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An examination of exposure measurement error from air pollutant spatial variability in time-series studies

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Relatively few studies have evaluated the effects of heterogeneous spatiotemporal pollutant distributions on health risk estimates in time-series analyses that use data from a central monitor to assign exposures. We present a method for examining the effects of exposure measurement error relating to spatiotemporal variability in ambient air pollutant concentrations on air pollution health risk estimates in a daily time-series analysis of emergency department visits in Atlanta, Georgia. We used Poisson generalized linear models to estimate associations between current-day pollutant concentrations and circulatory emergency department visits for the 1998–2004 time period. Data from monitoring sites located in different geographical regions of the study area and at different distances from several urban geographical subpopulations served as alternative measures of exposure. We observed associations for spatially heterogeneous pollutants (CO and NO_2) using data from several different urban monitoring sites. These associations were not observed when using data from the most rural site, located 38 miles from the city center. In contrast, associations for spatially homogeneous pollutants (O_3 and $PM_{2.5}$) were similar, regardless of the monitoring site location. We found that monitoring site location and the distance of a monitoring site to a population of interest did not meaningfully affect estimated associations for any pollutant when using data from urban sites located within 20 miles from the population center under study. However, for CO and NO_2, these factors were important when using data from rural sites located $\geq$30 miles from the population center, most likely owing to exposure measurement error. Overall, our findings lend support to the use of pollutant data from urban central sites to assess population exposures within geographically dispersed study populations in Atlanta and similar cities.
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Introduction

A common method for assigning exposure in population-based epidemiological studies of ambient air pollution is to use measurements obtained from central site ambient monitors (Wilson et al., 2005). However, uncertainties exist as to how well these concentrations represent true personal exposures to different pollutants, under different study designs and in different geographical settings, and how the resulting exposure measurement error may affect health risk estimates in epidemiological analyses.

There are several potential sources of exposure measurement error when using observed ambient measurements to estimate personal exposures, including (1) instrument error; (2) error resulting from the placement of a monitor (reflected by the representativeness of the monitoring site and spatial variability of the pollutant measured); and (3) differences between the ambient monitored concentration and average personal exposure (NRC, 1998). Simulation studies suggest that the difference between true and measured ambient pollutant levels most likely has only small effects on time-series health-risk estimates (Zeger et al., 2000; Sheppard et al., 2005). However, these studies either assumed spatial homogeneity in the air pollutant or only considered a pollutant ($PM_{2.5}$) with little spatiotemporal variation.

Total $PM_{2.5}$ and secondary pollutants, such as ozone (O_3), are often relatively homogeneous over space, in that their concentration levels as well as the temporal fluctuations in their concentrations are relatively consistent over metropolitan areas. However, other pollutants, including those emitted by motor vehicles, such as carbon monoxide (CO) and nitrogen dioxide (NO_2), are likely to show spatiotemporal heterogeneity, such that their concentration levels and/or the temporal fluctuations in their concentrations vary over metropolitan areas (also referred to as spatiotemporal variability). Spatially heterogeneous pollutants include both primary pollutants (e.g., CO and nitric oxide (NO)) and

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those formed by a relatively rapid conversion of a primary pollutant (e.g., NO_2).

The potential implications of heterogeneous spatiotemporal pollutant distributions on epidemiological findings are frequently discussed in the literature (Pinto et al., 2004; Ito et al., 2005; Wilson et al., 2005, 2006), but relatively few studies have directly evaluated the effects of such pollutant distributions on health risk estimates in time-series analyses that use data from a central monitor to assign exposures. Two recent publications have attempted to do so for particle exposures by comparing health effect estimates among models predicting outcome events for several geographical subpopulations located at different distances from a central monitoring site (Wilson et al., 2007), and among models using local (i.e., closest) site monitoring data in comparison with central monitoring data to assess exposures for geographical subpopulations (Chen et al., 2007).

In a daily time-series study of ambient particles and cardiovascular mortality in Phoenix, Wilson et al. (2007) found that effect estimates for $PM_{2.5}$, but not for $PM_{10\text{-}2.5}$, were lower for models predicting mortality in geographical subpopulations residing farther from a central monitoring site compared with analyses of the population residing closest to the site. Since socio-economic status (SES) of the three subpopulations increased with increasing distance from the central site, the authors suggested two factors that influenced the observed pattern of effects: (1) exposure error (poorer agreement between local population average exposure and the centrally monitored $PM_{2.5}$ concentrations with increasing distance from the central site); and (2) effect modification by SES (lesser sensitivity to the effects of $PM_{2.5}$ with increasing SES). It has been noted that SES may be a surrogate of various underlying characteristics that can modify the effects of ambient air pollution on a population, including susceptibility (e.g., because of poor health in general), health-related behaviors (e.g., smoking, nutrition), as well as disease diagnosis and treatment (e.g., less access to healthcare) (Bell et al., 2005). Individuals with low SES may also have higher personal exposures to ambient pollution (e.g., by living closer to roads or other specific pollution point sources or having lower air conditioning usage) compared with those with higher SES.

We previously presented the results of a geographical subanalysis of cardiorespiratory emergency department (ED) visits and ambient particle and gaseous pollutants (Sarnat et al., 2006), conducted as a part of the Study of Particles and Health in Atlanta (SOPHIA) (Tolbert et al., 2000). Observed associations between ambient pollutants and ED visits, particularly for circulatory diseases, were stronger when we limited the geographical domain of the study population analyzed to residential areas closer to the central monitoring sites compared with analyzing the full geographical domain of the study (Sarnat et al., 2006). These results were expected under the assumption that data from an ambient monitoring site provide better markers of exposure for populations residing in close proximity to the site compared with those residing farther away. However, in this analysis, associations were stronger for both spatially heterogeneous pollutants (e.g., CO and NO_2) and for pollutants with fairly homogeneous spatial distributions (e.g., $PM_{2.5}$ and sulfate), suggesting that decreased exposure measurement error in the geographical sub-analyses as compared with the full analysis may not have been the only explanation. It is possible, for example, that population characteristics that confer sensitivity to air pollution, such as socio-demographic factors, may have also affected our findings.

These analyses show the difficulty of disaggregating the effects of exposure measurement error from the effects of population characteristics in geographical subpopulation comparison studies. For example, if we observe stronger associations between air pollutant concentrations measured at a central ambient monitoring site and health outcomes in a population (A) residing close to the monitor compared with a population (B) residing farther from that monitor, the pattern could be partly because of (1) reduced exposure measurement error for population A and/or (2) greater susceptibility of population A to the pollutant of interest. Here, we present a method for examining the effects of exposure measurement error relating to spatiotemporal variability in ambient air pollutant concentrations on air pollution health risk estimates in our daily time-series analyses while controlling the potential modifying effects of population characteristics. Rather than using data from one central site and comparing health effect associations across different geographical subpopulations, our method examines single geographical subpopulations and compares health effect associations using pollutant data from different monitoring sites as alternative measures of exposure. Since we compare risk estimates within the same population over the same time period, any observed differences in risk when using different measures of exposure should not be attributed to differences in population susceptibility. For example, if we observe stronger associations for population A using ambient data from a monitor located in close proximity compared with those using data from a monitor located farther away, the difference in associations may be reasonably explained by differences in exposure measurement error between the two measures of exposure.

Our method relies on the availability of daily air monitoring data from multiple monitoring sites over a sufficiently long time period, as well as a population and health outcome supplying sufficient cases for geographical subpopulation analyses. In this analysis, we examined data from our Atlanta ED study over the 1998–2004 time period, for which daily CO, NO_2, O_3, and $PM_{2.5}$ concentrations were available from several monitoring sites located throughout the study area.

Methods

Ambient Air Quality Data

We obtained daily ambient concentration data for 1-h maximum CO, 1-h maximum NO_2, 8-h maximum O_3, and 24-h average $PM_{2.5}$ from all monitoring stations in the 20-county Atlanta study area that operated and collected daily measurements for one or more of these pollutants during all or a portion of the study period, 1 August 1998 through 31 December 2004. Data for all pollutants were available year-round, with the exception of O_3, for which data were generally only available between April and October. We also obtained daily meteorological data, including average temperature and dew point temperature, for the Hartsfield–Atlanta International Airport from the National Climatic Data Center.

The air monitoring stations, their characteristics, and their locations in the study area are described in Table 1 and Figure 1. The monitoring stations included those in the US Environmental Protection Agency's (EPA) Air Quality System (US EPA, 2007), the SouthEastern Aerosol Research and Characterization Study network (ARA, 2007), and the Assessment of the Spatial Composition in Atlanta network (Butler et al., 2003). In total, 10 sites provided data for this analysis, with four to five different sites per pollutant. On the basis of population density data and proximity to the Atlanta city center (e.g., within or close to the I-285 perimeter highway that circles the more central parts of the city), we considered the following sites as urban: Jefferson St. (JS), Georgia Tech (GT), Confederate Ave. (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), and Tucker (TU); and the following sites as rural: Conyers (CN) and Yorkville (YO) (Figure 1). JS is the site of the Aerosol Research Inhalation Epidemiology Study (ARIES) (Hansen et al., 2006) and the EPA Atlanta Supersites project (Solomon et al., 2003), and has been considered the primary site for particle pollutants in earlier publications by this research group (Metzger et al., 2004; Peel et al., 2005; Tolbert et al., 2007; Sarnat et al., 2008). In this analysis, we used JS as the default central site for CO, O_3, and $PM_{2.5}$ and GT as the central site for NO_2, located approximately 1 mile from JS. YO was the most rural site, at a distance of 38 miles from JS.

To compare descriptive statistics and epidemiological model results using data from different monitoring sites, data were matched across sites for each pollutant. For

Table 1. Ambient monitoring sites, including pollutants measured and site characteristics.

Site name (abbreviation)	Network	AQS site ID	Distance from JS (miles)	Pollutant[a]				AQS site characterization[b]		
				CO	NO_2	O_3	$PM_{2.5}$	Location setting	Land use	Monitoring objective
Jefferson St (JS)	SEARCH	N/A	0	✓		✓	✓[c]	Urban and center city	Industrial	N/A
Georgia Tech (GT)	AQS	131210048	0.92		✓			Urban and center city	Commercial	Highest concentration
Confederate Ave (CA)	AQS	131210055	5.2			✓		Suburban	Commercial	Population exposure
Roswell Rd (RR)	AQS	131210099	7.2	✓				Suburban	Commercial	Highest concentration
South Dekalb (SD)	AQS, ASACA	130890002	9.5		✓	✓	✓[c]	Suburban	Residential	Population exposure (NO_2, $PM_{2.5}$) Highest concentration (O_3)
Dekalb Tech (DT)	AQS	130891002	10.4	✓				Suburban	Residential	Population exposure
Doraville Health Center (DHC)	AQS	130892001	11.6				✓	Suburban	Commercial	Population exposure
Tucker (TU)	AQS	130893001	12.7		✓			Rural	Residential	Unknown
Conyers (CN)	AQS	132470001	24.1		✓	✓		Rural	Agricultural	Population exposure (NO_2, O_3) Max concentration (O_3)
Yorkville (YO)	SEARCH, AQS	132230003	37.6	✓	✓[c]	✓	✓[c]	Rural	Agricultural	General background (CO, NO_2, O_3) Upwind background ($PM_{2.5}$)

ASACA, Assessment of the Spatial Composition in Atlanta; AQS, US EPA Air Quality system; SEARCH, SouthEastern Aerosol Research and Characterization study.

[a]Check marks in pollutant columns indicate which sites measured each pollutant.

[b]All site characterization entries were obtained from the AQS data mart, with the exception of those for Jefferson St.

[c]When data from multiple instruments were available at the same site, primary instruments were selected and any missing values were modeled using data from the other instruments, as follows (FRM — federal reference method, PCM — particle composition monitor, TEOM — tapered element oscillating microbalance): at JS, $PM_{2.5}$ SEARCH FRM data were filled in with regression-adjusted SEARCH PCM and TEOM data; at SD, $PM_{2.5}$ AQS FRM data were filled in with regression-adjusted ASACA TEOM data; at YO, $PM_{2.5}$ SEARCH FRM data were filled in with regression-adjusted SEARCH TEOM data; at YO, NO_2 AQS data were filled in with regression-adjusted SEARCH data.

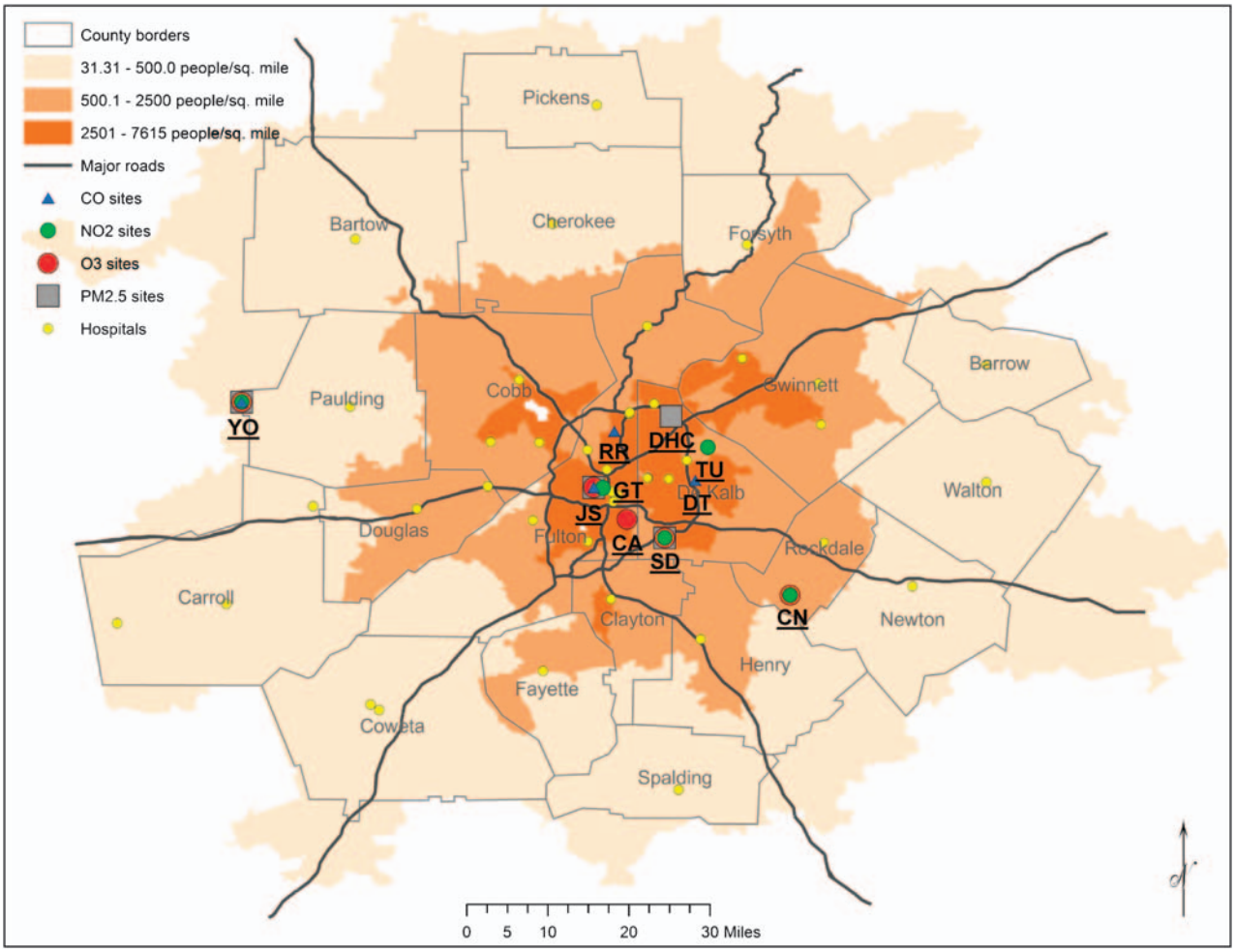

Figure 1. 20-county Atlanta study area with ZIP code level population density (# people/square mile; for 2001), location of air pollutant monitoring sites (including Jefferson St (JS), Georgia Tech (GT), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO)), and acute care hospitals.

example, if CO measurements from one monitor were missing for a particular day, the CO measurements from the other monitors were set to missing for the same day. This matching process resulted in slightly different time periods examined for each pollutant: 1 August 1998 to 30 June 2003 for CO, 1 August 1998 to 31 December 2004 for NO_2, 1 August 1998 to 31 December 2004 for O_3 (warm season only), and 1 March 1999 to 31 December 2004 for $PM_{2.5}$.

Emergency Department Data

We obtained individual-level data on ED visits for the 20-county (7964 sq. mile) Atlanta population through computerized billing records submitted by 41 of 42 acute care hospitals (Figure 1). For each patient visit, hospitals provided data on the date of admission, the primary International Classification of Diseases 9th Revision (ICD-9) diagnostic code, patient date of birth, gender, race, and 5-digit residential ZIP code. We defined our outcome of interest, circulatory disease, using primary ICD-9 diagnosis codes 390–459. We excluded repeat visits by patients visiting the same hospital within a single day.

In the overall analytic database, we included ED visits for patients living within any one of the 225 ZIP codes located wholly or partially in the 20-county Atlanta study area. We also created variables to delineate ED visits for specific geographical subpopulations living within 5 miles of each air monitoring site, identified using the distance between air monitoring sites and patient residential ZIP code centroids. The monitoring site around which each subpopulation was defined was considered to be "local", or closest, to that population. The 5-mile radius was chosen on the basis of the smallest distance from monitoring sites that allowed for sufficient daily ED visit counts for circulatory disease in epidemiological analyses. Analyses of the geographical subpopulations were limited to those around urban monitoring sites because of lack of population within 5 miles of rural

sites. In all, 0–6% of ZIP codes for CO, NO_2, and $PM_{2.5}$ epidemiological analyses, and 34% of ZIP codes for O_3 analyses, were counted in more than one geographical subpopulation.

Census Data

We obtained Census 2000 data to describe the socioeconomic characteristics of the geographic subpopulations. Using the 5-digit ZIP code tabulation area format, these data were linked to the hospital records by the residential ZIP code of each patient. On the basis of earlier research (Krieger et al., 2003), we used the percentage of persons with income below the federally defined poverty line (% below poverty (%BP)) as our primary indicator of SES (census variable P87) (US CB, 2002). We also examined other measures of deprivation (% public assistance (%PA)), as well as educational attainment (% high school graduation (%HS)) and income (median population housing income) as alternative metrics of SES.

Analyses

We examined the relationships between ED visits for circulatory disease and daily measures of air pollutants using Poisson generalized linear models. As in our earlier analyses of these data (Metzger et al., 2004; Peel et al., 2005; Tolbert et al., 2007; Sarnat et al., 2008), the model had the following form:

$$\begin{aligned}\log(E(Y_t)) = \alpha + \beta pollutant_t + \sum\nolimits_k \lambda_k \mathrm{DOW}_k \\ + \sum\nolimits_m \xi_m holiday_m + \sum\nolimits_n \nu_n hospital_n \\ + \sum\nolimits_p \xi_p season_p + g(\gamma_1, \ldots, \gamma_N;\ time_t) \\ + g(\delta_1, \ldots, \delta_N;\ temp_t) + (\eta_1, \ldots, \eta_N;\ dewpoint_t),\end{aligned}$$

where Y_t was the count of circulatory ED visits on day t in the population of interest (i.e., entire population or specific geographical subpopulation), and $pollutant_t$ was the corresponding ambient concentration on day t for the pollutant of interest from the monitoring site of interest. We used lag 0 as the exposure measure based on the literature (Ballester et al., 2006; Wellenius et al., 2006) as well as our data (Metzger et al., 2004), which suggest acute circulatory responses with air pollution. Moreover, the use of a single-day lag as opposed to a multi-day moving average allowed for minimization of missingness when matching the pollutant data across monitoring sites. Models included indicator variables for day of week (*DOW*) and holidays (*holiday*), as well as hospital indicator variables (*hospital*) to account for the entry and exit of hospitals during the study period. Long-term and seasonal trends in case presentation rates (*time*) were controlled with parametric cubic splines, $g(\gamma_1,\ldots,\gamma_N;\ \varkappa)$, with monthly knots. Owing to the missing wintertime O_3 data, O_3 models used separate time splines for each year. Finally, cubic splines were also used to control 3-day moving average (average of lags 0, 1, and 2 days) temperature (*temp*) and dew point temperature (*dewpoint*), with knots placed at the 25th and 75th percentiles. With this approach, the first and second derivatives of $g(\varkappa)$ are continuous so that time trends and meteorology are modeled as smooth functions. Variance estimates were scaled to account for Poisson overdispersion.

For the entire population, and for each geographical subpopulation, our analytical approach focused on comparing results among models incorporating pollution data from monitoring sites located in different geographical regions of the study area (e.g., urban *vs* rural sites) and with different distances from the geographical subpopulation of interest (e.g., local *vs* other sites). This approach allowed us to assess the effect of monitoring site location and the distance between monitoring sites and subpopulations on the estimated associations. Relative risks and 95% confidence intervals were calculated for interquartile range (IQR) increases in the site-specific pollutant data used. Interquartile ranges were used for comparing the results of associations based on pollutant data from different monitoring sites, which varied in their range of concentration.

In addition to examining the results for each geographical subpopulation individually, we calculated overall measures of association (using weighted averages) to summarize these results for each pollutant. Specifically, the weighted averages were used to compare the effects of using local urban *vs* other urban monitoring data on the geographical subpopulation associations, which were difficult to discern from the individual results. For a given set of geographical subpopulations, we compared the weighted averages of relative risk estimates obtained using only local monitoring data with estimates obtained using data from a central urban monitor. The weighted averages were computed on the log scale using the inverse of the variance of the estimates as the weights. To accommodate weighted averages that pooled estimates using data from different monitoring sites, the weighted average relative risks and 95% confidence intervals were calculated using common increments (i.e., 1 ppm for CO, 20 ppb for NO_2, 25 ppb for O_3, and 10 $\mu g/m^3$ for $PM_{2.5}$) that approximated urban IQRs.

Epidemiological analyses were carried out using SAS statistical software, V9.1 (SAS Institute, Inc., Cary, NC, USA), and mapping was conducted using ArcGIS ArcMAP V9.2 (ESRI Inc., Redlands, CA, USA).

Results

Air Quality Data

Descriptive statistics and Pearson correlations (Tables 2 and 3) for each pollutant and site, respectively, show that CO and NO_2 levels were spatially heterogeneous across the city, with respect to both their mean levels as well as site-to-site

Table 2. Descriptive statistics for air pollution data.

Pollutant	N^a	Site[b]	Mean	SD	Percentiles					
					Min	25th	50th	75th	Max	IQR
1-h max CO (ppm)	1374	JS	1.3	1.2	0.20	0.52	0.87	1.7	7.7	1.1
		RR	1.7	0.82	0.20	1.1	1.5	2.1	5.1	1.0
		DT	1.4	0.91	0.10	0.7	1.2	1.8	7.7	1.1
		YO	0.27	0.11	0.10	0.20	0.24	0.32	1.0	0.12
1-h max NO_2 (ppb)	1834	GT	40.6	18.0	1.0	27.0	38.4	51.0	172.0	24.0
		SD	34.4	15.3	1.0	23.0	33.0	44.0	139.0	21.0
		TU	32.7	13.8	3.0	23.0	32.0	41.0	100.0	18.0
		CN	14.5	9.9	1.0	8.0	13.0	19.0	242.0	11.0
		YO	10.9	9.3	1.0	5.0	8.0	14.0	70.0	9.0
8-h max O_3 (ppb)	1281	JS	52.8	21.6	2.3	37.5	50.3	67.3	130.8	29.8
		CA	53.3	22.1	2.9	37.9	51.0	67.3	139.0	29.4
		SD	49.4	20.7	2.0	34.9	48.0	62.6	135.3	27.8
		CN	51.9	20.0	5.4	37.5	49.8	63.3	129.3	25.8
		YO	57.4	18.7	9.1	43.6	55.5	70.4	133.1	26.7
24-h avg $PM_{2.5}$ ($\mu g/m^3$)	1641	JS	16.5	8.1	1.1	10.6	15.0	20.9	65.8	10.3
		SD	16.6	8.0	1.0	11.0	15.3	20.6	73.6	9.6
		DHC	17.1	8.5	3.0	11.2	15.5	21.0	80.0	9.8
		YO	13.6	7.4	1.9	8.3	11.8	17.3	65.6	9.0

IQR, interquartile range.
[a]Air pollution data were matched across sites for each pollutant. For example, if CO measurements from one monitor were missing for a particular day, the CO measurements from the other monitors were set to missing for the same day. Therefore, time periods of analysis differed by pollutant: CO = 08/01/1998–06/30/2003, NO_2 = 08/01/1998–12/31/2004, O_3 = 08/01/1998–12/31/2004, non-winter; $PM_{2.5}$ = 03/01/1999–12/31/2004.
[b]Air monitoring sites include Jefferson St (JS), Georgia Tech (GT), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO).

temporal correlations, whereas O_3 and $PM_{2.5}$ were more spatially homogeneous, as found in earlier analyses using these data (Wade et al., 2006). For example, urban–rural differences in mean concentrations were distinct for CO and NO_2 (e.g., rural concentrations were a fourth or less of urban concentrations), whereas concentrations were more similar across sites for O_3 and $PM_{2.5}$. In addition, Pearson correlations were moderate ($r = 0.61$–0.80) among urban sites for CO and NO_2, and weak ($r = 0.09$–0.37) between urban sites and the most rural site, YO. In comparison, correlations for O_3 and $PM_{2.5}$ were high ($r = 0.79$–0.98) among all sites. The observed patterns of correlations were consistent when analyses were stratified by warm and cool seasons.

Emergency Department and Socio-economic Data

Over the 1998–2004 time period, our database contained 7,616,029 ED visits, including 267,995 visits for circulatory disease (daily mean = 114.3 visits). Table 4 presents mean daily counts and demographic data for each geographical subpopulation living within 5 miles of each air monitoring site. ED visits for circulatory disease were predominantly made by adults and the elderly (mean age = 60.3 years), with some variation across the geographic subpopulations. Mean daily visit counts (ranging from 5 to 8 visits/day) and racial composition (ranging from 10% to 79% black) also varied across the geographical subpopulations. The visit counts for patients living within 5 miles of the rural monitors (CN and YO) were very low (<2 visits/day), which precluded these populations from being examined in the epidemiological subpopulation analyses.

Among the urban subpopulations, poverty (%BP) and public assistance (%PA), and educational attainment (%HS) and income were highly correlated ($r = 0.93$ and 0.91, respectively). %BP was negatively correlated with both %HS ($r = -0.63$) and income ($r = -0.85$), indicating the relationship between higher poverty and lower education and incomes in Atlanta. Using these measures, SES was typically lowest in the urban center and rural areas and highest in suburban areas.

Epidemiological Results — Entire Population

The results of epidemiological models predicting ED visits for circulatory disease in the entire study population are presented on the far left side of each graph in Figure 2 (closed circles) and in Supplementary Table S1. When using pollutant data from the central sites (i.e., JS and GT) as measures of population exposure, we observed significant

Table 3. Pearson correlation coefficients for matched air pollutant data (distance in miles between monitoring sites in parentheses).

Pollutant	Site[a]	CO JS	CO RR	CO DT	CO YO	NO_2 GT	NO_2 SD	NO_2 TU	NO_2 CN	NO_2 YO	O_3 JS	O_3 CA	O_3 SD	O_3 CN	O_3 YO	$PM_{2.5}$ JS	$PM_{2.5}$ SD	$PM_{2.5}$ DHC
CO	RR	0.61 (7)																
	DT	0.74 (10)	0.65 (10)															
	YO	0.15 (38)	0.37 (38)	0.18 (48)														
NO_2	GT	0.66 (0.9)	0.54 (7)	0.60 (10)	0.18 (39)													
	SD	0.53 (10)	0.45 (14)	0.51 (8)	0.12 (47)	0.77 (9)												
	TU	0.58 (13)	0.51 (10)	0.58 (4)	0.16 (48)	0.80 (12)	0.75 (12)											
	CN	0.32 (24)	0.22 (27)	0.27 (17)	0.08 (61)	0.46 (23)	0.53 (15)	0.45 (20)										
	YO	0.14 (38)	0.32 (38)	0.12 (48)	0.71 (0)	0.13 (39)	0.13 (47)	0.09 (48)	0.11 (61)									
O_3	JS	0.17 (0)	0.14 (7)	0.20 (10)	0.16 (38)	0.38 (1)	0.39 (10)	0.42 (13)	0.14 (24)	-0.06 (38)								
	CA	0.20 (5)	0.18 (11)	0.22 (8)	0.19 (42)	0.42 (5)	0.45 (5)	0.46 (12)	0.19 (19)	-0.03 (42)	0.98 (5)							
	SD	0.21 (10)	0.19 (14)	0.23 (8)	0.16 (47)	0.42 (9)	0.43 (0)	0.46 (12)	0.16 (15)	-0.03 (47)	0.96 (10)	0.98 (5)						
	CN	0.26 (24)	0.18 (27)	0.28 (17)	0.17 (61)	0.48 (23)	0.52 (15)	0.53 (20)	0.31 (0)	-0.03 (61)	0.88 (24)	0.92 (19)	0.92 (15)					
	YO	0.25 (38)	0.22 (38)	0.23 (48)	0.24 (0)	0.48 (39)	0.49 (47)	0.50 (48)	0.23 (61)	0.08 (0)	0.87 (38)	0.85 (42)	0.84 (47)	0.79 (61)				
$PM_{2.5}$	JS	0.43 (0)	0.39 (7)	0.40 (10)	0.28 (38)	0.45 (1)	0.35 (10)	0.41 (13)	0.17 (24)	0.03 (38)	0.63 (0)	0.64 (5)	0.63 (10)	0.63 (24)	0.57 (38)			
	SD	0.28 (10)	0.31 (14)	0.30 (8)	0.29 (47)	0.37 (9)	0.31 (0)	0.36 (12)	0.14 (15)	0.03 (47)	0.60 (10)	0.63 (5)	0.61 (0)	0.61 (15)	0.53 (47)	0.88 (10)		
	DHC	0.28 (12)	0.33 (6)	0.31 (8)	0.31 (44)	0.34 (11)	0.26 (15)	0.34 (5)	0.17 (25)	0.08 (44)	0.55 (12)	0.57 (13)	0.55 (15)	0.55 (25)	0.49 (44)	0.88 (12)	0.84 (15)	
	YO	0.18 (38)	0.24 (38)	0.17 (48)	0.35 (0)	0.24 (39)	0.18 (47)	0.25 (48)	-0.01 (61)	0.05 (0)	0.64 (38)	0.65 (42)	0.63 (47)	0.58 (61)	0.62 (0)	0.86 (38)	0.82 (47)	0.82 (44)

[a] Air monitoring sites include Jefferson St (JS), Georgia Tech (GT), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO)

Shaded cells indicate within-pollutant (between-site) correlations.

positive associations between circulatory visits and each pollutant (range of relative risks: 1.011–1.018 per IQR increase in pollutant concentration), which are consistent with those observed in our earlier analyses (Metzger et al., 2004). The results for CO and NO_2 are also consistent with traffic-related air pollution effects observed in our epidemiological analyses using source-apportioned $PM_{2.5}$ data (Sarnat et al., 2008). We found consistent results for all pollutants when using data from the other urban monitoring sites, located within 12 miles of the central sites, as measures of population exposure. When using data from the most rural site (YO), located 38 miles from the central sites, we also found consistent results for the spatially homogeneous pollutants, O_3 and $PM_{2.5}$. We did not find consistent results, however, for models examining effects associated with spatially heterogeneous pollutants, CO and NO_2, when using data from YO. For these models, associations were low in magnitude and consistent with the null hypothesis of no association.

Epidemiological Results — Geographical Subpopulations

Figure 2 also presents the results of models predicting ED visits for circulatory disease in the geographical subpopulations (open squares). Compared with the results of models predicting ED visits for the entire population, these results had much wider confidence intervals, primarily because of fewer visit counts contributing to the analyses. Similar to the results of the entire population analyses, the geographical subpopulation results showed clear urban–rural differences when using CO and NO_2 data from the different monitoring sites as different measures of exposure (e.g., associations were lowest in magnitude when using pollutant data from YO).

To aid in determining whether the distance between monitoring sites and geographical subpopulations affected the epidemiologic results within the urban area, we calculated weighted averages of the geographical subpopulation results (Figure 2, shaded triangles). The ''local'' weighted averages provided overall estimates for the relative risk using the local site pollution data across the geographical subpopulations for each pollutant (i.e., overall estimates of the circled results in Figure 2). We compared these estimates with corresponding results obtained using each urban site as a central monitor for the same geographical subpopulations. Weighted average results of models using local monitoring data were very similar to those using data from the other urban monitoring sites suggesting that, within the urban area, distance between monitoring sites and subpopulations did not affect our epidemiological results.

Table 4. Sociodemographic characteristics of the entire population and for each geographic subpopulation.

Population[c]	# ZIP codes	Circulatory ED visits[a]				SES indicators[b]				
		Daily *N* Mean (SD)	Age Mean (SD)	Race[d] %B	%O	# ZIP codes[e]	%BP Mean (SD)	%PA Mean (SD)	%HS Mean (SD)	Income Mean (SD)
Entire	225	114.3 (26.4)	60.3 (18.7) [0.13][f]	28.2 [13.5]	6.0					
⩽5 mi JS	15	8.3 (3.4)	61.3 (18.9) [0.5]	64.5 [14.7]	4.9	13	25.3 (14.5)	4.5 (3.7)	79.1 (12.8)	$36,544 ($18,011)
⩽5 mi CA	16	7.2 (3.2)	58.0 (18.3) [0.5]	76.9 [20.8]	4.3	13	28.6 (12.8)	5.9 (3.7)	71.9 (11.8)	$30,522 ($13,987)
⩽5 mi RR	10	5.4 (2.5)	68.8 (19.2) [0.2]	9.8 [4.1]	7.0	10	8.0 (4.0)	0.7 (0.4)	92.7 (5.4)	$67,168 ($21,513)
⩽5 mi SD	7	5.8 (2.8)	55.8 (17.5) [0.4]	79.3 [34.7]	5.1	6	15.3 (7.1)	4.4 (2.3)	75.7 (9.4)	$40,096 ($10,385)
⩽5 mi DT	11	8.0 (3.7)	57.6 (19.2) [0.3]	56.7 [38.9]	6.0	10	14.1 (9.6)	3.0 (2.1)	83.6 (10.0)	$43,892 ($8992)
⩽5 mi DHC	8	4.7 (2.5)	65.1 (18.8) [0.11]	11.8 [10.2]	9.6	8	9.8 (3.5)	1.2 (0.4)	85.3 (7.8)	$56,692 ($12,368)
⩽5 mi TU	8	5.3 (2.9)	57.4 (19.6) [0.13]	33.9 [23.8]	12.6	8	15.2 (10.1)	2.5 (2.4)	78.2 (8.6)	$44,807 ($11,410)
⩽5 mi CN	3	0.84 (0.95)	62.5 (16.9) [0.05]	15.7 [45.1]	1.8	1	3.4 (.)	0.7 (.)	88.4 (.)	$63,910 (.)
⩽5 mi YO	1	0.20 (0.45)	58.6 (18.3) [0.00]	8.2 [2.5]	1.3	1	13.7 (.)	2.5 (.)	67.5 (.)	$35,407 (.)

[a]Circulatory ED visits for the time period 1 August 1998 to 31 December 2004 ($N = 2345$ days).
[b]SES indicator data from Census 2000: %BP = percent below poverty; %PA = percent on public assistance; %HS = percent with high school graduation; Income = median population housing income.
[c]Subpopulations include all patients residing within 5 miles of Jefferson St (JS), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO).
[d]%B = mean percent of visits by black patients; %O = mean percent of visits by Hispanic and other races/ethnicities.
[e]Census data are missing for several ZIP codes that are included in ED database.
[f]Square brackets indicate percent unknown age and percent unknown race.

Discussion

Here, we present the results of time-series analyses of ambient air pollution and ED visits for circulatory disease in geographical subpopulations in Atlanta, Georgia, using air pollution data from monitors located in different regions of the study area as alternative measures of exposure. In doing so, we offer a method for evaluating the effects of an important component of exposure measurement error on air pollution health risk estimates in time-series analyses. Specifically, the method addresses the component of measurement error related to spatiotemporal variability in ambient air pollution concentrations when using fixed-site ambient monitoring data to estimate air pollution exposures. By comparing the results of models that use different exposure metrics for the same geographical subpopulation, our method effectively controls the potential modifying effects of population characteristics.

In our analysis, we assumed that a greater distance between the air pollution monitor used as the measure of exposure and the geographical subpopulation would result in a greater amount of exposure measurement error, particularly for pollutants showing spatiotemporal variability. Thus, differences in estimated relative risks when different air pollution monitors are used may serve to illustrate the degree of exposure measurement error. Classically, if exposure measurement error is non-differential with respect to a health outcome, we expect the bias to be towards the null when using an exposure measure containing error. According to this model, if the health outcome is caused by the exposure, using a more refined measure of exposure should result in less bias towards the null. For example, a model using data from a local monitoring site as the measure of exposure for a specific geographical subpopulation may yield higher estimated relative risks than a model using non-local data because of lower exposure measurement error, assuming that the correlation between measured ambient concentrations and unmeasured, true average population exposure is higher when the distance between the monitoring site and the population is small (Wilson et al., 2007). Comparing estimated relative risks is a crude way of evaluating measurement error, but descriptive comparisons may be informative. For example, in Figure 2, we compared the relative risks using different measures of exposure within each

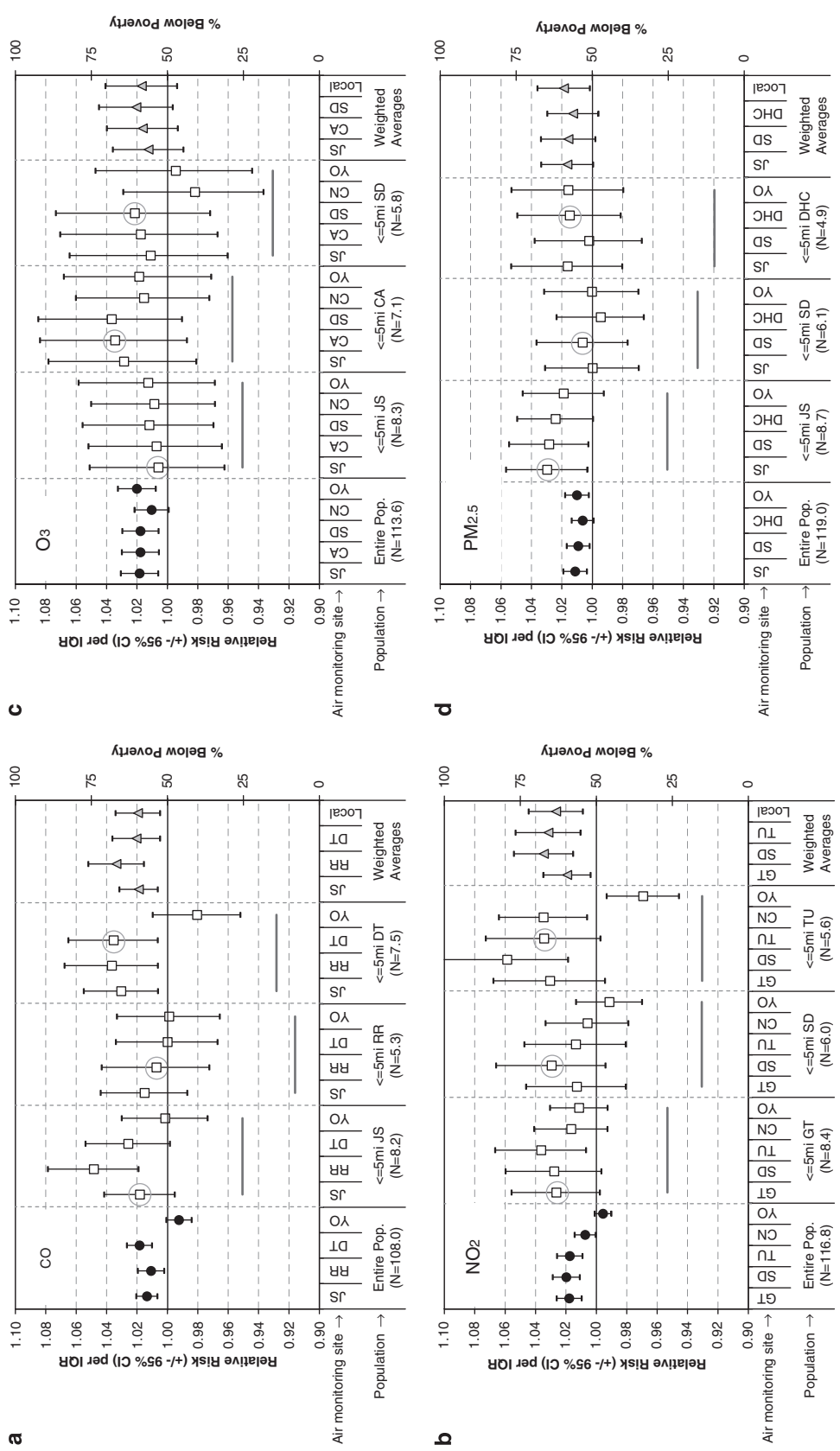

Figure 2. Associations between current-day ambient air pollutants and circulatory ED visits: (a) CO, (b) NO_2, (c) O_3, and (d) $PM_{2.5}$. ● = results of entire population analyses. □ = results of geographic subpopulation analyses. ○ = results of geographic subpopulation analyses using local (i.e., closest) monitoring site data. ▲ = weighted averages of geographic subpopulation results, where the "local" weighted averages provide overall estimates for the relative risk using the local site pollution data across the geographic subpopulations for each pollutant (i.e., overall estimates of the circled results) and "site-specific" weighted averages provide overall estimates of results obtained from using each urban site as a central monitor for the same geographic subpopulations. – = mean % below poverty of geographic subpopulations (on the secondary *y*-axis). IQR = interquartile range (approximate IQRs used for weighted average relative risks: CO = 1 ppm, NO_2 = 20 ppb, O_3 = 25 ppb, $PM_{2.5}$ = 10 $\mu g/m^3$). Air monitoring sites = Jefferson St (JS), Georgia Tech (GT), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO). Population = entire population and geographic subpopulations, which include all patients residing within 5 miles of Jefferson St (JS), Confederate Ave (CA), Roswell Rd (RR), South Dekalb (SD), Dekalb Tech (DT), Doraville Health Center (DHC), Tucker (TU), Conyers (CN), and Yorkville (YO). *N* = mean daily circulatory ED visits.

geographical subpopulation (e.g., for CO, we compared the four results obtained for the JS population, using monitoring data from JS, RR, DT, and YO). We anticipated that the distance between the population and the monitoring sites would provide an indication of the exposure measurement error and would thus dictate the observed associations for spatiotemporally heterogeneous pollutants (i.e., CO and NO_2), with strongest associations anticipated for each population when paired with its closest monitoring site (circled results in Figure 2).

Our results suggest that the effect of monitoring site location and the distance between monitoring sites and the population under study on observed relative risk estimates depend on the pollutant of interest, as expected. For spatially homogeneous pollutants (i.e., O_3 and $PM_{2.5}$), relative risk estimates were generally similar regardless of the monitoring site used as the exposure measure and regardless of distance between monitoring site and population. In contrast, for spatially heterogeneous pollutants (i.e., CO and NO_2), estimated associations varied by monitoring site location, particularly when the exposure measure included a rural monitoring site located far (e.g., greater than 30 miles) from the population center of interest. For example, associations that were observed using central site data for CO and NO_2 were not observed when using data from the most rural site as the measure of exposure.

Within the urban area, however, distances (e.g., <20 miles) between monitoring sites and geographical subpopulations did not meaningfully affect the estimates for any pollutant. Weighted averages of associations using local monitoring data (located within 5 miles of each subpopulation) were similar to those using data from other urban monitoring sites (located within 10–20 miles of the populations). If closer residential proximity to an ambient monitoring site provides better exposure assessment, as is often assumed to be the case (Jerrett et al., 2004; Chen et al., 2007; Wilson et al., 2007), we would have expected to observe larger relative risks when using local monitoring data than non-local monitoring data in the current analysis. These results suggest that, within urban Atlanta, use of local monitoring data as opposed to other urban monitoring data did not significantly modify exposure estimation for our pollutants of interest.

On the basis of our results, it appears that urban monitors served as similar surrogates of population exposures to CO and NO_2, and were better surrogates of these pollutants than rural monitors in our study. For CO and NO_2, the positioning of urban monitors may allow them to pick up specific sources (e.g., background traffic) that are more relevant to the health of the population compared with local effects near rural sites. For O_3 and $PM_{2.5}$, all monitors yielded very consistent epidemiological results given the fact that monitor siting criteria varied among our monitoring sites (Table 1).

It is important to note that the 5-mile radii used to define subpopulations in this analysis did not allow for highly refined exposure assessment to specific pollutant components associated with individual sources, such as traffic, whose concentrations vary considerably over short distances from roadways (100s of meters) (Zhu et al., 2002). Significant spatial variation in CO and NO_2 pollutant concentrations within the 5-mile capture areas may have reduced our ability to refine exposures sufficiently to observe substantial effects of residential proximity to monitoring sites on our epidemiological results. Other studies have indeed found higher relative risks when using more spatially refined estimates of exposure compared with using data from central sites (Jerrett et al., 2005). Moreover, data from certain monitors may not have been the most representative of corresponding local populations because of very local effects specific to the monitor, such as wind or point sources.

Another reason for the lack of consistent differences in results when using alternative (urban) measures of exposure may be because of the issue of subject mobility. Local monitoring data, assigned to patients on the basis of their residential ZIP codes, may not ultimately have improved exposure assessment in our study because of time-activity patterns that take individuals away from their location of residence for much of the day. Although time–activity studies show that people spend approximately 70% of their time inside their homes (Leech et al., 2002), the location of time spent away from home in Atlanta may be farther compared with studies of smaller geographic scale. As part of the Strategies for Metropolitan Atlanta's Regional Transportation and Air Quality (SMARTRAQ) study, Frank et al. (2004) reported the results of an activity-based survey of 8000 households in 2001, with participants recruited from different land use types, household sizes, and incomes . The authors found that the per capita daily vehicle miles traveled from home to work was 16.5 miles, with lower estimates for central counties (e.g., 12.2–13.8 miles for DeKalb and Fulton) than for outlying counties (e.g., 31.6 miles for Paulding). Therefore, our 5-mile radii may not have sufficiently captured the location of where patients spend their time throughout the day.

Differences in population characteristics, such as demographic or socio-economic factors, cannot explain differences in our epidemiological results when using alternative exposure measures for the same geographical subpopulation. They may, however, explain differences in results between different geographical subpopulations paired with their respective local sites (e.g., comparing circled results in Figure 2). Our demographic and SES data suggest that the geographical subpopulations differed with respect to these indicators (Table 4), and thus had potentially different susceptibilities to air pollution. However, we did not find a consistent link between the measured population characteristics and magnitude of the local site effect estimates. Our

comparison was limited by having only three results for each between-subpopulation comparison for each pollutant. Heterogeneity in the population characteristics within each geographical subpopulation as well as random variability because of small sample size may also have limited our ability to observe any potential effect.

As such, our results differ from other recent findings. Population characteristics, particularly SES (O'Neill et al., 2003; Jerrett et al., 2004; Cakmak et al., 2006; Zeka et al., 2006), have been shown earlier to affect the magnitude of observed associations between air pollution and health. In a geographical subpopulation study most similar to the current one, Jerrett et al. (2004) conducted a "zonal" analysis for associations between PM and sulfur dioxide and mortality in Hamilton, Canada, dividing the study area into five zones (Jerrett et al., 2004). They found that zonal estimates were 1/3 to 3 times higher than regional (entire population) estimates for both pollutants. They also found that the zone with the highest SES showed no effect in any models, whereas the zone with the lowest SES had the highest effects.

Our current analysis demonstrates a method for examining the effects of exposure measurement error relating to spatiotemporal heterogeneity in air pollutant concentrations on time-series health effect estimates, while controlling for population characteristics. In Atlanta, we found that monitoring site location and the distance of a monitoring site to a population of interest did not meaningfully affect estimated associations for any pollutant when using data from urban sites located within 20 miles from the population center under study. However, for CO and NO_2, these factors were important when using data from sites located greater than 30 miles from the population center, most likely because of exposure measurement error. Our results suggest that data from a rural site (Yorkville), the most distant site from our central, downtown monitors, introduced a substantial degree of exposure measurement error for estimating exposures to CO and NO_2. Using data from the urban monitors led to less exposure measurement error for our study population, and we found no important difference between these monitors for estimating associations for CO and NO_2. O_3 and $PM_{2.5}$ data from any monitoring site appeared to be similarly representative of population exposure.

These findings lend support to the use of limited ambient monitoring as a surrogate of population exposures in time-series settings. However, it is important to note that specific geographical features, source types, and resulting pollutant characteristics in Atlanta may influence the generalizability of our results to other locales. Atlanta provides a large and relatively flat geographical study area (e.g., a 20-county, 7964 sq. mile) the population of which is distributed in a concentric pattern around an urban core, with air pollution largely arising from power plants and traffic sources. The effect of distance between monitoring sites and subpopulations may be more prominent in areas with more spatial heterogeneity in pollutant levels than in those observed in Atlanta (e.g., because of differences in geographical features and/or geographical distribution of sources).

We did not attempt to examine the total effect of exposure measurement error in this analysis, which may in part explain differences in observed relative risks within and between pollutants. Although we explored the effects of exposure error among different pollutants, we did so only from the perspective of ambient spatiotemporal distributions. We did not consider several other factors that could potentially influence differences in health effect estimates, including differential instrument error between monitors and the spatial variation of pollutant-specific personal-ambient relationships (e.g., because of differential infiltration patterns).

Overall, the current analysis supports the use of pollutant data from urban central sites in Atlanta and similar cities to assess ambient exposures for geographically dispersed study populations, even for spatially heterogeneous pollutants (Metzger et al., 2004; Peel et al., 2005; Tolbert et al., 2007; Sarnat et al., 2008). In addition, our findings suggest the need to balance the advantages of improved exposure assessment that may hold if a smaller area is studied, with the increased variance of estimates that would result, in comparison with the study of a larger area with more people. Refining exposure assessment by limiting the population of interest to obtain more accurate local exposure estimates will increase the potential for random error, which could mask the association of interest.

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