Emergency Hospital Admissions for Cardiovascular Diseases and Ambient Levels of Carbon Monoxide

Results for 126 United States Urban Counties, 1999–2005

Michelle L. Bell, PhD; Roger D. Peng, PhD; Francesca Dominici, PhD; Jonathan M. Samet, MD

Background—Evidence on risk of cardiovascular disease (CVD) hospitalization associated with short-term exposure to outdoor carbon monoxide (CO), an air pollutant primarily generated by traffic, is inconsistent across studies. Uncertainties remain on the degree to which associations are attributable to other traffic pollutants and whether effects persist at low levels.

Methods and Results—We conducted a multisite time-series study to estimate risk of CVD hospitalization associated with short-term CO exposure in 126 US urban counties during 1999–2005 for >9.3 million Medicare enrollees aged ≥65 years. We considered models with adjustment by other traffic-related pollutants: NO_2, fine particulate matter (with aerodynamic diameter ≤2.5 μm), and elemental carbon. We found a positive and statistically significant association between same-day CO and increased risk of hospitalization for multiple CVD outcomes (ischemic heart disease, heart rhythm disturbances, heart failure, cerebrovascular disease, total CVD). The association remained positive and statistically significant but was attenuated with copollutant adjustment, especially NO_2. A 1-ppm increase in same-day daily 1-hour maximum CO was associated with a 0.96% (95% posterior interval, 0.79%, 1.12%) increase in risk of CVD admissions. With same-day NO_2 adjustment, this estimate was 0.55% (0.36%, 0.74%). The risk persisted at low CO levels <1 ppm.

Conclusions—We found evidence of an association between short-term exposure to ambient CO and risk of CVD hospitalizations, even at levels well below current US health-based regulatory standards. This evidence indicates that exposure to current CO levels may still pose a public health threat, particularly for persons with CVD. (***Circulation*. 2009;120:949-955.**)

Key Words: air pollution ■ carbon monoxide ■ cardiovascular diseases ■ heart diseases ■ hospitalization

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

Carbon monoxide (CO) is a tasteless, odorless gaseous pollutant ubiquitous in the outdoor atmosphere that is generated by combustion. Adverse health effects of CO exposure include death from asphyxiation at high exposure levels and, at lower levels, impaired neuropsychological performance and risk for myocardial ischemia and rhythm disturbances in persons with cardiovascular disease (CVD).[1,2] The most definitive evidence on CO and CVD comes largely from controlled exposure studies, involving CO inhalation at concentrations to mimic exposures previously typical of urban environments.[3] Findings of earlier epidemiological studies were mixed, and few recent epidemiological studies have been conducted.[3] Little research has been done on the potential adverse health effects in humans from current ambient exposure to generally low CO levels.[4]

Editorial see p 924
Clinical Perspective on p 955

Evidence on risk of CVD hospitalizations associated with CO exposure[5–10] is inconsistent across epidemiological studies,[3,4] perhaps because of their limited population sizes and the differing CVD causes considered. Although a few multicity CO studies have been conducted,[7,8] to the best of our knowledge a national-scale US study of CO and CVD hospitalizations has not been performed. Furthermore, because CO primarily results from traffic in most urban communities, risks associated with CO may be confounded or modified by other traffic-related air pollutants, such as NO_2 and fine particles (fine particulate matter with aerodynamic diameter ≤2.5 μm [$PM_{2.5}$]).[3] Human clinical studies provide useful scientific evidence but typically involve exposure to CO alone. Therefore, studies that better reflect CO and its existence in urban air as a component of a complex mixture are needed.

Currently, US outdoor CO levels are low and well below that specified by the US Environmental Protection Agency (EPA) health-based National Ambient Air Quality Standard (35 ppm for 1-hour daily maximum) in almost all areas.[11] However, the health risks of exposure to these low CO levels have not been addressed directly.[3] Rather, experimental

Received January 14, 2009; accepted June 9, 2009.

From the School of Forestry and Environmental Studies, Yale University, New Haven, Conn (M.L.B.); Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Md (R.D.P., F.D.); and Department of Preventative Medicine, University of Southern California, Keck School of Medicine, Los Angeles (J.M.S.).

The online-only Data Supplement is available with this article at http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.109.851113/DC1.

Correspondence to Michelle L. Bell, PhD, School of Forestry and Environmental Studies, Yale University, Kroon Hall, 195 Prospect St, New Haven, CT 06511. E-mail michelle.bell@yale.edu

© 2009 American Heart Association, Inc.

Circulation **is available at http://circ.ahajournals.org** **DOI: 10.1161/CIRCULATIONAHA.109.851113**

exposure studies have largely driven the standards. Should adverse health impacts occur at today's low CO levels, the public health burden could be considerable.

We conducted a national multisite time-series study to estimate the association between short-term exposure to outdoor CO and risk of CVD hospitalizations in a population of Medicare enrollees. We address key scientific questions about associations of CO with cause-specific CVD hospitalization categories; the shape of the exposure-response curve; the persistence of effects at low levels; and possible confounding by copollutants in the urban air pollution mixture, in particular those relating to traffic.

Methods

We constructed counts of emergency daily hospital admissions for Medicare enrollees aged ≥65 years during 1999–2005 for 126 US urban counties with populations ≥200 000 and CO data for ≥75% of days in the study period. On average, across the study period, >9.3 million subjects were included. Admission rates were based on the total number of Medicare enrollees for a county on a given day. Cause-specific CVD hospitalizations were considered on the basis of primary diagnosis according to *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes: heart failure (*ICD-9* 428); heart rhythm disturbances (*ICD-9* 426 to 427); cerebrovascular events (*ICD-9* 430 to 438); ischemic heart disease (*ICD-9* 410 to 414, 429); and peripheral vascular disease (*ICD-9* 440 to 448). Total CVD admissions were calculated as the sum of these causes. We considered hospitalizations for injuries and other external causes (*ICD-9* 800 to 849) as a test outcome for which we anticipate no association with CO, an approach that has been used in earlier research.[12,13]

Air pollution data were obtained from the US EPA. The highest hourly value recorded for a given day (daily 1-hour maximum) was used as the exposure metric for CO, and daily averages were used for $PM_{2.5}$, NO_2, and elemental carbon (EC). Because the copollutant data were applied as daily averages, we performed sensitivity analysis with daily (24-hour average) CO levels. On average across the communities, CO data were available for 99% of study days. Daily temperature and dew point temperature for each county were obtained from the National Climatic Data Center. Air pollution and weather data from multiple monitors within a county were averaged to generate county-level estimates.

Within each county, we first estimated risk of CVD hospitalization associated with CO in a log-linear overdispersed Poisson time-series model with variables to adjust for long-term trend, seasonality, day of the week, temperature and dew point temperature, and potentially different long-term trends for ages 65 to 74 and ≥75 years. Natural cubic splines were used to address nonlinearity in variables for long-term trend, seasonality, and weather. Separate regression models were fit to data from each county. We conducted separate analyses for CO exposure concentrations for the following: (1) the same day as the hospitalization (L0); (2) the day before (L1); and (3) 2 days previous (L2). For each analysis, we then combined the adjusted county-specific risk estimates across counties and estimated a national average with Bayesian hierarchical models, which accounts for within-county statistical error and between-county variability of the "true" relative risks (also called "heterogeneity").[14] The model produces a posterior probability distribution of the national average effect, which we summarize by reporting the posterior mean. We used this statistical approach in previous multisite time-series studies of particulate matter for mortality and morbidity.[12,13]

Results are presented as the percent increase in risk of CVD hospitalization per 1-ppm increase in the daily 1-hour maximum CO. This increment (1 ppm) approximates the average interquartile range (difference between 75th and 25th percentiles) across all communities. Statistical significance was determined by the posterior probability of an estimate >0 being ≥0.95. We investigated whether results were robust to the degrees of freedom for control of seasonality and long-term trends.

Given the strong role of traffic as a source for CO, we investigated whether associations between CO and CVD hospitalizations were robust to adjustment by traffic-related pollutants $PM_{2.5}$ or NO_2 individually or together in multipollutant models. We considered same-day $PM_{2.5}$ because previous studies found that same-day (L0) $PM_{2.5}$ concentration was associated with the largest risk of CVD admissions.[13] We considered NO_2 also on the same day (L0) because we found that this lag had the strongest effect in single-lag models. To focus more on the traffic-related components of $PM_{2.5}$ total mass, we also adjusted for the portion of $PM_{2.5}$ that is EC on the basis of EPA PM chemical component monitoring data.[15]

Because not all counties had data for all pollutants, we examined potential confounding by each copollutant by comparing the association between CO and CVD hospitalizations as follows: (1) with copollutant adjustment and (2) without copollutant adjustment, but only considering days for which copollutant data were available. For NO_2 and $PM_{2.5}$, we considered counties with copollutant data available for ≥75% of the study days, resulting in 92 counties for NO_2, with data for this pollutant available an average 97.0% of the study days. For $PM_{2.5}$, 67 counties were used, with data available for an average 91.9% of days in the study period. There were 58 counties with both NO_2 and $PM_{2.5}$ data available. Limited data are available for EC, which is not measured in all counties and is typically measured at a frequency of 1 in 6 days. Using a criterion of at least 60 observations corresponding to approximately a year of measurements at a frequency of 1 in 6 days, 81 counties were included in the EC analysis. Data were available for an average of 56.5% days in the study period. Because of the limited data for EC, this copollutant was not considered in conjunction with NO_2 or $PM_{2.5}$ total mass.

We performed sensitivity analysis to investigate whether the effect estimates for CO and hospital admissions were affected by monitor coverage based on the county's area and number of CO monitors. A second-stage regression analysis was performed with county-specific health effect estimates as the outcome variable and the county area per number of CO monitors for each county as the independent variable.

To investigate risk at low CO levels, we performed subset analyses using data sets including only days with CO levels below a specified value, *s*. We repeated the subset analysis for *s* values from 1 to 10 ppm in 1-ppm increments. Under the threshold hypothesis, no association would be observed in analysis of CO values at or below the threshold. We investigated the exposure-response curve as sensitivity analysis using a nonlinear function of CO.[16] This study was exempted by the institutional review board at Johns Hopkins Bloomberg School of Public Health.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Table 1 provides descriptive statistics on pollution and hospitalization data. Ischemic heart disease and heart failure were the most common causes of CVD hospitalizations. Although CO levels varied across communities, all counties had low levels during the study period. County-specific pollutant and health data summaries are available in Tables I and II in the online-only Data Supplement. A plot of county-specific average CO levels versus CVD hospitalization rates is provided in Figure I in the online-only Data Supplement. The correlations between daily 1-hour maximum CO and other pollutants, on average across communities, were 0.26 for daily $PM_{2.5}$ (67 counties, average of 2326 observation days per county), 0.56 for NO_2 (92 counties, average of 2464 days per county), and 0.48 for EC (81 counties, average of 328 days per county). Correlations among copollutants are provided in Table III in the online-only Data Supplement.

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

Table 1. Summary Statistics of Pollution and Health Data for 126 US Urban Counties, 1999–2005

	No. of Counties	Median	25th to 75th Percentiles	Minimum to Maximum
Pollution levels				
Daily 1-hour maximum CO, ppm	126	1.3	0.9 to 1.9	0.2 to 9.7
Daily 24-hour CO, ppm	126	0.5	0.4 to 0.7	0.05 to 2.5
Daily $PM_{2.5}$, $\mu g/m^3$	67	11.6	8.0 to 16.8	0.3 to 71.1
Daily NO_2, ppb	92	15.8	11.6 to 21.0	1.1 to 53.7
Daily EC $PM_{2.5}$, $\mu g/m^3$	81	0.60	0.41 to 0.89	0.01 to 3.3
Hospitalization rates/100 000 persons				
Ischemic heart disease	126	5.56	3.33 to 8.05	0.01 to 22.4
Heart rhythm disturbances	126	2.68	1.11 to 4.52	0.00 to 15.3
Heart failure	126	4.81	2.90 to 7.26	0.00 to 21.1
Cerebrovascular disease	126	3.79	2.08 to 5.97	0.00 to 17.7
Peripheral vascular disease	126	0.18	0.02 to 1.05	0.00 to 8.18
Total CVD	126	19.0	14.5 to 23.8	0.35 to 47.6
Injury	126	4.16	2.22 to 6.34	0.00 to 19.2
Study subjects (population at risk on a given day)	126	74 747	68 998 to 78 152	67 059 to 80 304

These data represent the average of county-specific values.

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

On average across the 126 counties, the 1-hour maximum CO level was 1.6 ppm, well below the National Ambient Air Quality Standard (35 ppm). Figure 1A provides box plots showing the distribution of the communities' CO levels. We also described the change of CO levels with comparison of CO on adjacent days within cities (Figure 1B).

Table 2 summarizes estimated associations between CO and risk of CVD hospitalizations with adjustment by copollutants. Associations between CO and CVD hospitalizations remained positive and statistically significant with adjustment by any copollutant, although estimates were attenuated, especially with NO_2 adjustment. Figure II in the online-only Data Supplement provides county-specific and national estimates with and without copollutant adjustment. Associations between the copollutants (NO_2, $PM_{2.5}$, and EC) and CVD hospitalizations are provided in Table IV in the online-only Data Supplement. Subsequent analyses were adjusted for L0 NO_2 because of the change in CO estimates with adjustment by this pollutant.

Figure 2 shows the percent increase in risk of cause-specific and total CVD hospitalizations per 1-ppm increase in daily 1-hour maximum CO, adjusted by same-day NO_2. For most CVD outcomes, associations were positive and statistically significant for same-day CO. Statistically significant associations were not observed between the outcome of accidents and injuries and CO at any lag.

Because daily values were used for copollutants, we performed sensitivity analysis with a 24-hour average metric of CO (Table V in the online-only Data Supplement). Results were similar to those with the daily 1-hour maximum CO. Effect estimates were generally lowered with copollutant adjustment, especially NO_2, but remained positive and statistically significant.

Sensitivity analysis found that results for the association between same-day daily 1-hour maximum CO and total CVD hospitalizations were robust to the degree of adjustment for seasonality and trend (Figure III in the online-only Data Supplement). Similarly, effect estimates for injury, showing no association, were robust to the degree of adjustment for trend and seasonality.

The average number of CO monitors per county was 2.3 (interquartile range=1.9), and the monitor coverage (county area per number of monitors) averaged 1614 km^2 per monitor across all counties. The median correlation of the daily 1-hour

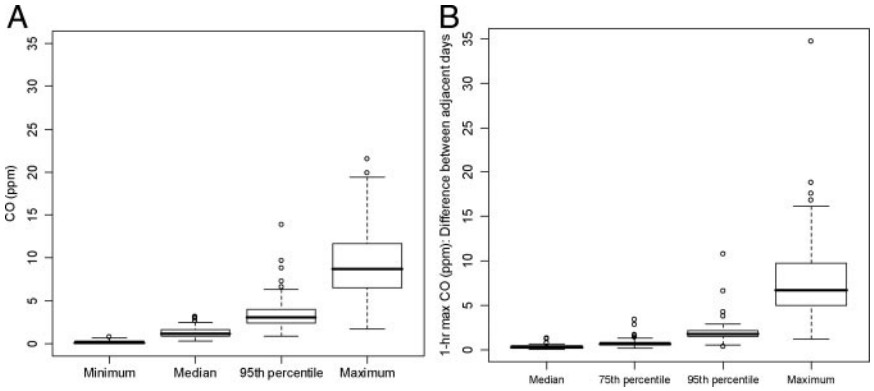


Figure 1. Distribution of daily 1-hour maximum CO levels for 126 communities. A, Minimum, median, 95th percentile, and maximum 1-hour daily maximum CO levels. B, Median, 75th percentile, 95th percentile, and maximum of 126 communities for the difference between adjacent days' 1-hour daily maximum CO levels.

Table 2. Percent Increase in Risk of Cardiovascular Hospital Admissions per 1-ppm Increase in the Same-Day 1-Hour Maximum CO for Those Aged ≥65 Years (1999–2005), With and Without Adjustment for Copollutants NO_2, $PM_{2.5}$, and EC

Copollutant Adjustment	No. of Counties	Percent Change in Risk (95% Posterior Interval)
None, all days included	126	0.96 (0.79, 1.12)
None, but days with NO_2 data available	92	1.05 (0.85, 1.24)
NO_2	92	0.55 (0.36, 0.74)
None, but days with $PM_{2.5}$ data available	67	0.84 (0.64, 1.03)
$PM_{2.5}$	67	0.76 (0.57, 0.96)
None, but days with NO_2 and $PM_{2.5}$ data available	58	0.93 (0.72, 1.14)
NO_2 and $PM_{2.5}$	58	0.52 (0.29, 0.75)
None, but days with EC data available	81	1.05 (0.54, 1.56)
EC	81	0.97 (0.38, 1.57)

To aid comparison across identical data sets, effect estimates without copollutant adjustment were generated for the subset of data with copollutant data available. All pollutants (CO, NO_2, $PM_{2.5}$, EC) were based on same-day levels (L0).

maximum CO from monitor pairs within the same county was 0.66. An interquartile range increase in monitor coverage (1500 km^2 per monitor decrease) was associated with an 8% (95% interval, −7%, 24%) increase in same-day daily 1-hour maximum CO effect estimates for CVD hospitalizations based on all 126 counties, and a 20% (95% interval, −11%, 52%) increase based on NO_2 adjusted estimates for 92 counties. Although the associations are not statistically significant, they are suggestive of higher effect estimates with denser monitor coverage.

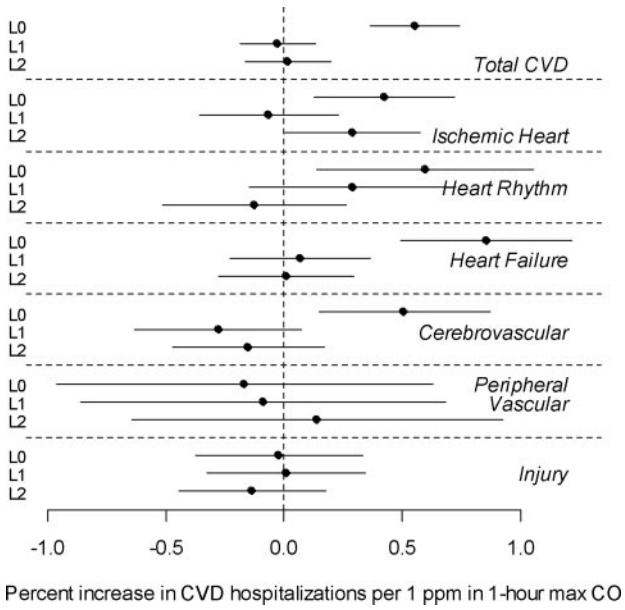


Figure 2. Percent increase in risk of cardiovascular and injury-related hospital admissions for those aged ≥65 years for 92 US counties (1999–2005) per 1-ppm increase in the same-day 1-hour daily maximum CO for multiple lag structures and causes of hospitalizations, with adjustment by L0 NO_2. The points indicate central estimates; horizontal lines, 95% posterior intervals. Exposures are represented as L0 for the same day, L1 for the previous day, and L2 for 2 days previous.

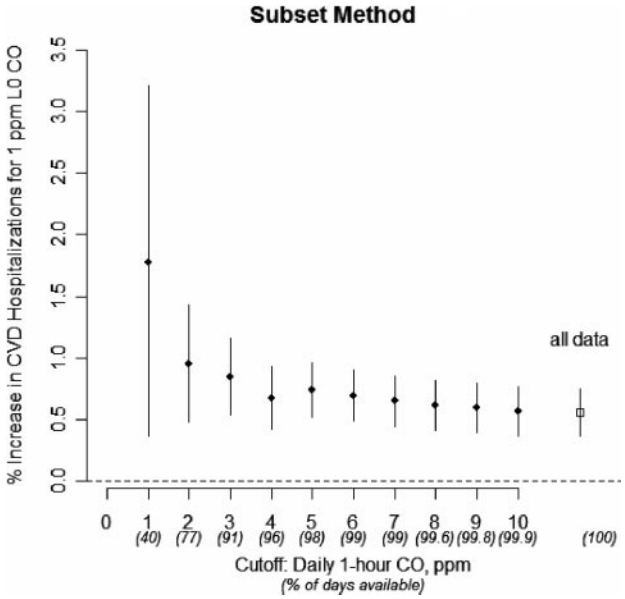


Figure 3. Percent increase in risk of cardiovascular hospitalizations per 1-ppm increase in same-day daily 1-hour maximum CO, using the subset method for 92 US counties, adjusted for same-day NO_2. The solid diamonds indicate the central estimate; vertical lines, 95% posterior intervals. Estimates are based on the subset of data only including days with CO levels at or below the cutoff value (*s*) specified on the *x* axis. The estimate on the far right (open box) reflects results based on the entire data set. The italicized numbers in parentheses represent the percentage of days used in each threshold analysis, on average across the communities, compared with the data used in the nonthreshold analysis.

Figure 3 shows results of the subset analyses. For all values of *s*, from 1 to 10 ppm, associations between CO and CVD admissions adjusted by NO_2 remained positive and statistically significant. When we restricted analysis to days with a 1-hour daily maximum CO less than the current US EPA health-based standard (35 ppm), we found that a 1-ppm increase in CO is associated with a 0.55% (95% interval, 0.36%, 0.74%) increase in risk of CVD admissions. This estimate is identical to the estimated risk obtained with the entire data set.

We estimated an exposure-response curve allowing a nonlinear relationship between CO and risk of CVD admissions (Figure IV in the online-only Data Supplement). We found no evidence of departure for a linear exposure-response curve. These findings support the subset analysis and do not indicate a threshold level below which CO levels are not associated with the health response.

Discussion

We performed a study of CO and CVD hospitalizations using data on >9.3 million Medicare enrollees in 126 US urban counties over a 7-year period. Other recent time-series studies of CO and morbidity include a study of 10 Canadian cities investigating congestive heart failure[5] and the 2 largest US -based studies, which investigated conges-

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

tive heart failure admissions in 7 communities[10] and total CVD admissions in 8 communities.[17] Mortality was examined in 19 European cities by the Air Pollution and Health: A European Approach (APHEA-2) investigators, finding independent associations of CO with total and CVD mortality.[18] Ambient CO levels have also been associated with heart rate variability in a human exposure study of persons with coronary artery disease[19] and other adverse health outcomes in multiple population-based studies, such as low birth weight[20] and mortality.[18,21]

Our results provide strong evidence of an association between outdoor CO concentrations and risk of CVD hospitalizations for an older population. The patterns of association by lag, with strongest effects on the same day, are consistent with CO kinetics and the likely mechanisms by which CO has adverse CVD effects. For the "control" category of injury, we found no evidence of an association, implying satisfactory adjustment for time-varying potential confounders.

Because the primary CO source in urban centers is traffic, we considered confounding by other traffic-related pollutants (NO_2, $PM_{2.5}$, EC). With adjustment for these copollutants, the association remained, although it was attenuated, particularly with NO_2 adjustment. We cannot exclude the possibility that the observed associations could reflect pollution from traffic emissions generally, which have been associated with cardiovascular end points[22,23] and not from CO specifically. CO levels were moderately correlated with NO_2, also resulting from vehicle emissions, among other sources.[24] Our analyses estimate the effects of CO adjusted by other traffic-related pollutants. The total health impacts of air pollution from the traffic source, or from the air pollution mixture more broadly, are as yet unknown. Understanding the public health consequences of multiple pollutants is an area needing further research, as indicated by reports from the National Resource Council.[25,26]

Because of the spatial distribution of ambient CO in urban areas, we anticipate potential misclassification of personal exposures for city dwellers by our reliance on regulatory monitors. Extensive research has not been conducted on the relationship between personal exposure to CO and ambient measurements. Such work is needed, especially relative to which subpopulations (eg, outdoor workers) may have differential exposure. A study of 56 subjects found little agreement between ambient and personal CO measurements.[27] An examination of in-home CO distribution in Washington, DC, found higher levels for those living in the metropolitan area than those in the suburbs.[28] We did not find that the health effect estimates vary by the monitor coverage within a county, although the results were suggestive of potential higher estimates with more dense monitor coverage. The exposure misclassification would tend to reduce estimates, implying that our results could underestimate risk of hospitalization associated with CO.

The present National Ambient Air Quality Standard for CO, promulgated in 1994, is based largely on results of studies involving exposure of volunteers with coronary heart disease to concentrations of CO sufficient to raise blood carboxyhemoglobin concentrations from the typical level of 1% in nonsmokers to as high as 6%.[29,30] The study participants had documented coronary heart disease, and study outcomes were clinically relevant indicators (increased arrhythmias,[31,32] time to ischemia or angina[33,34]). Effects on indicators of myocardial ischemia were identified at carboxyhemoglobin concentrations as low as 2%[34] and for arrhythmias at 6%.[31] The Coburn-Forster-Kane equation, which describes the relationship between inhaled CO and blood carboxyhemoglobin, was used by the EPA to calculate ambient exposures that could result in carboxyhemoglobin concentrations associated with adverse effects, although the equation's original aim was to estimate the rate of endogenous CO production.[35] In another study, carboxyhemoglobin measurements did not correlate with clinical status in CO poisoning.[36]

Our results are consistent with clinical and animal model studies finding that CO exposure can adversely affect cardiac function.[4,37,38] Many of these studies investigated high CO concentrations, often elevated by cigarette smoking, which far exceed the ambient levels studied here; an early review of this literature noted that few studies explored low CO levels.[37] One critical finding of our research is the perhaps unexpectedly strong effect observed at current ambient levels (Table 1). A 1-ppm increase in CO concentration, approximating the interquartile range across communities, would correspond to an ≈0.1% to 0.2% increase in blood carboxyhemoglobin on average. The maximum changes in CO concentration within city, based on comparison of CO levels on adjacent days, are at a level that would be expected to increase carboxyhemoglobin by ≈1%, sufficient to increase the level from the baseline of 1% typical of nonsmokers to the 2% value at which effects were observed in some exposure studies (Figure 1B). Additionally, clinical CO studies, which used volunteers and involved an exercise protocol, may have underestimated potential susceptibility of persons with coronary heart disease.

Although physiological responses to CO have been well studied, much of the scientific evidence involves concentrations that are quite high in relation to current US ambient levels. The acute and lethal toxicity of CO at high levels is well documented, and human exposure studies have shown acute CO poisoning at very high concentrations,[2] although debate still exists on the biological mechanisms of CO toxicity.[39–41] Additional information on physiological mechanisms continues to be gained. CO exposure causes adverse health responses through binding to hemoglobin and subsequent lessened delivery of oxygen, as the affinity of hemoglobin for CO is >200 times that of oxygen.[38] Other mechanisms have also been hypothesized, including detriment to myoglobin function, generation of reactive oxygen species, and interruption of the terminal oxidase of the electron transport chain.[40,42–45] Recent in vitro and animal model studies indicate that low levels of CO may have therapeutic effects on tissue such as antioxidative and anti-inflammatory responses.[46–49]

This study provides one of the first population-based investigations of the health effects of current low ambient CO levels. We provided evidence that the association between CO and risk of cardiovascular hospitalizations persists at levels of daily 1-hour maximum CO <1 ppm and that daily excursions of CO concentration occur that are sufficient to

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

elevate carboxyhemoglobin to a level at which adverse effects have been observed experimentally. Most of the United States is in regulatory compliance with health-based CO regulations (35 ppm for the daily 1-hour maximum).[11,30] Higher levels of CO exist in some regions, including areas with developing transportation networks, such as urban Chinese centers, where CO primarily results from traffic.[50] Although much of the current research on health and traffic-related air pollution focuses on particulate matter, our study indicates that ambient CO and traffic may present a far larger health burden than suspected previously.

Sources of Funding

Funding was provided by an Oak Ridge Institute for Science and Education Fellowship with the US EPA, the EPA (RD-83241701), and the National Institutes of Health National Institute of Environmental Health Sciences Outstanding New Environmental Scientist Award (RO1 ES015028). The views expressed do not necessarily represent those of the funding agencies.

Disclosures

None.

References

1. Chambers CA, Hopkins RO, Weaver LK, Key C. Cognitive and affective outcomes of more severe compared to less severe carbon monoxide poisoning. *Brain Inj*. 2008;22:387–395.
2. Varon J, Marik PE, Fromm RE, Gueler A. Carbon monoxide poisoning: a review for clinicians. *J Emerg Med*. 1999;17:87–93.
3. US EPA. *Air Quality Criteria for Carbon Monoxide*. Washington, DC: US Environmental Protection Agency, Office of Research and Development; 2000.
4. Chen TM, Gokhale J, Shofer S, Kuschner WG. Outdoor air pollution: nitrogen dioxide, sulfur dioxide, and carbon monoxide health effects. *Am J Med Sci*. 2007;333:249–256.
5. Burnett RT, Dales RE, Brooke JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. *Epidemiology*. 1997;8:162–167.
6. Schwartz J. Is carbon monoxide a risk factor for hospital admission for heart failure? *Am J Public Health*. 1995;85:1343–1345.
7. Barnett AG, Williams GM, Schwartz J, Best TL, Neller AH, Petroeschevsky AL, Simpson RW. The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in Australian and New Zealand cities. *Environ Health Perspect*. 2006;114:1018–1023.
8. Von Klot S, Peters A, Aalto P, Bellander T, Berglind N, D'Ippoliti D, Elosua R, Hörmann A, Kulmala M, Lanki T, Löwel H, Pekkanen J, Picciotto S, Sunyer J, Forastiere F. Ambient air pollution is associated with increased risk of hospital cardiac readmissions of myocardial infarction survivors in five European cities. *Circulation*. 2005;112:3073–3079.
9. Yang W, Jennison BL, Omaye ST. Cardiovascular disease hospitalization and ambient levels of carbon monoxide. *J Toxicol Environ Health A*. 1998;55:185–196.
10. Morris RD, Naumova EN, Munasinghe RL. Ambient air pollution and hospitalization for congestive heart failure among elderly people in seven large US cities. *Am J Public Health*. 1995;85:1361–1365.
11. US Environmental Protection Agency. The Green Book nonattainment areas for criteria pollutants: 2008. Available at: http://www.epa.gov/oar/oaqps/greenbk/index.html. Accessed July 25, 2008.
12. Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. *JAMA*. 2008;299:2172–2179.
13. Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *JAMA*. 2006;295:1127–1134.
14. Richardson S, Best N. Bayesian hierarchical models in ecological studies of health-environment effects. *Environmetrics*. 2003;14:129–147.
15. Bell ML, Dominici F, Ebisu K, Zeger SL, Samet JM. Spatial and temporal variation in $PM_{2.5}$ chemical composition in the United States for health effects studies. *Environ Health Perspect*. 2007;115:989–995.
16. Bell ML, Peng RD, Dominici F. The exposure-response curve for ozone and risk of mortality and the adequacy of current ozone regulations. *Environ Health Perspect*. 2006;114:532–536.
17. Schwartz J. Air pollution and hospital admissions for heart disease in eight U.S. counties. *Epidemiology*. 1999;10:17–22.
18. Samoli E, Touloumi G, Schwartz J, Anderson HR, Schindler C, Forsberg B, Vigotti MA, Vonk J, Kosnik M, Skorkovsky J, Katsouyanni K. Short-term effects of carbon monoxide on mortality: an analysis within the APHEA project. *Environ Health Perspect*. 2007;115:1578–1583.
19. Dales R, Air Pollution-Cardiac Health Research Group. Ambient carbon monoxide may influence heart rate variability in subjects with coronary artery disease. *J Occup Environ Med*. 2004;46:1217–1221.
20. Salam MT, Millstein J, Li YF, Lurmann FW, Margolis HG, Gilliland FD. Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the Children's Health Study. *Environ Health Perspect*. 2005;113:1638–1644.
21. Burnett RT, Cakmak S, Raizenne ME, Stieb D, Vincent R, Krewski D, Brook JR, Philips O, Ozkaynak H. The association between ambient carbon monoxide levels and daily mortality in Toronto, Canada. *J Air Waste Manag Assoc*. 1998;48:689–700.
22. Fan ZT, Meng Q, Weisel C, Laumbach R, Ohman-Strickland P, Shalat S, Hernandez MZ, Black K. Acute exposure to elevated $PM_{2.5}$ generated by traffic and cardiopulmonary health effects in healthy older adults. *J Expo Sci Environ Epidemiol*. 2009;19:525–533.
23. Peretz A, Sullivan JH, Leotta DF, Trenga CA, Sands FN, Allen J, Carlsten C, Wilkinson CW, Gill EA, Kaufman JD. Diesel exhaust inhalation elicits acute vasoconstriction in vivo. *Environ Health Perspect*. 2008;116:937–942.
24. Ross Z, English PB, Scalf R, Gunier R, Smorodinsky S, Wall S, Jerrett M. Nitrogen dioxide prediction in Southern California using land use regression modeling: potential for environmental health analyses. *J Exp Sci Environ Epidemiol*. 2006;16:106–114.
25. National Research Council (NRC) Committee on Air Quality Management in the United States. *Air Quality Management in the United States*. Washington, DC: National Academies Press: 2004.
26. NRC Committee on Research Priorities for Airborne Particulate Matter. *Research Priorities for Airborne Particulate Matter IV: Continuing Research Progress*. Washington, DC: National Academies Press; 2004.
27. Sarnat JA, Schwartz J, Catalano PJ, Suh HH. Gaseous pollutants in particulate matter epidemiology: confounders or surrogates? *Environ Health Perspect*. 2001;109:1053–1061.
28. Schwab M. An examination of the intra-SMSA distribution of carbon monoxide exposure. *J Air Waste Manag Assoc*. 1990;40:331–336.
29. US Environmental Protection Agency. *Review of the National Ambient Air Quality Standards for Carbon Monoxide Assessment of Scientific and Technical Information: OAQPS Staff Paper*. Research Triangle Park, NC: US EPA Office of Air Quality Planning and Standards; 1992.
30. US Environmental Protection Agency. National ambient air quality standards for carbon monoxide: final decision. *Fed Reg*. 1994;59:38906–38917.
31. Sheps DS, Herbst MC, Hinderliter AL, Adams KF, Ekelund LG, O'Neil JJ, Goldstein GM, Bromberg PA, Dalton JL, Ballenger MN, Davis SM, Koch GG. Production of arrhythmias by elevated carboxyhemoglobin in patients with coronary artery disease. *Ann Intern Med*. 1990;113:343–351.
32. Dahms TE, Younis LT, Wiens RD, Zarnegar S, Byers SL, Chaitman BR. Effects of carbon monoxide exposure in patients with documented cardiac arrhythmias. *J Am Coll Cardiol*. 1993;21:442–450.
33. Kleinman MT, Davidson DM, Vandagriff RB, Caiozzo VJ, Whittenberger JL. Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease. *Arch Environ Health*. 1989;44:361–369.
34. Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. *N Engl J Med*. 1989;32:1426–1432.
35. Coburn RF, Forster RE, Kane PB. Considerations of the physiological variables that determine the blood carboxyhemoglobin concentration in man. *J Clin Invest*. 1965;44:1899–1910.
36. Hampson NB, Hauff NM. Carboxyhemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture? *Am J Emerg Med*. 2008;26:665–669.
37. Kuller LH, Radford EP. Epidemiological bases for the current ambient carbon monoxide standards. *Environ Health Perspect*. 1983;52:131–139.

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

38. Prockop LD, Chichkova RI. Carbon monoxide intoxication: an updated review. *J Neurol Sci*. 2007;262:122–130.
39. Seger D, Welch L. Carbon monoxide controversies: neuropsychologic testing, mechanism of toxicity, and hyperbaric oxygen. *Ann Emerg Med*. 1994;24:242–248.
40. Penney DG. Acute carbon monoxide poisoning: animal models: a review. *Toxicology*. 1990;62:123–160.
41. Omaye ST. Metabolic modulation of carbon monoxide toxicity. *Toxicology*. 2002;180:139–150.
42. Piantadosi CA. Carbon monoxide, reactive oxygen signaling, and oxidative stress. *Free Radic Biol Med*. 2008;45:562–569.
43. McGrath JJ. Biological plausibility for carbon monoxide as a copollutant in PM epidemiologic studies. *Inhal Toxicol*. 2000;12:S91–S107.
44. Iheagwara KN, Thom SR, Deutschman CS, Levy RJ. Myocardial cytochrome oxidase activity is decreased following carbon monoxide exposure. *Biochim Biophys Acta*. 2007;1772:1112–1116.
45. Turcanu V, Dhouib M, Gendrault JL, Poindron P. Carbon monoxide induces murine thymocyte apoptosis by a free radical-mediated mechanism. *Cell Biol Toxicol*. 1998;14:47–54.
46. Ryter SW, Kim HP, Nakahira K, Zuckerbraun BS, Morse D, Choi AM. Protective functions of heme oxygenase-1 and carbon monoxide in the respiratory system. *Antioxid Redox Signal*. 2007;9:2157–2173.
47. Ryter SW, Morse D, Choi AM. Carbon monoxide and bilirubin: potential therapies for pulmonary/vascular injury and disease. *Am J Respir Cell Mol Biol*. 2007;36:175–182.
48. Zhou Z, Song R, Fattman CL, Greenhill S, Alber S, Oury TD, Choi AM, Morse D. Carbon monoxide suppresses bleomycin-induced lung fibrosis. *Am J Pathol*. 2005;166:27–37.
49. Otterbein LE, Otterbein SL, Ifedigbo E, Liu F, Morse DE, Fearns C, Ulevitch RJ, Knicklebein R, Flavell RA, Choi AM. MKK3 mitogen activated protein kinase pathway mediates carbon monoxide–induced protection against oxidant-induced lung injury. *Am J Pathol*. 2003; 163:2555–2563.
50. NRC Committee on Energy Futures and Air Pollution in Urban China and the United States. *Energy Futures and Urban Air Pollution: Challenges for China and the United States*. Washington, DC: National Academies Press; 2007.

CLINICAL PERSPECTIVE

With growing traffic in many urban centers, the health impacts of traffic-related air pollution are a current public health concern. This national study of 126 US urban counties during 1999–2005 examines whether exposure to carbon monoxide (CO) on the same day and previous few days increases risk of cardiovascular disease (CVD) hospitalizations for an older population based on >9.3 million Medicare enrollees aged ≥65 years. Our findings indicate that higher levels of CO exposure are associated with an increased risk of CVD hospitalizations on the same day for multiple cause-specific CVD outcomes (ischemic heart disease, heart rhythm disturbances, heart failure, cerebrovascular disease, and total CVD admissions). Although it is not possible to fully disentangle the effects of CO and of other air pollutants produced by traffic, the association between CO and CVD hospital admissions remained after adjustment for other traffic-related pollutants: NO_2, fine particulate matter (with aerodynamic diameter ≤2.5 μm) total mass, and elemental carbon. The risk persisted even at low CO levels <1 ppm, which are well below the current US health-based regulatory standard. This study provides one of the first population-based investigations of the health effects of current low ambient CO levels and indicates that exposure to current CO levels may still pose a threat to public health, particularly for persons with CVD. It adds to other research showing that air pollution harms the health of people with CVD.

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

Circulation

American Heart Association®

Emergency Hospital Admissions for Cardiovascular Diseases and Ambient Levels of Carbon Monoxide: Results for 126 United States Urban Counties, 1999–2005

Michelle L. Bell, Roger D. Peng, Francesca Dominici and Jonathan M. Samet

Circulation. 2009;120:949-955; originally published online August 31, 2009;
doi: 10.1161/CIRCULATIONAHA.109.851113
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/120/11/949

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2009/08/31/CIRCULATIONAHA.109.851113.DC1.html

Downloaded from http://circ.ahajournals.org/ by guest on January 6, 2017

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/

SUPPLEMENTAL MATERIAL: Emergency Hospital Admissions for Cardiovascular Diseases and Ambient Levels of Carbon Monoxide: Results for 126 U.S. Urban Counties, 1999-2005

Table I. Summary statistics of county-specific pollution data for 126 U.S. counties (1999 to 2005)

Note: Pollutant data were averaged across monitors to protect against the influence of outliers, as was conducted in previous research. A 10% trimmed mean was used to average across monitors after correction for yearly averages for each monitor. After taking the trimmed mean, the median of the yearly averages was added back to the time series. As a result, it is possible for the time series of pollutant values to contain some negative values. However, because time-series analysis depends only on the data's temporal variation, the presence of these values should not directly influence results.

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Jefferson, AL	4.3	2.7	0.1 to 36.9	3.3	NA	NA	NA	NA	15.6	13.6	-3.1 to 69.3	10.9
Maricopa, AZ	3.5	3.2	0.5 to 18.4	2.7	23.3	22.6	2.1 to 64.9	11.9	NA	NA	NA	NA
Pima, AZ	2.5	2.3	0.5 to 10.6	1.6	16.6	15.9	3.1 to 34.5	9.9	NA	NA	NA	NA
Pulaski, AR	1.4	1.2	0.0 to 6.7	1.1	14.6	13.8	1.0 to 58.7	7.4	14.3	13.0	1.6 to 48.6	9.0
Alameda, CA	1.6	1.2	0.3 to 7.7	1.4	17.9	17.1	3.3 to 61.2	11.3	NA	NA	NA	NA
Contra Costa, CA	1.3	1	0.3 to 7.8	1	13.0	12.1	2.6 to 38.9	7.6	NA	NA	NA	NA
Fresno, CA	1.7	1.2	0.2 to 11.9	1.5	15.7	14.9	3.3 to 47.9	8.4	20.0	13.3	-7.0 to 149.0	15.8
Kern, CA	1.6	1.3	0.2 to 10.1	1.1	13.9	13.2	2.1 to 37.6	6.5	16.2	10.9	-3.0 to 149.0	11.8
Los Angeles, CA	3.5	2.7	0.6 to 19.0	3	26.7	25.7	5.8 to 66.4	13.1	18.9	16.4	1.9 to 86.9	11.8
Riverside, CA	2.1	1.9	0.4 to 8.8	1.6	17.9	16.9	0.9 to 59.5	10.9	20.4	17.6	-6.1 to 112.7	16.3
Sacramento, CA	1.8	1.4	0.2 to 10.0	1.5	14.1	13.1	1.9 to 49.3	8.0	12.5	9.0	-2.1 to 109.3	8.2
San Bernardino, CA	1.6	1.4	0.2 to 10.3	1.1	24.0	24.0	3.7 to 61.6	10.9	NA	NA	NA	NA
San Diego, CA	2.7	2.2	0.4 to 12.7	2.2	19.9	17.8	5.2 to 56.7	11.4	14.2	12.5	-1.4 to 170.5	7.9

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
San Francisco, CA	1.5	1.3	0.4 to 8.6	0.8	15.2	12.8	-0.5 to 55.6	15.0	NA	NA	NA	NA
San Joaquin, CA	1.4	1	0.2 to 11.3	0.9	13.3	12.7	-0.6 to 50.4	8.8	NA	NA	NA	NA
San Mateo, CA	1.6	1.2	0.0 to 9.8	1.4	16.5	15.4	1.9 to 63.9	11.9	NA	NA	NA	NA
Santa Clara, CA	1.7	1.2	0.1 to 8.8	1.4	22.5	20.9	4.1 to 86.0	13.0	NA	NA	NA	NA
Stanislaus, CA	1.2	0.8	0.2 to 11.4	1	16.6	15.5	4.3 to 58.2	8.7	NA	NA	NA	NA
Adams, CO	1.4	1.2	0.2 to 6.4	1.1	20.3	19.6	0.0 to 62.2	15.5	NA	NA	NA	NA
Denver, CO	2.4	2.1	0.5 to 17.1	1.6	32.6	32.5	0.9 to 91.9	13.6	10.1	8.8	-0.1 to 58.5	4.7
Fairfield, CT	1.6	1.4	0.1 to 7.6	0.8	17.3	16.2	0.0 to 65.6	10.8	NA	NA	NA	NA
Hartford, CT	2.9	2.5	0.3 to 18.0	1.6	17.1	15.3	0.0 to 57.0	10.8	12.0	9.9	1.9 to 68.1	8.7
New Haven, CT	1.1	1	0.2 to 4.4	0.5	21.0	19.9	0.2 to 62.2	11.7	12.6	10.5	-4.1 to 78.8	9.9
New Castle, DE	1	0.86	0.0 to 4.7	0.6	18.0	17.3	-3.5 to 174.0	11.5	14.9	12.9	0.9 to 114.6	10.3
District of Columbia	2	1.7	0.2 to 10.9	1	22.1	21.1	4.5 to 58.3	10.3	15.2	13.5	0.0 to 61.5	10.0
Broward, FL	1.9	1.7	0.4 to 8.0	1	8.8	7.9	-0.3 to 38.0	7.1	8.4	7.5	0.5 to 66.6	4.7
Duval, FL	1.5	1.3	0.3 to 8.7	1	14.4	13.6	0.0 to 76.9	7.4	10.7	9.6	0.6 to 49.4	6.3
Hillsborough, FL	2.1	2	0.2 to 9.0	1.1	7.2	6.4	-2.1 to 30.6	5.1	11.6	10.6	1.7 to 46.3	6.1
Miami-Dade, FL	1.9	1.7	0.4 to 11.9	1.1	10.4	9.0	1.0 to 54.7	7.2	8.6	7.7	1.1 to 53.8	4.7
Orange, FL	1.4	1.3	0.1 to 8.6	0.7	11.1	10.0	0.2 to 42.3	6.7	10.4	9.4	1.9 to 56.2	5.6
Palm Beach, FL	1.3	1.04	0.0 to 6.6	1.4	13.9	14.2	1.1 to 32.7	6.6	7.9	7.1	-1.0 to 48.7	4.4
Pinellas, FL	1.6	1.5	0.3 to 5.8	0.7	11.2	10.1	0.1 to 39.5	8.8	10.4	9.4	0.6 to 62.5	5.8
DeKalb, GA	1.2	1	0.0 to 7.7	1	16.3	15.1	0.5 to 54.7	10.7	16.9	15.5	0.8 to 74.6	10.0
Fulton, GA	1.4	1.3	0.0 to 6.1	0.9	20.0	18.5	1.0 to 71.3	13.8	17.2	15.7	-0.6 to 140.0	9.7
Honolulu, HI	1.3	1.2	0.3 to 4.6	0.6	4.0	3.8	0.0 to 11.1	1.9	4.3	3.6	1.0 to 88.0	2.0
Ada, ID	2.1	1.9	0.3 to 10.7	1.1	NA	NA	NA	NA	NA	NA	NA	NA

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Cook, IL	2.3	2.3	0.5 to 6.8	1.2	22.5	22.0	3.9 to 54.0	10.0	15.9	14.3	1.5 to 61.0	10.6
Winnebago, IL	1.5	1.4	0.1 to 6.9	1	NA	NA	NA	NA	NA	NA	NA	NA
Allen, IN	1.4	1.2	0.2 to 6.5	0.9	NA	NA	NA	NA	NA	NA	NA	NA
Marion, IN	1.7	1.5	0.3 to 16.6	0.9	16.7	16.2	2.0 to 44.0	8.7	16.4	14.9	2.9 to 60.3	10.3
Polk, IA	1.5	1.3	0.2 to 18.4	0.7	NA	NA	NA	NA	10.5	8.8	0.9 to 48.8	7.8
Sedgwick, KS	1.5	1.2	0.0 to 16.2	1.2	NA	NA	NA	NA	NA	NA	NA	NA
Jefferson, KY	1.8	1.5	0.0 to 13.2	1.1	16.5	15.9	2.4 to 38.7	7.9	16.4	14.6	2.1 to 67.5	10.4
East Baton Rouge, LA	1.2	1	0.0 to 7.0	0.7	12.2	11.5	1.1 to 37.5	5.1	13.3	12.0	-1.1 to 47.7	7.4
Orleans, LA	1.6	1.5	0.0 to 6.8	0.8	17.9	17.0	0.1 to 48.3	9.5	13.7	12.2	0.7 to 45.8	7.1
Baltimore City, MD	1.2	0.9	0.0 to 14.9	0.7	21.3	20.5	-0.6 to 59.1	9.8	15.9	13.8	0.3 to 66.5	11.4
Hampden, MA	1.4	1.2	0.0 to 11.2	1.2	12.4	11.0	-3.6 to 49.8	9.0	13.0	10.8	0.7 to 67.1	8.8
Middlesex, MA	0.9	0.7	0.0 to 8.6	0.6	NA	NA	NA	NA	NA	NA	NA	NA
Suffolk, MA	1.2	1	0.0 to 9.1	0.8	21.2	20.4	5.1 to 49.2	8.5	13.5	11.7	-0.1 to 63.3	8.3
Worchester, MA	1.1	1	0.0 to 9.5	0.6	16.6	15.5	1.5 to 51.3	10.4	NA	NA	NA	NA
Kent, MI	0.9	0.7	0.0 to 6.0	0.5	NA	NA	NA	NA	13.5	11.3	1.3 to 75.3	11.1
Macomb, MI	0.7	0.5	0.0 to 5.2	0.6	NA	NA	NA	NA	NA	NA	NA	NA
Oakland, MI	0.8	0.6	0.0 to 9.8	0.7	NA	NA	NA	NA	NA	NA	NA	NA
Wayne, MI	1.4	1.2	0.2 to 8.2	1	19.9	19.0	0.9 to 90.9	10.4	15.6	13.6	1.8 to 80.3	11.9
Dakota, MN	0.4	0.4	0.0 to 1.7	0.3	10.0	9.4	0.0 to 30.2	5.5	NA	NA	NA	NA
Hennepin, MN	1.2	1	0.0 to 12.3	1	NA	NA	NA	NA	NA	NA	NA	NA
Ramsey, MN	1.9	1.8	0.0 to 11.4	1.4	NA	NA	NA	NA	NA	NA	NA	NA
St. Louis, MN	0.9	0.8	0.0 to 6.4	0.7	NA	NA	NA	NA	NA	NA	NA	NA
Hinds, MS	0.9	0.6	0.0 to 8.6	0.7	NA	NA	NA	NA	NA	NA	NA	NA

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Jackson, MO	1.5	1.3	0.0 to 15.0	1.2	NA	NA	NA	NA	12.6	11.4	1.8 to 55.9	8.2
St. Louis, MO	1.1	1	0.0 to 6.8	0.6	15.2	14.4	1.1 to 38.2	8.1	NA	NA	NA	NA
St. Louis City, MO	1.4	1.1	0.1 to 12.0	0.9	20.9	20.1	4.1 to 53.3	8.9	15.0	13.7	2.2 to 57.9	9.7
Clark, NV	3.2	2.95	0.4 to 10.4	2.3	8.7	8.3	-3.1 to 26.7	6.2	8.3	7.6	-1.9 to 53.5	4.5
Washoe, NV	2.7	2.45	0.3 to 10.0	1.9	NA	NA	NA	NA	NA	NA	NA	NA
Hillsborough, NH	1.6	1.2	0.0 to 15.0	1.1	11.8	10.4	-2.6 to 47.1	7.4	NA	NA	NA	NA
Bergen, NJ	1.8	1.6	0.2 to 9.5	1.1	NA	NA	NA	NA	NA	NA	NA	NA
Camden, NJ	1	0.8	0.1 to 8.2	0.5	20.6	19.5	3.0 to 67.8	12.0	NA	NA	NA	NA
Hudson, NJ	2.2	2	0.2 to 10.5	1.2	24.6	23.6	3.2 to 72.5	13.0	NA	NA	NA	NA
Middlesex, NJ	1.4	1.3	0.2 to 6.0	0.8	17.9	16.3	3.0 to 64.0	10.9	NA	NA	NA	NA
Morris, NJ	1.5	1.3	0.2 to 9.9	1	11.1	9.1	1.1 to 41.4	8.3	NA	NA	NA	NA
Union, NJ	2.1	1.8	0.3 to 9.8	1.4	36.7	35.9	6.0 to 87.9	16.5	13.8	11.7	-0.5 to 85.7	11.0
Bernalillo, NM	2.1	1.8	0.2 to 13.9	1.6	12.1	11.1	-3.6 to 37.3	9.3	7.1	6.1	1.5 to 46.8	3.3
Albany, NY	0.6	0.6	0.0 to 4.3	0.3	NA	NA	NA	NA	NA	NA	NA	NA
Bronx, NY	1.1	0.9	0.1 to 6.2	0.6	31.6	30.6	10.8 to 75.0	11.6	15.2	12.8	0.2 to 79.7	10.7
Erie, NY	0.9	0.8	0.0 to 5.4	0.5	17.1	16.1	2.8 to 47.0	9.5	NA	NA	NA	NA
Kings, NY	2	1.8	0.4 to 8.5	1	NA	NA	NA	NA	NA	NA	NA	NA
Monroe, NY	1	0.8	0.2 to 6.2	0.5	NA	NA	NA	NA	NA	NA	NA	NA
New York, NY	1.9	1.8	0.3 to 9.3	1.3	37.0	36.5	-0.6 to 82.1	11.4	NA	NA	NA	NA
Niagara, NY	0.6	0.5	0.0 to 7.0	0.4	NA	NA	NA	NA	NA	NA	NA	NA
Onondaga, NY	1	0.9	0.1 to 6.1	0.5	NA	NA	NA	NA	NA	NA	NA	NA
Queens, NY	1	0.9	0.0 to 13.4	0.6	27.4	26.4	6.0 to 66.4	12.4	NA	NA	NA	NA
Suffolk, NY	0.6	0.3	0.0 to 3.9	0.7	15.5	14.1	0.0 to 52.6	9.5	NA	NA	NA	NA

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Forsyth, NC	1.7	1.5	0.3 to 6.3	0.9	14.5	13.4	0.3 to 47.9	9.0	14.6	13.2	0.5 to 68.2	9.8
Mecklenburg, NC	1.5	1.2	0.1 to 14.1	1.1	17.5	16.6	3.9 to 56.1	9.6	15.3	14.2	2.2 to 83.8	9.1
Wake, NC	1.6	1.3	0.2 to 7.0	1.5	NA	NA	NA	NA	14.0	12.8	2.0 to 54.4	8.9
Cuyahoga, OH	2.1	1.8	0.2 to 21.5	1.2	17.6	16.7	0.9 to 48.3	9.4	16.8	14.8	0.3 to 63.0	12.4
Franklin, OH	1.2	1.1	0.3 to 11.7	0.6	NA	NA	NA	NA	16.4	14.8	1.4 to 157.1	10.0
Hamilton, OH	1.3	1.2	0.1 to 8.4	0.7	21.3	21.0	3.8 to 46.5	8.6	16.7	15.0	2.6 to 54.4	10.2
Lake, OH	0.9	0.81	0.0 to 3.4	0.5	NA	NA	NA	NA	NA	NA	NA	NA
Montgomery, OH	1.1	0.9	0.2 to 5.9	0.6	NA	NA	NA	NA	16.2	14.7	2.1 to 54.2	10.2
Stark, OH	0.9	0.8	0.0 to 5.5	0.7	NA	NA	NA	NA	NA	NA	NA	NA
Summit, OH	1.4	1.3	0.0 to 10.3	0.9	NA	NA	NA	NA	16.1	14.4	2.5 to 56.6	10.4
Oklahoma, OK	1.3	1	0.1 to 7.9	1	11.1	9.9	1.6 to 39.5	6.9	10.3	9.1	1.2 to 44.9	6.8
Tulsa, OK	1.4	1.1	0.1 to 9.1	0.9	10.6	10.0	1.0 to 38.6	7.3	11.9	10.6	1.6 to 35.4	7.6
Lane, OR	2.1	1.9	0.4 to 8.0	1.2	NA	NA	NA	NA	8.3	6.0	-5.0 to 64.1	7.0
Multnomah, OR	2.4	2.2	0.4 to 19.4	1.5	NA	NA	NA	NA	NA	NA	NA	NA
Allegheny, PA	1.3	1.2	0.0 to 7.3	0.9	20.7	19.8	3.5 to 54.4	10.0	15.2	12.8	-2.9 to 69.9	12.3
Berks, PA	0.9	0.8	0.0 to 5.5	0.5	19.0	18.2	3.7 to 65.9	8.5	NA	NA	NA	NA
Dauphin, PA	0.8	0.7	0.0 to 5.4	0.5	16.6	15.4	0.9 to 65.0	9.7	15.6	13.6	1.5 to 70.9	12.0
Erie, PA	1.4	0.8	0.0 to 12.5	0.9	12.5	11.8	0.0 to 42.6	7.1	NA	NA	NA	NA
Lackawanna, PA	0.6	0.5	0.0 to 5.2	0.7	14.1	13.0	0.3 to 43.7	9.0	12.3	10.2	0.6 to 61.8	10.0
Lancaster, PA	0.7	0.6	0.0 to 3.7	0.6	14.2	13.1	0.8 to 50.6	8.5	NA	NA	NA	NA
Northampton, PA	0.6	0.5	0.0 to 15.7	0.6	15.2	13.9	1.5 to 57.0	9.0	14.2	11.7	1.0 to 75.2	11.2
Philadelphia, PA	1.7	1.5	0.4 to 12.3	1	27.0	26.2	6.7 to 59.5	10.9	14.4	12.5	0.5 to 91.1	10.4
York, PA	0.7	0.6	0.0 to 5.3	0.7	18.0	17.0	1.8 to 61.8	10.4	NA	NA	NA	NA

County	CO Daily 1-Hour Maximum (ppm)				NO_2 Daily Mean (ppb)				$PM_{2.5}$ Daily Mean ($\mu g/m^3$)			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Providence, RI	1.6	1.4	0.3 to 12.7	0.9	15.1	14.0	-2.7 to 49.8	8.9	12.1	10.1	1.6 to 75.3	7.4
Charleston, SC	1	0.8	0.0 to 6.5	0.7	7.5	6.9	-3.0 to 27.8	5.6	12.1	11.0	1.7 to 44.3	7.4
Greenville, SC	1.2	0.9	0.0 to 7.0	1	13.9	12.6	-1.2 to 50.6	9.5	12.9	11.9	-1.2 to 60.9	9.4
Richland, SC	1.3	1.1	0.0 to 5.3	0.9	2.3	1.7	-12.0 to 20.3	4.5	NA	NA	NA	NA
Davidson, TN	2.2	1.9	0.4 to 7.9	1.3	16.2	15.5	0.9 to 74.9	10.1	14.4	13.2	0.6 to 45.8	8.7
Shelby, TN	1.8	1.5	0.3 to 11.7	1.2	12.3	11.1	-9.2 to 57.9	11.1	14.1	12.8	-0.5 to 47.8	8.6
Bexar, TX	1.1	0.9	0.0 to 7.2	0.6	7.4	6.4	-0.7 to 31.4	4.4	NA	NA	NA	NA
Cameron, TX	0.8	0.6	0.0 to 5.5	0.4	NA	NA	NA	NA	NA	NA	NA	NA
Dallas, TX	0.8	0.6	0.0 to 4.6	0.5	15.1	13.8	0.3 to 46.2	9.1	12.7	11.4	2.2 to 51.3	7.7
El Paso, TX	3.5	2.3	0.4 to 19.9	3.2	15.8	14.6	1.8 to 44.0	9.3	NA	NA	NA	NA
Harris, TX	1.5	1.2	0.3 to 7.8	0.9	13.7	12.9	-0.4 to 36.9	8.0	12.5	11.5	0.6 to 55.3	6.9
Tarrant, TX	1	0.8	0.1 to 8.1	0.7	12.2	11.1	-0.7 to 41.9	8.9	12.1	11.1	1.8 to 51.4	7.3
Travis, TX	0.5	0.4	0.0 to 2.4	0.3	4.3	3.5	-1.1 to 32.1	3.3	NA	NA	NA	NA
Salt Lake, UT	2.2	1.7	0.3 to 11.3	1.7	24.6	22.7	3.1 to 73.3	13.8	11.7	7.6	0.3 to 94.2	6.4
Fairfax, VI	1.2	1.1	0.3 to 9.7	0.6	18.5	17.5	3.7 to 49.3	8.5	14.1	12.5	1.3 to 54.7	9.1
Norfolk City, VI	1.2	0.9	0.0 to 9.9	0.9	16.7	16.2	0.3 to 40.1	8.7	NA	NA	NA	NA
Clark, WA	2.3	1.9	0.4 to 13.5	1.5	NA	NA	NA	NA	NA	NA	NA	NA
King, WA	2.7	2.4	0.8 to 16.1	1.3	18.8	18.5	2.2 to 49.4	9.5	8.8	7.3	0.3 to 54.9	6.1
Pierce, WA	1.9	1.6	0.0 to 13.7	1.4	NA	NA	NA	NA	NA	NA	NA	NA
Spokane, WA	3.3	3.1	0.7 to 12.3	1.8	NA	NA	NA	NA	NA	NA	NA	NA
Milwaukee, WI	1.1	0.9	0.1 to 10.8	0.7	16.8	16.0	1.1 to 49.1	10.0	NA	NA	NA	NA

Table II. Summary statistics of county-specific hospitalization data for 126 U.S. counties (1999 to 2005)

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Jefferson, AL	13.5	13.0	0.0 to 29.0	7.0	61,770	60,960	59,890 to 64,140	2,880
Maricopa, AZ	30.1	30.0	0.0 to 59.0	10.0	187,800	185,300	164,200 to 220,700	39,000
Pima, AZ	10.1	10.0	0.0 to 24.0	4.0	64,540	67,590	51,060 to 76,000	19,260
Pulaski, AR	7.4	7.0	0.0 to 19.0	4.0	38,450	40,450	33,530 to 42,250	5,640
Alameda, CA	12.5	12.0	0.0 to 28.0	5.0	66,520	67,620	61,100 to 72,630	9,440
Contra Costa, CA	7.8	8.0	0.0 to 20.0	4.0	49,300	51,760	42,510 to 55,880	11,180
Fresno, CA	9.8	10.0	0.0 to 28.0	5.0	53,760	54,780	47,710 to 58,260	8,210
Kern, CA	6.6	6.0	0.0 to 19.0	3.0	33,690	33,580	29,820 to 38,410	6,410
Los Angeles, CA	87.6	89.0	1.0 to 150.0	27.0	476,400	476,700	438,200 to 520,500	51,800
Riverside, CA	15.6	15.0	0.0 to 34.0	7.0	83,820	84,220	67,340 to 102,100	26,120
Sacramento, CA	8.9	9.0	0.0 to 22.0	4.0	57,910	59,490	49,590 to 66,550	13,930
San Bernardino, CA	11.4	11.0	1.0 to 31.0	5.0	57,970	58,160	47,340 to 69,530	17,160
San Diego, CA	22.5	22.0	0.0 to 43.0	8.0	143,200	146,500	122,700 to 165,700	35,400
San Francisco, CA	8.8	9.0	0.0 to 19.0	5.0	58,160	59,080	54,420 to 62,620	6,750
San Joaquin, CA	7.1	7.0	0.0 to 21.0	4.0	36,060	34,800	29,140 to 43,490	13,620
San Mateo, CA	6.5	6.0	0.0 to 17.0	3.0	45,000	47,520	36,560 to 51,160	11,680
Santa Clara, CA	11.1	11.0	0.0 to 27.0	4.0	80,070	80,090	69,910 to 92,010	15,010
Stanislaus, CA	3.9	4.0	0.0 to 12.0	3.0	22,730	23,690	19,140 to 26,400	6,310
Adams, CO	2.0	2.0	0.0 to 10.0	2.0	13,250	13,580	11,670 to 14,820	2,320
Denver, CO	4.7	5.0	0.0 to 15.0	3.0	29,920	30,460	28,360 to 31,370	2,140

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Fairfield, CT	16.8	17.0	1.0 to 36.0	7.0	91,930	94,100	83,120 to 97,540	11,510
Hartford, CT	18.3	18.0	0.0 to 39.0	7.0	104,000	113,400	86,770 to 114,900	26,770
New Haven, CT	18.7	18.0	1.0 to 38.0	7.0	92,950	99,580	80,370 to 101,000	19,180
New Castle, DE	10.9	11.0	0.0 to 28.0	5.0	54,000	54,550	50,620 to 56,660	4,020
District of Columbia	11.1	11.0	0.0 to 27.0	6.0	54,500	54,630	52,420 to 55,880	1,170
Broward, FL	25.0	25.0	0.0 to 51.0	8.0	111,000	110,600	107,900 to 115,100	3,400
Duval, FL	14.0	14.0	0.0 to 31.0	7.0	62,310	61,590	47,440 to 75,120	25,230
Hillsborough, FL	15.9	16.0	2.0 to 35.0	7.0	78,150	81,860	67,020 to 87,410	16,210
Miami-Dade, FL	33.0	33.0	1.0 to 59.0	11.0	135,100	132,800	130,800 to 143,600	8,200
Orange, FL	16.1	16.0	1.0 to 37.0	8.0	67,710	74,730	49,420 to 80,280	26,340
Palm Beach, FL	34.3	34.0	0.0 to 68.0	13.0	154,900	157,800	139,600 to 166,400	20,700
Pinellas, FL	23.5	23.0	1.0 to 49.0	8.0	120,300	116,800	111,800 to 130,700	12,900
DeKalb, GA	5.4	5.0	0.0 to 15.0	3.0	41,040	41,240	37,090 to 45,730	5,860
Fulton, GA	9.0	9.0	0.0 to 22.0	4.0	52,280	52,280	50,160 to 55,370	2,970
Honolulu, HI	8.7	8.0	0.0 to 20.0	4.0	70,650	70,350	67,080 to 75,510	3,030
Ada, ID	2.7	3.0	0.0 to 10.0	3.0	23,400	23,340	21,800 to 25,210	1,370
Cook, IL	113.2	114.0	8.0 to 182.0	30.0	481,000	492,000	449,500 to 511,600	55,000
Winnebago, IL	6.6	6.0	0.0 to 18.0	3.0	33,680	33,880	32,140 to 34,500	790
Allen, IN	6.2	6.0	0.0 to 17.0	4.0	36,240	36,400	35,060 to 36,710	290
Marion, IN	15.4	15.0	0.0 to 31.0	6.0	84,550	84,820	82,500 to 86,360	2,070
Polk, IA	6.7	7.0	0.0 to 17.0	3.0	39,620	39,740	38,560 to 40,340	740
Sedgwick, KS	8.5	8.0	0.0 to 22.0	5.0	47,600	48,850	44,640 to 50,090	4,340
Jefferson, KY	15.6	15.0	0.0 to 32.0	5.0	82,320	84,710	78,080 to 85,650	6,580

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
East Baton Rouge, LA	5.5	5.0	0.0 to 15.0	3.0	29,140	31,380	24,050 to 34,370	8,170
Orleans, LA	7.0	7.0	0.0 to 21.0	4.0	30,230	31,710	15,890 to 36,560	2,460
Baltimore City, MD	18.8	19.0	1.0 to 41.0	7.0	69,080	67,750	62,690 to 76,220	6,850
Hampden, MA	9.6	9.0	0.0 to 21.0	5.0	47,210	47,230	46,790 to 47,900	340
Middlesex, MA	27.6	28.0	1.0 to 54.0	9.0	127,700	125,200	123,100 to 135,200	8,800
Suffolk, MA	12.4	12.0	1.0 to 29.0	5.0	55,750	54,320	53,800 to 58,300	3,820
Worchester, MA	11.2	11.0	0.0 to 28.0	5.0	49,170	48,210	47,810 to 51,850	2,610
Kent, MI	10.3	10.0	0.0 to 25.0	5.0	58,990	58,820	58,200 to 60,260	980
Macomb, MI	27.1	27.0	0.0 to 49.0	10.0	99,220	102,100	93,540 to 104,700	9,750
Oakland, MI	30.5	30.0	1.0 to 56.0	11.0	126,100	128,800	118,700 to 134,500	11,800
Wayne, MI	60.4	61.0	1.0 to 96.0	19.0	212,300	213,800	205,300 to 217,700	4,300
Dakota, MN	2.4	2.0	0.0 to 9.0	2.0	16,980	17,160	15,630 to 17,910	1,040
Hennepin, MN	11.6	11.0	0.0 to 27.0	5.0	78,270	78,690	74,720 to 80,920	2,730
Ramsey, MN	6.9	7.0	0.0 to 21.0	4.0	43,830	44,040	42,190 to 44,850	1,220
St. Louis, MN	5.6	5.0	0.0 to 17.0	3.0	29,090	29,340	26,370 to 30,770	1,890
Hinds, MS	4.4	4.0	0.0 to 13.0	3.0	25,230	25,300	23,910 to 26,070	620
Jackson, MO	9.8	10.0	0.0 to 22.0	5.0	56,230	54,790	52,900 to 59,960	5,920
St. Louis, MO	19.0	19.0	0.0 to 38.0	6.0	99,310	99,090	96,550 to 102,400	3,880
St. Louis City, MO	6.2	6.0	0.0 to 15.0	4.0	27,670	27,470	24,670 to 31,610	2,720
Clark, NV	13.6	13.0	1.0 to 33.0	5.0	86,820	87,000	72,070 to 102,200	17,360
Washoe, NV	3.4	3.0	0.0 to 11.0	3.0	28,030	27,520	24,040 to 33,310	5,870
Hillsborough, NH	6.0	6.0	0.0 to 17.0	4.0	37,130	38,220	29,040 to 40,160	2,260

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Bergen, NJ	22.0	22.0	0.0 to 48.0	8.0	111,500	112,300	107,500 to 114,100	3,700
Camden, NJ	11.8	12.0	0.0 to 28.0	5.0	47,250	48,800	42,520 to 50,730	6,980
Hudson, NJ	13.2	13.0	0.0 to 33.0	6.0	49,970	50,020	48,700 to 50,850	380
Middlesex, NJ	17.3	17.0	0.0 to 35.0	7.0	73,920	76,870	67,250 to 77,770	7,750
Morris, NJ	8.6	8.0	0.0 to 20.0	5.0	49,530	50,600	44,420 to 54,090	6,630
Union, NJ	12.8	12.0	0.0 to 27.0	6.0	59,020	59,330	57,060 to 60,180	820
Bernalillo, NM	3.7	3.0	0.0 to 14.0	3.0	35,610	36,520	31,710 to 38,560	4,000
Albany, NY	6.0	6.0	0.0 to 18.0	4.0	32,110	31,960	30,530 to 34,120	2,080
Bronx, NY	19.1	19.0	2.0 to 40.0	8.0	76,940	77,090	73,020 to 81,890	4,000
Erie, NY	19.5	19.0	2.0 to 42.0	7.0	91,270	92,330	78,890 to 103,700	14,560
Kings, NY	38.5	38.0	1.0 to 75.0	14.0	154,400	149,100	140,400 to 176,000	22,700
Monroe, NY	9.1	9.0	0.0 to 22.0	4.0	41,370	40,700	38,690 to 45,560	3,130
New York, NY	24.3	24.0	0.0 to 50.0	10.0	140,900	138,800	137,400 to 150,300	5,700
Niagara, NY	5.8	6.0	0.0 to 17.0	3.0	22,880	22,810	20,470 to 25,730	2,890
Onondaga, NY	9.8	10.0	0.0 to 25.0	5.0	59,800	59,660	58,390 to 60,890	1,100
Queens, NY	33.4	34.0	1.0 to 62.0	12.0	155,800	155,300	147,800 to 166,200	6,700
Suffolk, NY	32.7	32.0	0.0 to 65.0	15.0	133,100	137,000	110,300 to 148,300	29,700
Forsyth, NC	5.0	5.0	0.0 to 14.0	3.0	26,830	26,530	25,890 to 28,190	1,320
Mecklenburg, NC	12.0	12.0	0.0 to 26.0	6.0	57,990	58,060	55,190 to 60,580	2,140
Wake, NC	8.4	8.0	0.0 to 22.0	4.0	48,280	48,470	42,240 to 53,930	6,850
Cuyahoga, OH	37.2	37.0	2.0 to 74.0	12.0	148,500	149,400	144,900 to 151,500	3,800
Franklin, OH	17.3	17.0	0.0 to 37.0	7.0	81,830	83,990	75,030 to 87,130	9,570
Hamilton, OH	17.3	17.0	3.0 to 41.0	7.0	84,360	84,360	80,740 to 87,280	4,330

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Lake, OH	5.3	5.0	0.0 to 16.0	4.0	25,520	26,730	21,340 to 28,170	5,640
Montgomery, OH	11.0	11.0	0.0 to 26.0	5.0	63,390	63,620	60,810 to 65,990	2,840
Stark, OH	10.6	10.0	1.0 to 24.0	5.0	45,180	44,730	44,230 to 46,790	1,470
Summit, OH	13.2	13.0	1.0 to 30.0	6.0	53,790	53,680	53,080 to 55,450	740
Oklahoma, OK	13.6	13.0	0.0 to 31.0	6.0	67,240	67,440	63,940 to 70,730	4,930
Tulsa, OK	10.1	10.0	0.0 to 23.0	4.0	50,110	49,590	48,740 to 52,480	2,230
Lane, OR	3.2	3.0	0.0 to 11.0	2.0	23,690	24,030	20,910 to 26,630	3,340
Multnomah, OR	4.2	4.0	0.0 to 14.0	3.0	31,190	31,630	28,600 to 33,830	3,750
Allegheny, PA	33.6	33.0	3.0 to 66.0	13.0	122,500	122,100	98,160 to 145,600	23,300
Berks, PA	10.6	10.0	0.0 to 27.0	5.0	46,550	48,250	41,580 to 48,890	6,430
Dauphin, PA	6.2	6.0	0.0 to 19.0	4.0	28,590	29,340	26,640 to 29,830	2,770
Erie, PA	5.9	6.0	0.0 to 16.0	4.0	29,110	29,220	28,520 to 29,540	480
Lackawanna, PA	7.8	8.0	0.0 to 20.0	5.0	30,500	30,170	28,960 to 32,360	1,870
Lancaster, PA	11.3	11.0	0.0 to 29.0	6.0	61,150	63,820	52,260 to 65,980	12,280
Northampton, PA	9.3	9.0	0.0 to 23.0	5.0	35,960	38,160	32,320 to 38,770	5,560
Philadelphia, PA	31.0	30.0	0.0 to 61.0	11.0	103,300	99,810	93,910 to 120,600	13,390
York, PA	9.1	9.0	0.0 to 23.0	4.0	48,790	50,710	41,890 to 52,740	9,180
Providence, RI	10.8	11.0	1.0 to 23.0	5.0	48,280	48,020	45,120 to 52,350	4,300
Charleston, SC	6.0	6.0	0.0 to 18.0	4.0	35,520	35,270	33,770 to 38,090	1,610
Greenville, SC	9.3	9.0	0.0 to 23.0	5.0	44,740	44,790	42,970 to 46,840	1,410
Richland, SC	6.3	6.0	0.0 to 18.0	4.0	30,420	30,380	29,750 to 31,480	710
Davidson, TN	9.4	9.0	0.0 to 30.0	4.0	49,520	49,430	46,020 to 52,520	2,990
Shelby, TN	18.2	18.0	0.0 to 36.0	8.0	83,620	84,080	79,800 to 85,270	750

County	Total CVD Hospitalizations / Day				Study Subjects (Population at Risk) / Day			
	Mean	Median	Minimum to Maximum	IQR	Mean	Median	Minimum to Maximum	IQR
Bexar, TX	13.6	13.0	2.0 to 32.0	5.0	90,190	95,760	74,560 to 104,300	26,400
Cameron, TX	6.8	7.0	0.0 to 17.0	4.0	32,000	32,120	30,450 to 33,330	970
Dallas, TX	26.3	26.0	1.0 to 58.0	8.0	147,300	153,600	125,100 to 161,600	27,500
El Paso, TX	9.7	9.0	0.0 to 25.0	5.0	62,970	64,850	55,580 to 67,480	8,100
Harris, TX	40.6	40.0	2.0 to 73.0	15.0	204,600	214,200	162,200 to 228,500	55,700
Tarrant, TX	16.3	16.0	1.0 to 39.0	7.0	84,460	87,620	66,650 to 99,250	27,320
Travis, TX	8.5	8.0	0.0 to 21.0	5.0	51,140	52,220	44,200 to 56,380	7,540
Salt Lake, UT	7.8	8.0	0.0 to 19.0	4.0	67,280	66,980	65,010 to 70,160	2,210
Fairfax, VI	7.7	7.0	0.0 to 19.0	4.0	52,700	52,920	45,520 to 61,220	7,650
Norfolk City, VI	4.7	4.0	0.0 to 16.0	3.0	22,290	22,300	20,910 to 23,720	1,570
Clark, WA	2.8	3.0	0.0 to 9.0	2.0	18,260	17,980	16,220 to 21,210	3,240
King, WA	16.1	16.0	2.0 to 35.0	6.0	122,400	123,700	106,900 to 137,800	22,800
Pierce, WA	7.1	7.0	0.0 to 21.0	4.0	52,950	54,450	45,180 to 61,960	12,410
Spokane, WA	5.9	6.0	0.0 to 19.0	4.0	44,410	49,330	32,930 to 51,130	12,850
Milwaukee, WI	20.3	20.0	0.0 to 46.0	7.0	101,400	100,800	95,610 to 107,800	5,950

Table III. Correlation between daily levels of co-pollutants $PM_{2.5}$, EC, and NO_2

Pollutants	Average correlation	Number of counties	Average number of days included per county
$PM_{2.5}$ and NO_2	0.42	58	2292
$PM_{2.5}$ and EC	0.42	50	331
NO_2 and EC	0.61	62	323

Table IV. Percent increase in risk of cardiovascular hospital admissions per approximate IQR increase in the same day daily NO_2, $PM_{2.5}$, or EC $PM_{2.5}$ for those $\geq$65 years (1999-2005)

Note: The IQR increment is 9.4 ppb for NO_2, 9.8 $\mu g/m^3$ for $PM_{2.5}$, and 0.5 $\mu g/m^3$ for EC $PM_{2.5}$.

Pollutant:	*Co-pollutant adjustment:*	*Number of counties*	*Percent change in risk (95% posterior interval)*
NO_2	CO	92	1.34% (1.06, 1.62%)
	CO and $PM_{2.5}$	58	1.30% (0.87, 1.73%)
$PM_{2.5}$	CO	67	0.33% (0.08, 0.59%)
	CO and NO_2	58	-0.18% (-0.49, 0.14%)
EC	CO	81	0.23% (-0.39%, 0.85%)

Table V. Percent increase in risk of cardiovascular hospital admissions per 0.3 ppm increase in the same day 24-hour average CO for those ≥65 years (1999-2005), with and without adjustment for co-pollutants

Note: In order to aid comparison across identical datasets, effect estimates without co-pollutant adjustment were generated for the subset of data with co-pollutant data available. All pollutants (CO, NO_2 $PM_{2.5}$, EC) were based on same day levels (L0). The increment of CO approximates the IQR (see Table 1).

Co-pollutant adjustment:	*Number of counties*	*Percent change in risk (95% posterior interval)*
None, all days included	126	1.19% (1.03, 1.35%)
None, but days with NO_2 data available	92	1.28% (1.08, 1.48%)
NO_2	92	0.60% (0.36, 0.85%)
None, but days with $PM_{2.5}$ data available	67	1.15% (0.94, 1.36%)
$PM_{2.5}$	67	1.13% (0.90, 1.36%)
None, but days with NO_2 and $PM_{2.5}$ data available	58	1.32% (1.07, 1.57%)
NO_2 and $PM_{2.5}$	58	0.64% (0.32, 0.97%)
None, but days with EC data available	81	1.35 (0.74, 1.96)
EC	81	1.36 (0.62, 2.10)

Figure I. County-specific average daily 1-hour maximum CO and average CVD hospitalization rates

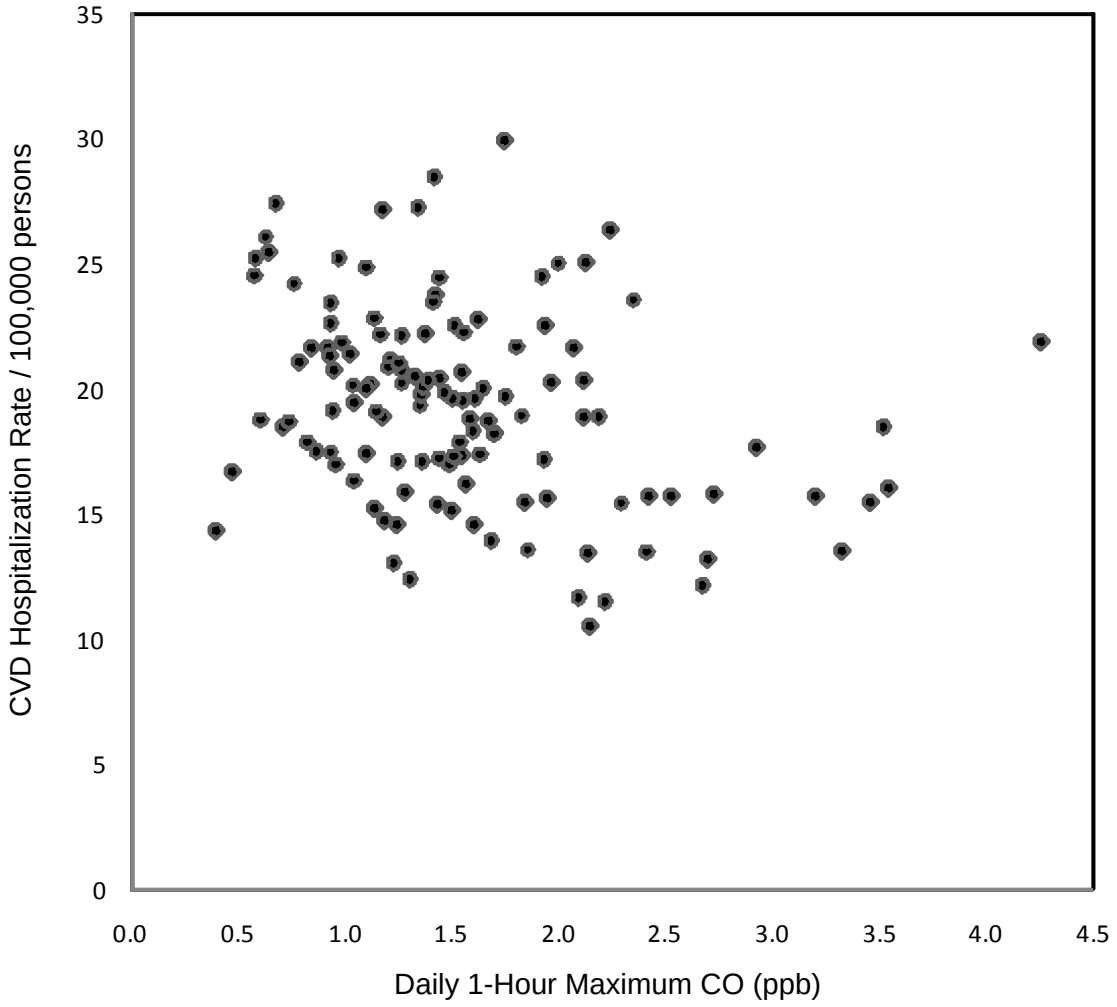


Figure II. Percent increase in risk of CVD hospital admissions per 1 ppm increase in same day 1-hour maximum CO for those ≥65 years (1999-2005), with and without adjustment for co-pollutants for 92 U.S. counties for adjustment by same day NO_2 (Figure IIa), for 67 counties for adjustment by same day $PM_{2.5}$ (Figure IIb), for 58 counties for adjustment by same day NO_2 and $PM_{2.5}$ (Figure IIc), and for 81 counties for adjustment by same day EC (Figures IId).

Note: Estimates without adjustment for co-pollutants (x-axis) were based on a subset of data with data available for that co-pollutant; estimates on the y-axis were adjusted for the co-pollutant. Each point represents a single county. The red point reflects the overall estimate; the red horizontal and vertical lines represent the 95% posterior intervals for the overall estimate. A point on the dashed diagonal line would reflect perfect agreement between results with and without adjustment by the co-pollutant. Not that the figures' axes have different scales.

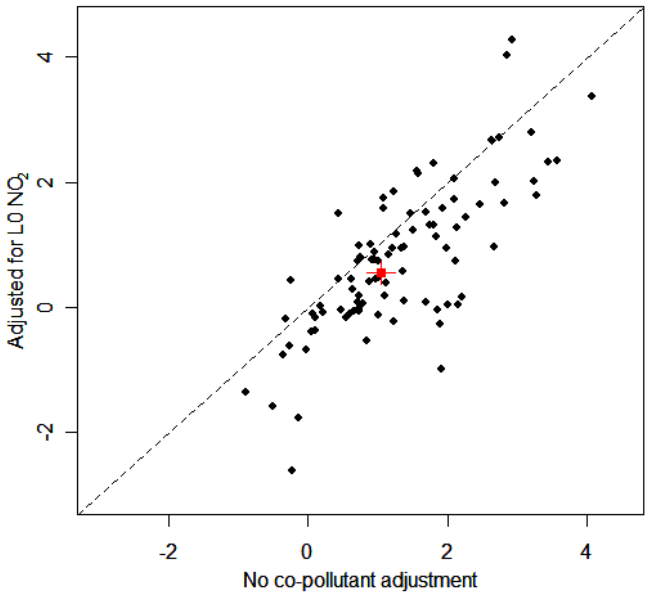


Fig. IIa. With and without adjustment by same day NO_2

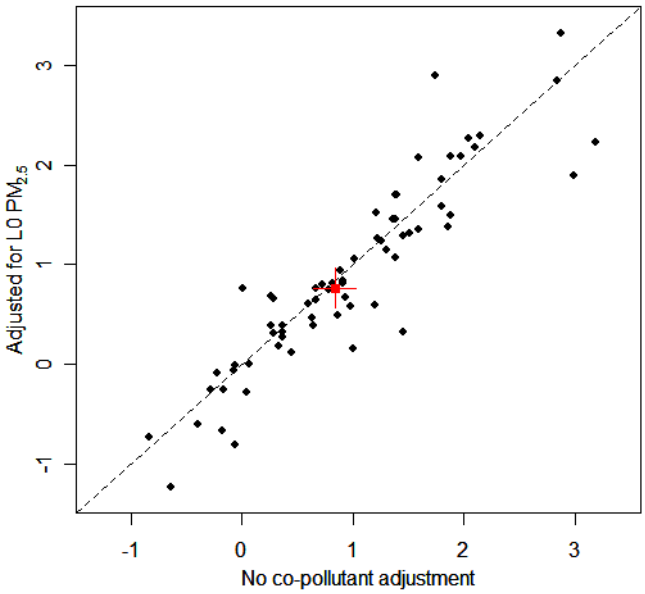


Fig. IIb. With and without adjustment by same day $PM_{2.5}$

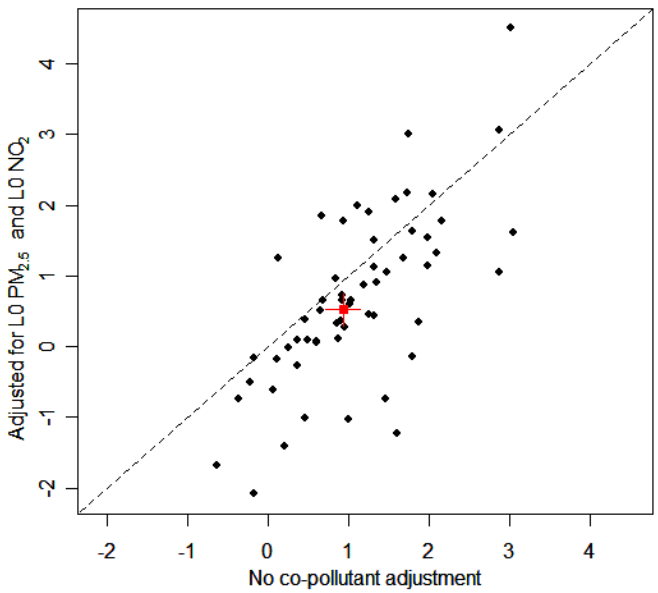


Fig. IIc. With and without adjustment by same day $PM_{2.5}$ and same day NO_2

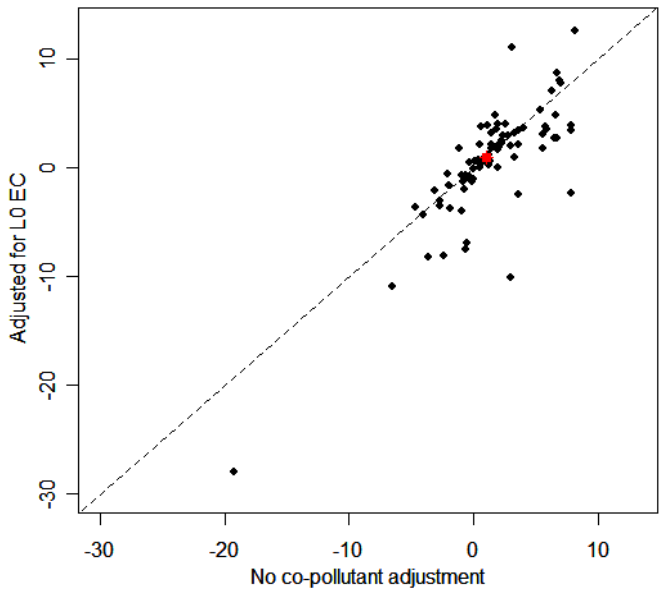


Fig. IId. With and without adjustment by same day EC

Figure III. Percent increase in risk of cardiovascular hospital admissions per 1 ppm increase in the same day 1-hour maximum CO for those ≥65 years (1999-2005) adjusted for same day NO_2, with varying degrees of freedom for the natural cubic spline of time

Note: The points represent central estimates; the horizontal lines represent 95% posterior intervals.

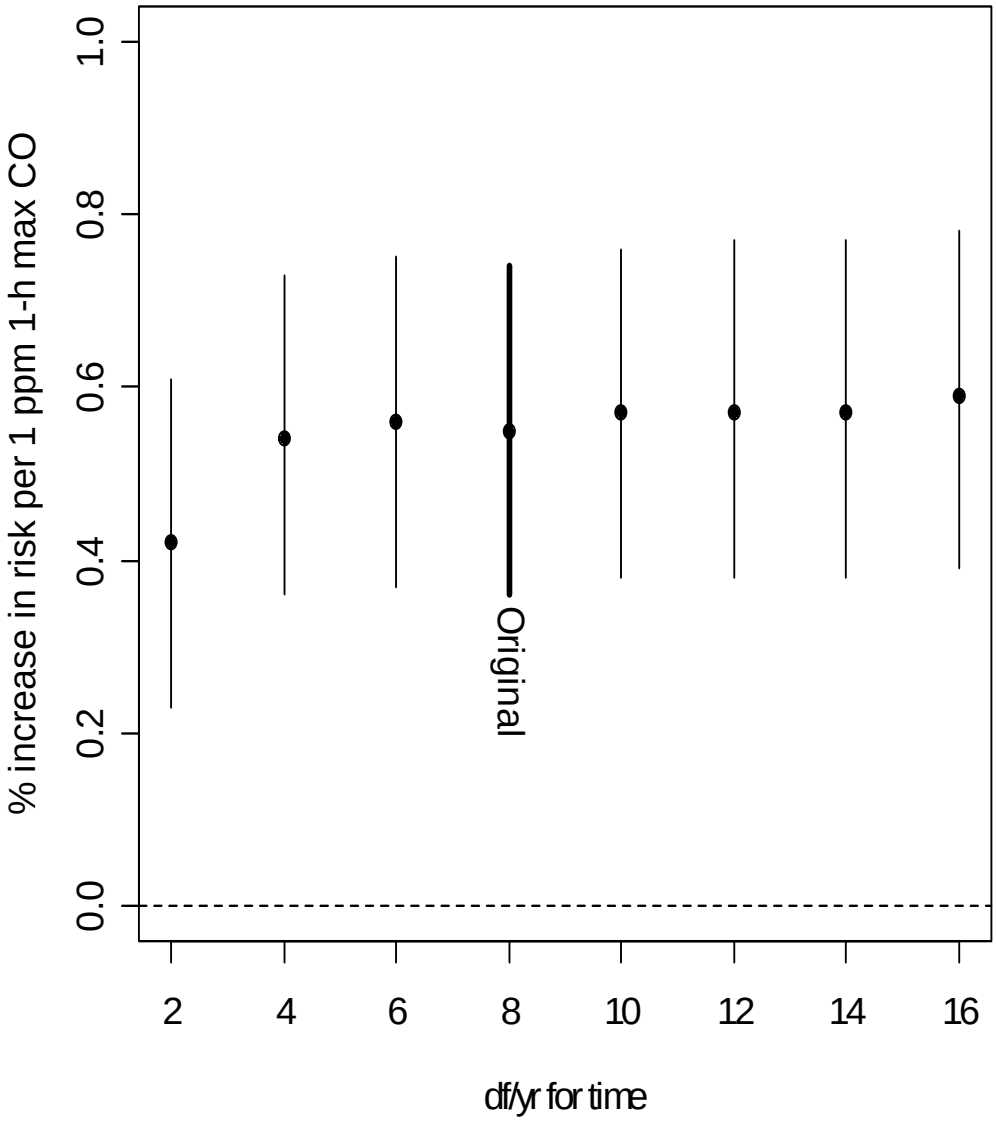
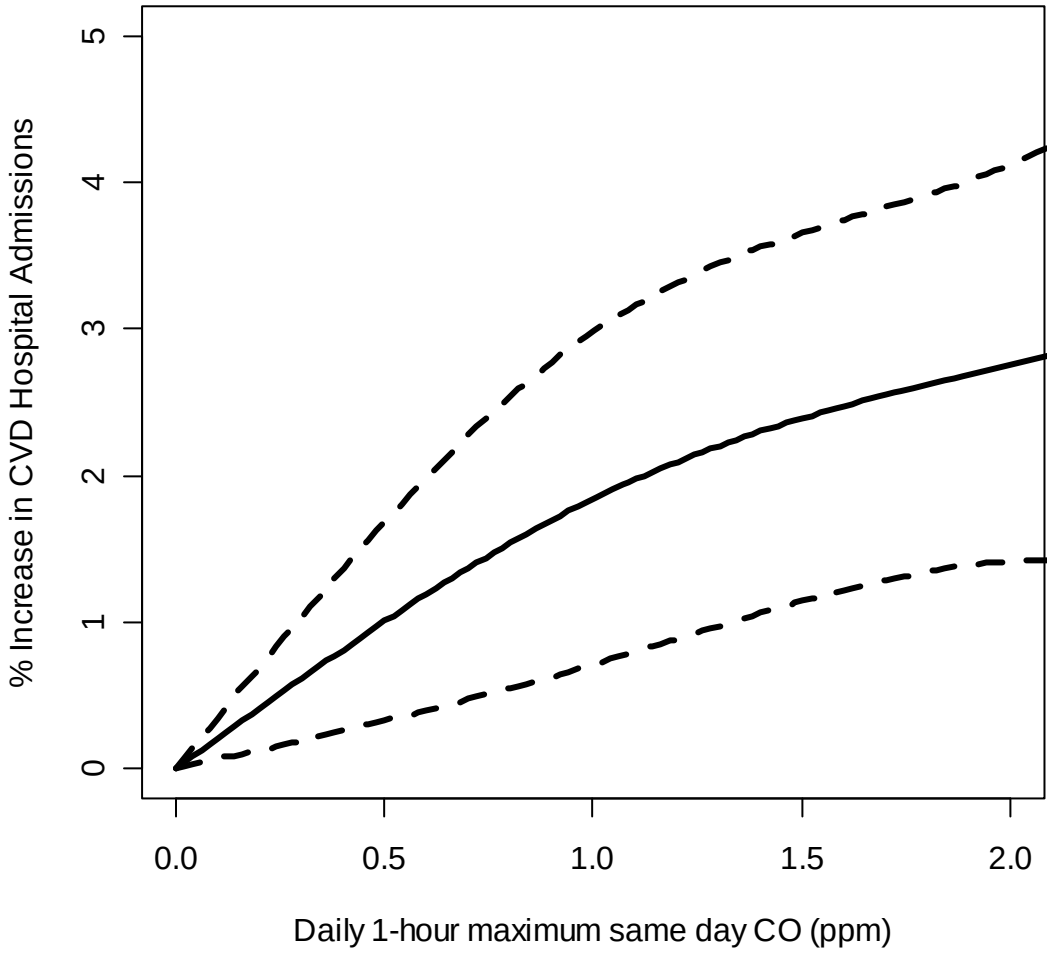


Figure IV. Exposure-response curve for daily 1-hour maximum same day CO and risk of cardiovascular hospitalizations for 92 U.S. counties, adjusted for same day NO_2

Note: The solid line represents central estimates; the dashed lines represent 95% posterior intervals. These results were generated by applying a natural cubic spline of daily 1-hour maximum CO levels (interior knots 1 and 2 ppm, boundary knots 0 and 10 ppm). This non-linear approach to develop exposure-response relationships has been applied to study of particulate matter and ozone (Bell et al. 2006, Daniels et al. 2000, Dominici et al. 2002).



References

Bell ML, Peng RD, Dominici F. The exposure-response curve for ozone and risk of mortality and the adequacy of current ozone regulations. *Environ Health Perspect.* 2006; 114:532-536.

Daniels MJ, Dominici F, Samet JM, Zeger SL. Estimating particulate matter-mortality dose-response curves and threshold levels: an analysis of daily time-series for the 20 largest US cities. *Am J Epidemiol* 2000; 152:397-406.

Dominici F, Daniels M, Zeger SL, Samet JM. Air pollution and mortality: estimating regional and national dose-response relationships. *J Am Stat Assoc* 2002; 97:100-111.