diabetes	15,796	15	5,705	17	1,562	6	3,737	16	4,793	24
Dysrhythmia	12,839	12	5,407	17	NA*	NA	2,741	12	4,692	23
COPD*	8,378	8	2,651	8	993	4	1,405	6	3,329	17
Congestive heart failure	5,746	6	3,475	11	1,111	4	1,160	5	NA	NA
Pneumonia	1,507	2	404	1	153	1	322	1	628	3
Asthma	1,552	2	347	1	362	1	264	1	579	3
Upper respiratory infection	756	1	151	1	155	1	126	1	324	2
Atherosclerosis	941	1	302	1	60	0	357	1	222	1

* NA, not applicable; COPD, chronic obstructive pulmonary disease.

to nitrogen dioxide among patients with diabetes was markedly stronger than that among patients without diabetes (per 20 ppb: OR = 1.158, 95 percent CI: 1.046, 1.282 vs. OR = 1.014, 95 percent CI: 0.988, 1.040). Associations of peripheral and cerebrovascular disease visits in relation to ozone, nitrogen dioxide, and carbon monoxide were considerably larger among patients with comorbid COPD than in patients without COPD (table 6). The estimated associations for these pollutants among patients with comorbid COPD expressed as a range were odds ratios of 1.11–1.24 per unit increase of pollutant compared with 1.01–1.03 per same unit increase in patients without comorbid COPD.

TABLE 3. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days), Atlanta, Georgia, 1993–2000

Air quality measurement (unit) and method	All cardiovascular disease		Ischemic heart disease		Dysrhythmia		Peripheral and cerebrovascular disease		Congestive heart failure	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
PM_{10}* (10 μg/m^3)										
Case-crossover	1.010	1.000, 1.020	1.009	0.991, 1.027	1.011	0.991, 1.031	1.017	0.996, 1.039	1.001	0.978, 1.024
Time series†	1.009	0.998, 1.019	1.011	0.992, 1.030	1.008	0.989, 1.029	1.020	0.999, 1.043	0.992	0.968, 1.016
Ozone (25 ppb)										
Case-crossover	1.000	0.980, 1.020	1.001	0.966, 1.038	1.012	0.973, 1.052	1.021	0.979, 1.064	0.952	0.908, 0.997
Time series†	1.008	0.987, 1.030	1.019	0.981, 1.059	1.008	0.967, 1.051	1.028	0.985, 1.073	0.965	0.918, 1.014
Nitrogen dioxide (20 ppb)										
Case-crossover	1.025	1.012, 1.038	1.026	1.003, 1.049	1.022	0.997, 1.047	1.033	1.006, 1.061	1.017	0.988, 1.047
Time series†	1.025	1.012, 1.039	1.029	1.005, 1.053	1.019	0.994, 1.044	1.041	1.013, 1.069	1.010	0.981, 1.040
Carbon monoxide (1 ppm)										
Case-crossover	1.020	1.010, 1.030	1.016	0.999, 1.034	1.017	0.998, 1.036	1.031	1.010, 1.052	1.019	0.997, 1.041
Time series†	1.017	1.008, 1.027	1.016	0.999, 1.034	1.012	0.993, 1.031	1.031	1.010, 1.052	1.010	0.988, 1.032
Sulfur dioxide (20 ppb)										
Case-crossover	1.009	0.995, 1.024	1.013	0.988, 1.039	1.003	0.975, 1.031	1.024	0.993, 1.055	0.993	0.961, 1.026
Time series†	1.007	0.993, 1.022	1.007	0.981, 1.033	1.001	0.975, 1.028	1.028	0.999, 1.059	0.992	0.961, 1.025

* PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.
† Time-series results from Metzger et al. (15).

TABLE 4. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days) in visits with and without comorbid hypertension, Atlanta, Georgia, 1993–2000

	Ischemic heart disease		Dysrhythmia		Peripheral and cerebrovascular disease		Congestive heart failure	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
With comorbid hypertension*								
PM_{10}†	1.003	0.973, 1.034	1.037	0.988, 1.089	1.024	0.990, 1.060	1.041‡	0.999, 1.084
Ozone	1.022	0.962, 1.086	0.980	0.888, 1.082	1.006	0.939, 1.077	0.969	0.890, 1.054
Nitrogen dioxide	1.036	0.997, 1.076	1.095‡	1.030, 1.165	1.031	0.987, 1.076	1.037	0.985, 1.090
Carbon monoxide	1.007	0.978, 1.037	1.065‡	1.015, 1.118	1.038	1.004, 1.074	1.037	0.997, 1.079
Sulfur dioxide	1.024	0.980, 1.070	1.034	0.964, 1.110	1.041	0.989, 1.095	1.012	0.954, 1.074
No comorbid hypertension*								
PM_{10}	1.013	0.991, 1.036	1.006	0.985, 1.028	1.013	0.987, 1.040	0.982‡	0.955, 1.010
Ozone	0.991	0.948, 1.036	1.018	0.975, 1.063	1.029	0.977, 1.084	0.943	0.891, 0.998
Nitrogen dioxide	1.021	0.992, 1.050	1.009‡	0.982, 1.036	1.035	1.001, 1.070	1.007	0.973, 1.043
Carbon monoxide	1.022	1.000, 1.043	1.008‡	0.988, 1.029	1.027	1.002, 1.054	1.010	0.985, 1.037
Sulfur dioxide	1.008	0.976, 1.040	0.997	0.968, 1.028	1.015	0.978, 1.053	0.985	0.947, 1.024

* Determined from secondary *International Classification of Diseases*, Ninth Revision, codes listed for the same visit.
† PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.
‡ Comparing the pollution regression coefficients for visits with and without comorbid hypertension: $p < 0.05$.

The results from models assessing effect modification by comorbid congestive heart failure provided little evidence of effect modification with the notable exception of primary ischemic heart disease visits (table 7). The associations for ischemic heart disease among persons with comorbid congestive heart failure were substantially more negative in

TABLE 5. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days) in visits with and without comorbid diabetes, Atlanta, Georgia, 1993–2000

	Ischemic heart disease		Dysrhythmia		Peripheral and cerebrovascular disease		Congestive heart failure	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
With comorbid diabetes*								
PM_{10}†	1.022	0.979, 1.067	1.049	0.968, 1.137	1.016	0.965, 1.069	1.029	0.982, 1.078
Ozone	1.025	0.940, 1.118	1.010	0.859, 1.189	0.958	0.862, 1.065	0.956	0.868, 1.053
Nitrogen dioxide	1.003	0.950, 1.059	1.158‡	1.046, 1.282	1.012	0.947, 1.082	1.017	0.959, 1.078
Carbon monoxide	0.985	0.945, 1.027	1.058	0.976, 1.146	1.065	1.012, 1.121	1.020	0.975, 1.067
Sulfur dioxide	0.995	0.934, 1.060	1.025	0.911, 1.153	1.026	0.951, 1.106	1.018	0.952, 1.090
No comorbid diabetes*								
PM_{10}	1.006	0.987, 1.026	1.009	0.989, 1.029	1.018	0.995, 1.042	0.992	0.966, 1.019
Ozone	0.996	0.958, 1.037	1.012	0.972, 1.054	1.033	0.987, 1.080	0.950	0.900, 1.003
Nitrogen dioxide	1.030	1.005, 1.057	1.014‡	0.988, 1.040	1.037	1.008, 1.068	1.018	0.985, 1.052
Carbon monoxide	1.023	1.004, 1.042	1.014	0.995, 1.034	1.025	1.003, 1.048	1.018	0.993, 1.044
Sulfur dioxide	1.017	0.989, 1.045	1.002	0.973, 1.031	1.023	0.990, 1.058	0.986	0.949, 1.023

* Determined from secondary *International Classification of Diseases*, Ninth Revision, codes listed for the same visit.
† PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.
‡ Comparing the pollution regression coefficients for visits with and without comorbid diabetes: $p < 0.05$.

TABLE 6. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days) in visits with and without comorbid chronic obstructive pulmonary disease, Atlanta, Georgia, 1993–2000

	Ischemic heart disease		Dysrhythmia		Peripheral and cerebrovascular disease		Congestive heart failure	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
With comorbid COPD*,†								
PM_{10}*	0.981	0.921, 1.044	0.984	0.889, 1.088	1.086	0.998, 1.181	1.010	0.954, 1.069
Ozone	0.938	0.825, 1.067	0.959	0.779, 1.180	1.237‡	1.039, 1.473	0.972	0.864, 1.093
Nitrogen dioxide	0.960	0.886, 1.040	1.064	0.934, 1.213	1.142	1.026, 1.271	1.051	0.980, 1.128
Carbon monoxide	0.996	0.938, 1.057	0.972	0.878, 1.077	1.113	1.027, 1.205	1.058	1.003, 1.115
Sulfur dioxide	0.991	0.905, 1.086	1.085	0.936, 1.256	1.065	0.944, 1.202	1.035	0.956, 1.122
No comorbid COPD†								
PM_{10}	1.012	0.993, 1.031	1.012	0.992, 1.032	1.013	0.991, 1.035	0.999	0.974, 1.025
Ozone	1.007	0.970, 1.045	1.014	0.974, 1.055	1.009‡	0.967, 1.053	0.948	0.900, 0.998
Nitrogen dioxide	1.032	1.007, 1.056	1.020	0.995, 1.046	1.026	0.998, 1.054	1.011	0.979, 1.043
Carbon monoxide	1.018	1.000, 1.036	1.018	0.999, 1.038	1.026	1.004, 1.047	1.011	0.987, 1.036
Sulfur dioxide	1.015	0.988, 1.042	1.000	0.972, 1.029	1.020	0.989, 1.053	0.985	0.950, 1.021

* COPD, chronic obstructive pulmonary disease; PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.
† Determined from secondary *International Classification of Diseases*, Ninth Revision, codes listed for the same visit.
‡ Comparing the pollution regression coefficients for visits with and without comorbid COPD: $p < 0.05$.

relation to air pollution than those for patients without comorbid congestive heart failure, particularly for PM_{10}, nitrogen dioxide, and carbon monoxide. Results from models assessing effect modification by comorbid dysrhythmia did not provide evidence of effect modification (table 8).

DISCUSSION

Despite numerous studies providing evidence of an association between ambient air pollution and acute cardiovascular morbidity in the general population, relatively little is known regarding potentially susceptible populations. Using a case-crossover framework in this investigation, we took advantage of a large database of emergency department visits collected over a 7-year time period to examine potential heterogeneity of risk for adverse cardiovascular events in relation to air pollution in people with specific comorbid conditions. Stronger associations were observed for cardiovascular visits in relation to ambient air pollution levels among patients with comorbid hypertension, diabetes, and COPD compared with patients without these comorbid conditions.

Our results provide evidence that underlying hypertension may increase the risk for cardiovascular morbidity, specifically for dysrhythmia and congestive heart failure, in relation to increased air pollution levels, particularly PM_{10}, nitrogen dioxide, and carbon monoxide. Relatively few studies have examined comorbid hypertension as a potential effect modifier. Results from D'Ippoliti et al. (2) did not provide evidence of effect modification by hypertension for the association of air pollution and risk of myocardial infarction. Goldberg et al. (3) reported no increased association of mortality in relation to air pollution among persons with hypertension. However, several studies have found evidence of effect modification by hypertensive status when examining the association of air pollution and heart rate variability (4, 8, 21), suggesting that hypertension may increase the risk of cardiovascular events in relation to air pollution via a reduction in cardiac autonomic control. This hypothesis is consistent with our results, in which we observed the strongest evidence for effect modification by hypertensive status for dysrhythmia visits.

Our results suggesting that existing diabetes modifies the association of air pollution and cardiovascular outcomes are generally consistent with previously reported associations among persons with diabetes (1, 2, 7, 8, 11, 12). The plausibility of this association is strengthened by evidence that air pollution exposure is associated with reduced heart rate variability (4, 21–26), increased C-reactive protein levels (27), increased fibrinogen levels (28−32), and elevated inflammatory markers (31, 32). Diabetes is associated with similar changes in these cardiovascular risk factors (33–35).

Our results also provide evidence that persons with comorbid COPD may be at increased risk of adverse cardiovascular events in relation to air pollution. These results are similar to those reported previously (3, 10, 36). Zanobetti et al. (10) reported similar increased risk for hospital admissions for cardiovascular disease in relation to PM_{10} among persons with COPD as well as with pneumonia and acute respiratory infections. The number of visits for cardiovascular disease in our data set with an underlying diagnosis of pneumonia or acute respiratory infections was very low, so we were not able

TABLE 7. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days) in visits with and without comorbid congestive heart failure, Atlanta, Georgia, 1993–2000

	Ischemic heart disease		Dysrhythmia		Peripheral and cerebrovascular disease	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
With comorbid congestive heart failure*						
PM_{10}†	0.927‡	0.877, 0.980	1.016	0.924, 1.117	1.076	0.979, 1.183
Ozone	1.015	0.910, 1.132	0.981	0.815, 1.180	1.089	0.903, 1.314
Nitrogen dioxide	0.911‡	0.850, 0.977	1.136	1.006, 1.282	1.043	0.928, 1.172
Carbon monoxide	0.956‡	0.907, 1.007	1.065	0.968, 1.173	1.072	0.981, 1.172
Sulfur dioxide	0.981	0.905, 1.063	1.034	0.902, 1.186	1.067	0.931, 1.223
No comorbid congestive heart failure*						
PM_{10}	1.020‡	1.000, 1.039	1.011	0.991, 1.031	1.014	0.993, 1.036
Ozone	1.000	0.963, 1.039	1.013	0.973, 1.055	1.017	0.975, 1.061
Nitrogen dioxide	1.041‡	1.016, 1.066	1.017	0.992, 1.043	1.032	1.005, 1.061
Carbon monoxide	1.024‡	1.006, 1.042	1.015	0.996, 1.034	1.029	1.008, 1.051
Sulfur dioxide	1.017	0.990, 1.045	1.002	0.974, 1.030	1.021	0.990, 1.053

* Determined from secondary *International Classification of Diseases*, Ninth Revision, codes listed for the same visit.

† PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.

‡ Comparing the pollution regression coefficients for visits with and without comorbid congestive heart failure: $p < 0.05$.

TABLE 8. Estimated odds ratios and 95% confidence intervals for the association of cardiovascular disease visits with daily ambient air quality measurements (average of pollution levels lagged 0, 1, and 2 days) in visits with and without comorbid dysrhythmia, Atlanta, Georgia, 1993–2000

	Ischemic heart disease		Peripheral and cerebrovascular disease		Congestive heart failure	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
With comorbid dysrhythmia*						
PM_{10}†	1.019	0.975, 1.065	1.047	0.985, 1.113	0.983	0.939, 1.030
Ozone	0.969	0.887, 1.060	1.033	0.913, 1.169	0.914	0.830, 1.006
Nitrogen dioxide	1.059	1.001, 1.120	1.067	0.988, 1.152	1.014	0.956, 1.076
Carbon monoxide	1.028	0.985, 1.072	1.072	1.011, 1.138	1.004	0.960, 1.051
Sulfur dioxide	1.015	0.953, 1.082	1.000	0.914, 1.092	0.992	0.927, 1.061
No comorbid dysrhythmia*						
PM_{10}	1.007	0.987, 1.027	1.014	0.991, 1.036	1.006	0.980, 1.034
Ozone	1.008	0.969, 1.048	1.019	0.975, 1.065	0.964	0.913, 1.017
Nitrogen dioxide	1.019	0.994, 1.045	1.028	1.000, 1.058	1.018	0.985, 1.052
Carbon monoxide	1.014	0.995, 1.033	1.026	1.004, 1.048	1.023	0.998, 1.049
Sulfur dioxide	1.013	0.985, 1.041	1.027	0.994, 1.060	0.994	0.957, 1.032

* Determined from secondary *International Classification of Diseases*, Ninth Revision, codes listed for the same visit.

† PM_{10}, particulate matter with an average aerodynamic diameter of less than 10 μm.

to examine this stratification. Sunyer et al. (36) reported an increased risk of mortality in relation to PM_{10} among patients with severe COPD; Bateson and Schwartz (1), however, reported no increased risk of mortality in relation to PM_{10} in persons with existing COPD.

Our results did not corroborate the results from Mann et al. (6), who reported an increased risk of hospital admissions for ischemic heart disease in relation to carbon monoxide among persons with a secondary diagnosis of congestive heart failure. We observed the opposite trend in our results; patients with comorbid congestive heart failure had a decreased risk of emergency department visits for ischemic heart disease compared with patients without comorbid congestive heart failure. These differences may have resulted from the different populations; Mann et al. (6) examined hospital admissions among members of a health maintenance organization in southern California, while our study was a population-based assessment of emergency department visits. Different air pollution mixtures in the two areas or instability due to low numbers of patients with comorbid congestive heart failure may have also contributed to the contrasting results. Additionally, the different sources of information for primary diagnosis and comorbid conditions (medical records in Mann et al. (6) vs. emergency department billing records in our study) may have different amounts of measurement error, particularly in assessing secondary diagnoses. Goldberg et al. (3) also reported an increased risk of death in relation to particles among persons with existing congestive heart failure, while D'Ippoliti et al. (2) did not observe an increased risk of acute myocardial infarction admissions in relation to air pollution among patients with congestive heart failure. Moreover, consistent with our results, D'Ippoliti et al. (2) did not observe evidence of effect modification by dysrhythmia of the association of air pollution and acute myocardial infarction.

There were limitations in our assessment of comorbid illness. Hospitals provided various numbers of secondary diagnostic codes (the number provided ranged from three to 35 secondary codes); moreover, we used only the concurrent secondary diagnoses rather than including diagnoses from previous visits, potentially reducing the sensitivity of our comorbid illness assessment and subsequently limiting power to observe any effect modification by these conditions. However, Zanobetti et al. (10) reported little or no difference when using concurrent or previous admissions when assessing secondary conditions. Additionally, we examined only one comorbid illness at a time; an alternative method would be to examine multiple secondary diagnoses (e.g., patients with secondary diabetes and hypertension compared with patients with either one or none of the underlying conditions). However, the proportions of cardiovascular disease visits with combinations of comorbid conditions were too low for reliable models. An additional limitation in our assessment of comorbid illness stems from the possibility that the diagnosis of certain primary outcomes may be affected by the presence of one or more comorbid conditions, or vice versa, making certain primary outcomes more or less likely to have comorbid conditions listed at the same visit in the billing records. We are not able to examine this issue in our database.

Additional limitations of this study include the use of a central monitor for pollution measurements and the potential for spurious associations due to the number of statistical tests performed. The measurement error resulting from using centrally located monitors for ambient air pollution measures could potentially attenuate observed associations but is not likely to be responsible for spurious associations. We have attempted to reduce the potential problems associated with multiple testing by using an a priori approach for choosing the pollutant metric, pollutant lag structure, comorbid conditions, and modeling approach. Additionally, behavior such as air conditioning use or time spent outdoors may affect personal exposure levels. This could affect the magnitude of the observed associations in comparison with other geographic locations.

The magnitude of the estimates and standard errors obtained using the case-crossover approach for the primary case groups were comparable with those from our previously published time-series analysis for cardiovascular visits (15). The largest degree of inconsistency was observed for congestive heart failure and for ozone across the outcomes, and this inconsistency was minor. Congestive heart failure is the smallest of the cardiovascular disease subgroups, and ozone was not measured throughout the year (measured April through October); the smaller number of observations in these models may make the results more prone to random error compared with the other subgroups or pollutants with more observations. As discussed by Kunzli and Schindler (37), case-crossover methods may reduce the power to detect associations compared with time-series studies, because there may be less variability in the difference between air pollution concentrations on event and control days compared with using the full distributions of air pollution values as in time-series methodology. Additionally, case-crossover and time-series methods differ in the way the models control long-term time trends. The case-crossover analysis inherently controls for long-term time trends when a sufficiently small referent time period is used (18, 19, 38); therefore, the differences observed for the ozone models may indicate that there is some residual confounding by time in the time-series results. However, the differences are not extensive enough to alter the conclusions drawn from the results. The overall similarity of the time-series and case-crossover estimates provides evidence of the robustness of our results.

This study took advantage of a large database of emergency department visits to examine the issue of increased susceptibility among persons with underlying conditions. The results provide further evidence of increased susceptibility to adverse cardiovascular events in relation to air pollution in persons with comorbid hypertension, diabetes, and COPD.

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