

# Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Stroke  
Association<sup>SM</sup>

A Division of American  
Heart Association



## **Air Pollution and Hospital Admissions for Ischemic and Hemorrhagic Stroke Among Medicare Beneficiaries**

Gregory A. Wellenius, Joel Schwartz and Murray A. Mittleman

*Stroke* 2005;36:2549-2553; originally published online Oct 27, 2005;

DOI: 10.1161/01.STR.0000189687.78760.47

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214  
Copyright © 2005 American Heart Association. All rights reserved. Print ISSN: 0039-2499. Online  
ISSN: 1524-4628

The online version of this article, along with updated information and services, is  
located on the World Wide Web at:

<http://stroke.ahajournals.org/cgi/content/full/36/12/2549>

Subscriptions: Information about subscribing to *Stroke* is online at  
<http://stroke.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters  
Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax:  
410-528-8550. E-mail:  
[journalpermissions@lww.com](mailto:journalpermissions@lww.com)

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

# Air Pollution and Hospital Admissions for Ischemic and Hemorrhagic Stroke Among Medicare Beneficiaries

Gregory A. Wellenius, ScD; Joel Schwartz, PhD; Murray A. Mittleman, MD, DrPH

**Background and Purpose**—The association between short-term elevations in ambient air particles and increased cardiovascular morbidity and mortality is well documented. Ambient particles may similarly increase the risk of stroke.

**Methods**—We evaluated the association between daily levels of respirable particulate matter (aerodynamic diameter  $\leq 10 \mu\text{m}$ ,  $\text{PM}_{10}$ ) and hospital admission for ischemic and hemorrhagic stroke among Medicare recipients (age  $\geq 65$  years) in 9 US cities using a 2-stage hierarchical model. In the first stage, we applied the time-stratified case-crossover design to estimate the effect of  $\text{PM}_{10}$  in each city. We used a 3-day unconstrained, distributed lag model to simultaneously estimate the effect of  $\text{PM}_{10}$  0 to 2 days before the admission day and controlled for meteorological covariates in all of the models. In the second stage, we used random-effects metaanalytic techniques to combine the city-specific effect estimates.

**Results**—Ischemic ( $n=155\,503$ ) and hemorrhagic (19 314) stroke admissions were examined separately. For ischemic stroke, an interquartile range increase in  $\text{PM}_{10}$  was associated with a 1.03% (95% CI, 0.04% to 2.04%) increase in admissions on the same day only. Similar results were observed with  $\text{CO}$ ,  $\text{NO}_2$ , and  $\text{SO}_2$ . For hemorrhagic stroke, no association was observed with any pollutant 0 to 2 days before admission.

**Conclusions**—These results suggest that elevations in ambient particles may transiently increase the risk of ischemic, but not hemorrhagic, stroke. Studies with more accurate assessment of timing of stroke onset are necessary to confirm or refute these findings. (*Stroke*. 2005;36:2549-2553.)

**Key Words:** ischemic stroke ■ hemorrhagic stroke ■ air pollution ■ environmental exposure ■ epidemiology

Epidemiological studies have demonstrated a consistent increased risk for cardiac morbidity and mortality associated with acute exposure to ambient air particles, including triggering of acute myocardial infarction,<sup>1,2</sup> discharge of implanted cardioverter defibrillators,<sup>3</sup> and hospital admission for acute decompensation of patients with congestive heart failure.<sup>4</sup> Although the mechanisms have not been fully elucidated, current evidence suggests that alterations in hemodynamics,<sup>5,6</sup> hemostatic factors,<sup>7-9</sup> and autonomic function<sup>10,11</sup> may underlie the cardiovascular effects of particulate air pollution.

Exposure to particulate air pollution may similarly increase the risk of stroke. Studies of small-area variation have found a positive association between stroke mortality rates and living in areas of high-ambient pollution.<sup>12</sup> Time series studies using hospital discharge summaries report a statistically significant positive association between daily measures of respirable particles (particulate matter with aerodynamic diameter  $< 10 \mu\text{m}$ ,  $\text{PM}_{10}$ ) and cerebrovascular hospitalizations,<sup>13-16</sup> but the results have been inconsistent.<sup>17-19</sup> Moreover, few studies have distinguished between ischemic and

hemorrhagic strokes.<sup>15,16,20</sup> Given the putative mechanisms of particulate-related cardiovascular effects, we hypothesized that short-term elevations in  $\text{PM}_{10}$  would be associated with increased hospitalizations for ischemic but not hemorrhagic stroke. We evaluated this hypothesis among Medicare beneficiaries  $\geq 65$  years of age in 9 US cities with daily  $\text{PM}_{10}$  monitoring.

## Methods

### Study Population

This study was approved by the Institutional Review Boards of the Harvard School of Public Health and Beth Israel Deaconess Medical Center. We evaluated the association between mean daily  $\text{PM}_{10}$  levels and the rate of admission for stroke among Medicare beneficiaries in 9 cities chosen a priori based on their large populations, many years of daily  $\text{PM}_{10}$  monitoring, and geographic diversity (Table 1). The observation period in each city was limited by the range of dates for which both hospital admissions and daily  $\text{PM}_{10}$  data were available.

We obtained information on hospital admissions from the Centers for Medicare and Medicaid Services. Ischemic stroke cases were defined as persons admitted from the emergency room with a primary discharge diagnosis of acute but ill-defined cerebrovascular

Received August 5, 2005; accepted August 25, 2005.

From the Cardiovascular Epidemiology Research Unit (G.A.W., M.A.M.), Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center, and Departments of Environmental Health (G.A.W., J.S., M.A.M.) and Epidemiology (J.S., M.A.M.), Harvard School of Public Health, Boston, Mass.

Correspondence to Gregory A. Wellenius, ScD, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Deaconess 306, Boston, MA 02215. E-mail gwelleni@bidmc.harvard.edu

© 2005 American Heart Association, Inc.

Stroke is available at <http://www.strokeaha.org>

DOI: 10.1161/01.STR.0000189687.78760.47

**TABLE 1. No. of Hospital Admissions for Ischemic and Hemorrhagic Stroke Among Medicare Beneficiaries (age  $\geq 65$ ) in 9 US Cities During the Study Period**

City	County	Time Period	Person-Years (Thousands)*	Stroke Cases	
				Ischemic	Hemorrhagic
Birmingham	Jefferson, Shelby	1/1/1986–12/31/1993	792	6642	770
Chicago	Cook	5/1/1986–11/30/1999	8603	54 797	7182
Cleveland	Cuyahoga	10/1/1988–11/30/1999	2468	20 142	2298
Detroit	Wayne	4/1/1986–11/30/1999	3606	26 585	2854
Minneapolis	Hennepin, Ramsey	1/1/1987–12/31/1997	1940	6903	1119
New Haven	New Haven	4/1/1988–11/30/1999	1373	7546	1043
Pittsburgh	Allegheny	1/1/1987–11/30/1999	2995	23 139	2590
Salt Lake City	Salt Lake	1/1/1986–11/30/1999	853	2559	380
Seattle	King	1/1/1986–12/31/1995	1671	7190	1078
Total	...	...	24 300	155 503	19 314

\*Based on estimated no. of residents  $\geq 65$  years of age according to the US Bureau of the Census, 1990 Census of Population and Housing.

disease or occlusion of cerebral arteries, excluding those without cerebral infarction.<sup>21</sup> In a sensitivity analysis, we limited the definition of ischemic stroke to patients admitted from the emergency room with a primary discharge diagnosis of occlusion of cerebral arteries.<sup>21</sup> Hemorrhagic stroke cases were defined as persons admitted from the emergency room with a primary discharge diagnosis of intracerebral hemorrhage.<sup>21</sup>

### Exposure Information

We obtained daily measures of PM<sub>10</sub> and hourly measures of CO, NO<sub>2</sub>, and SO<sub>2</sub> from the US Environmental Protection Agency and computed daily mean concentrations in each city.<sup>22</sup> To evaluate the effect of PM<sub>10</sub> within the range of exposure deemed acceptable in the United States under current regulations, we excluded from analysis 31 days (of 37 203 possible) on which PM<sub>10</sub> levels exceeded 150  $\mu\text{g}/\text{m}^3$ , the current 24-hour US Environmental Protection Agency standard. We considered pollutant data unavailable for a given city if  $>10\%$  of days in the observation period had missing values. Using this criterion, data on CO was missing in New Haven, Conn; NO<sub>2</sub> in Birmingham, Ala, Salt Lake City, Utah, and Seattle, Wash; and SO<sub>2</sub> in Birmingham, Ala. We obtained National Weather Service data on climatologic variables (National Climatic Data Center) and calculated the apparent temperature (an index of human discomfort that incorporates ambient temperature and relative humidity) as described previously.<sup>23</sup>

Data on PM<sub>10</sub> were missing on 4.0% of the days. In a sensitivity analysis, we used city-specific prediction models to impute single missing values. Specifically, we modeled PM<sub>10</sub> as smooth functions of PM<sub>10</sub> on the previous and following day, available copollutants, and climatologic variables. City-specific model  $R^2$  values ranged from 0.50 to 0.85 (mean, 0.71). We imputed missing values of PM<sub>10</sub>

for days preceded and followed by nonmissing days. This time-series, referred to as "PM<sub>10</sub> with imputed values," had missing values on 1.7% of days.

### Data Analysis

We used a 2-stage hierarchical model to evaluate the association between ambient pollution and the rate of hospital admission, as described previously.<sup>24</sup> In the first stage, we used the time-stratified case-crossover study design<sup>25</sup> to separately estimate the effect of air pollution in each city. In this design, each subject's exposure before a case-defining event (case period) is compared with his or her own exposure experience during  $\geq 1$  control period when the subject did not become a case. Control periods were chosen such that exposures during the case period were compared with exposures occurring on other days of the same month falling on the same day of the week as the case period. Exposure during the case period was defined as pollutant concentrations 0 to 2 days before admission (lags 0 to 2 days). This design has been shown to be effective in controlling for seasonality, time trends, and chronic and slowly varying potential confounders.<sup>24</sup>

We performed conditional logistic regression, stratifying on each day, to obtain estimates of odds ratios and 95% CIs. We report effect estimates as the percentage of change in the rate of hospitalization associated with an interquartile range increase in mean daily pollutant levels. For each pollutant, we simultaneously evaluated the effect at lags of 0 to 2 days using unconstrained distributed lag models<sup>26</sup> and controlled for meteorological covariates. We modeled the mean apparent temperature at lag 0 as a quadratic function and mean apparent temperature at lags 1 and 2, mean barometric pressure at lags 0 and 1, and pollutants at lags 0 to 2 as linear functions of continuous variables.

**TABLE 2. Summary of Mean Daily Concentrations of Air Pollutants and Climatologic Variables in 9 US Cities**

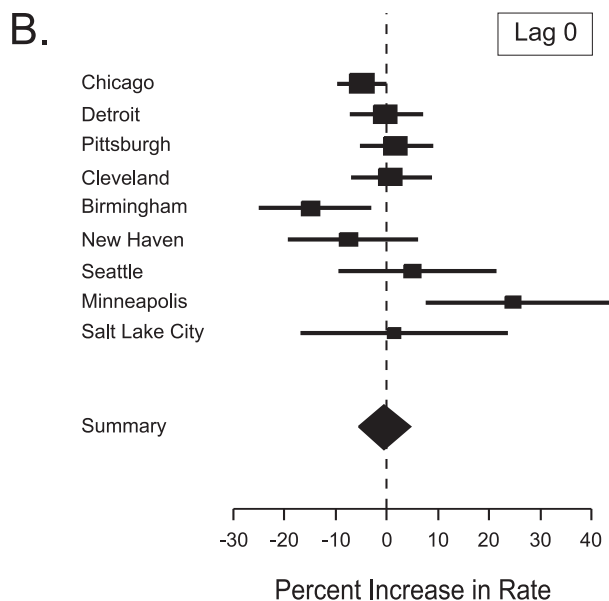
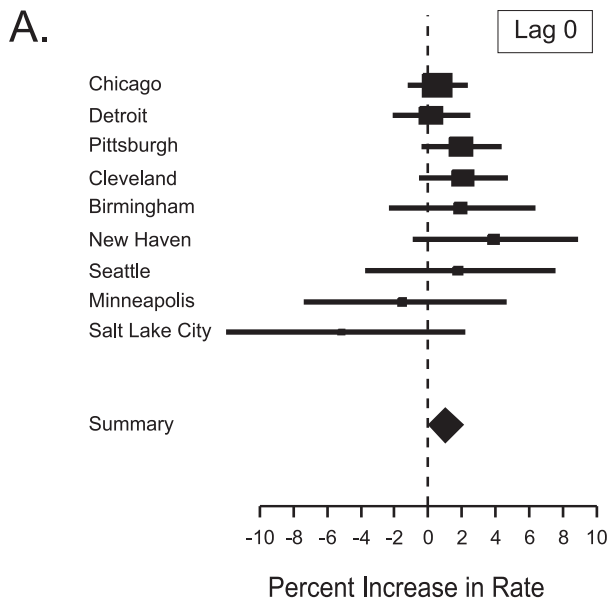
Variable	Percentiles					Correlation With PM <sub>10</sub>
	10	25	50	75	90	
PM <sub>10</sub> , $\mu\text{g}/\text{m}^3$	12.91	18.88	28.36	41.84	57.89	...
PM <sub>10</sub> with imputed values, $\mu\text{g}/\text{m}^3$	12.94	18.95	28.44	41.83	58.00	...
CO, ppm	0.54	0.73	1.02	1.44	1.98	0.43
NO <sub>2</sub> , ppb	13.71	18.05	23.54	29.98	36.54	0.53
SO <sub>2</sub> , ppb	2.17	3.57	6.22	10.26	16.17	0.39
Apparent temperature, °C	−3.93	0.95	9.47	19.33	25.42	0.22

In the second stage, we obtained a combined random-effects estimate from the city-specific effect estimates using standard random-effects meta-analysis methods.<sup>27</sup> All of the reported *P* values are based on 2-sided tests at the  $\alpha=0.05$  level. Analyses were performed using SAS V9 and the R statistical package.

## Results

### Ischemic Stroke Admissions

There were 155 503 hospital admissions from the emergency department with a primary discharge diagnosis of ischemic stroke among Medicare beneficiaries  $\geq 65$  years of age in 9 US cities (Table 1). The overall mean PM<sub>10</sub> level was 32.69



City-specific (■, height inversely proportional to variance of estimate) and random-effects summary (◆, horizontal limits indicate 95% CIs) estimates of the percentage change in rate of hospital admission for ischemic (A) and hemorrhagic (B) stroke associated with an interquartile range increase in PM<sub>10</sub> (22.96  $\mu\text{g}/\text{m}^3$ ) on the same day (lag 0).

$\mu\text{g}/\text{m}^3$  (SD  $\pm 19.75$ ; Table 2). Age on admission ranged from 65 to 117 years with a mean of  $78.6 \pm 7.7$  years. Cases were mostly white (75.4%) and female (60.7%).

We simultaneously estimated the effect of PM<sub>10</sub> at lags of 0 to 2 days in each city and then obtained summary estimates using standard random-effects meta-analysis techniques. A positive association between PM<sub>10</sub> and hospital admissions on the same day was observed in 7 of the 9 cities examined ( $P_{\text{heterogeneity}}=0.71$ ; Figure, A). Overall, an interquartile range increase in PM<sub>10</sub> on the day of admission was associated with a 1.03% (95% CI, 0.04% to 2.04%) increase in the rate of hospital admission for ischemic stroke. PM<sub>10</sub> levels 1 or 2 days before admission were not associated with increased risk. Using the alternate definition of ischemic stroke yielded a 1.39% (95% CI, 0.26% to 2.52%) increase for an interquartile range increase in PM<sub>10</sub> on the admission day and no significant increase associated with PM<sub>10</sub> levels 1 or 2 days before admission. Using PM<sub>10</sub> with imputed values as the exposure did not materially alter the results.

Ambient measures of CO, NO<sub>2</sub>, and SO<sub>2</sub> were correlated with ambient PM<sub>10</sub> levels (Table 2). An interquartile range increase in each pollutant was associated with a qualitatively similar increase in admissions on the same day (Table 3). No association was observed with any pollutant 1 or 2 days before the admission date.

### Hemorrhagic Stroke Admissions

There were 19 314 hospital admissions with a primary discharge diagnosis of hemorrhagic stroke (Table 1). Compared with patients admitted for ischemic stroke, these patients tended to be younger (mean age,  $77.9 \pm 7.6$  years), more likely to be white (78.2%), and less likely to be female (58.8%).

PM<sub>10</sub> levels on the day of admission were not associated with hemorrhagic stroke admissions although there was evidence of statistical heterogeneity between cities ( $P_{\text{heterogeneity}}=0.013$ ; Figure, B). PM<sub>10</sub> levels 1 to 2 days before admission were also not associated with increased risk. Likewise, no association was observed between hemorrhagic stroke admissions and PM<sub>10</sub> with imputed values, CO, NO<sub>2</sub>, or SO<sub>2</sub> (Table 3).

## Discussion

Previous studies using administrative data from 1 to 3 cities suggest an association between daily fluctuations in PM<sub>10</sub> and cerebrovascular hospital admissions.<sup>13–16</sup> We evaluated the association between PM<sub>10</sub> and hospital admissions for ischemic and hemorrhagic stroke among Medicare beneficiaries  $\geq 65$  years of age in 9 US cities and found that a transient increase in ambient particles was associated with an increased risk of hospital admission for ischemic but not hemorrhagic stroke. Specifically, for ischemic stroke, we found that an interquartile range increase in PM<sub>10</sub> was associated with a 1.03% (95% CI, 0.04% to 2.04%) increase in the risk of admission on the same day. In contrast, for hemorrhagic stroke, we found no evidence of an association with PM<sub>10</sub> or any other pollutant examined.

Few published studies have examined the effects of ambient particles specifically on ischemic or hemorrhagic stroke.<sup>15,16,20</sup> Using hospital admission records from Taiwan,

**TABLE 3. Percentage Change in Rate of Hospital Admission for Ischemic and Hemorrhagic Stroke for an Interquartile Range Increase in Mean Daily Pollutant Concentrations\***

Pollutant	Unit Increase (interquartile range)	Percent Increase in Hospitalization Rate	
		Ischemic Stroke	Hemorrhagic Stroke
PM <sub>10</sub>	22.96 $\mu\text{g}/\text{m}^3$	1.03 (0.04, 2.04)	−0.58 (−5.48 to 4.58)
PM <sub>10</sub> with imputed values	22.96 $\mu\text{g}/\text{m}^3$	2.33 (1.22, 3.45)	0.05 (−5.01 to 5.39)
CO	0.71 ppm	2.83 (1.23, 4.46)	−1.61 (−4.79 to 1.68)
NO <sub>2</sub>	11.93 ppb	2.94 (1.78, 4.12)	0.38 (−2.66 to 3.51)
SO <sub>2</sub>	6.69 ppb	1.35 (0.43, 2.29)	0.68 (−1.77 to 3.19)

\*Random-effects summary estimates for lag 0 from single-pollutant models controlling for meteorological covariates.

Tsai et al<sup>16</sup> found a statistically significant positive association between PM<sub>10</sub> and both ischemic and hemorrhagic strokes after excluding days with mean daily temperature <20°C. Similarly, Hong et al<sup>20</sup> analyzed death certificates in Seoul, Korea, with similar statistically significant results for ischemic and hemorrhagic stroke. Linn et al<sup>15</sup> also found a significant increase in hospitalization rates for ischemic stroke in metropolitan Los Angeles, but did not consider hemorrhagic strokes. The discrepant results in relation to hemorrhagic stroke may be explained by differences in case definitions, analytic methods, average pollutant levels, or population characteristics between the current and previous studies.

Exposure to ambient particles may plausibly increase the risk of ischemic stroke by promoting atherosclerotic plaque disruption and thrombosis. This could be mediated by a combination of  $\geq 3$  different mechanisms. First, particulate exposure can induce an acute systemic inflammatory response with an increased number of circulating neutrophils<sup>28</sup> and increased levels of C-reactive protein.<sup>9</sup> Second, particulate-related changes in hemostatic factors have been reported, including increased levels of fibrinogen<sup>7,8</sup> and von Willebrand factor<sup>9</sup> and enhanced peripheral arterial thrombosis.<sup>29</sup> Third, particulate-related changes in autonomic nervous system activity, as assessed by heart rate variability, are well documented and are consistent with relative sympathoexcitation.<sup>10,11</sup>

The observed association between ischemic stroke and air pollution was similar for all of the pollutants considered. Likewise, we consistently failed to find evidence of an association between hemorrhagic stroke and any pollutant considered. Because ambient measures are correlated, separating the effects of individual pollutants is problematic. However, PM<sub>10</sub> is relatively spatially homogenous within a metropolitan area,<sup>30</sup> and ambient measures at a central site are well correlated with personal exposure measures.<sup>31</sup> In contrast, personal exposures to CO, NO<sub>2</sub>, and SO<sub>2</sub> are relatively poorly predicted by ambient measures.<sup>32</sup> For example, ambient measures of NO<sub>2</sub> are likely more strongly correlated with personal exposure to particulate matter than to personal NO<sub>2</sub> exposure.<sup>32</sup> Thus, the present study is consistent with the interpretation that sources of pollution that lead to concurrent elevation of these pollutants may be responsible for the observed associations.

The health effects of exposure to air pollution from indoor sources (eg, from tobacco smoke or cooking) are also of interest, but evaluating these effects requires a different study design and indoor, as well as ambient, pollutant monitors. Although ambient particles have been shown to penetrate indoors, there is little correlation between exposure to particles originating from indoor sources and those from outdoor sources.<sup>33</sup>

This study has several potential limitations. First, misclassification of the outcome is expected as a result of diagnostic or coding errors. However, these errors are likely unrelated to pollutant levels and are expected to reduce the precision of our estimates and potentially bias the relative risk toward the null. In fact, using the alternate definition of ischemic stroke, which is likely to be more specific, albeit less sensitive, than the primary definition,<sup>34,35</sup> we found a stronger association with PM<sub>10</sub>. Similarly, we expect that the incidence of clinically unrecognized or nonhospitalized stroke is unrelated to pollutant levels after adjusting for meteorological covariates and month-of-year and day-of-week effects. Therefore, exclusion of these cases is expected to reduce the precision of our estimates but not otherwise bias our results. Second, the use of ambient rather than personal exposure measures is expected to result in exposure misclassification. However, this misclassification is expected to lead one to underestimate the relative risk.<sup>36</sup> Third, the date of symptom onset likely preceded the date of admission in a proportion of cases, leading to nondifferential exposure misclassification and bias of the relative risk toward the null. Fourth, residual confounding by short-term respiratory epidemics remains a possibility. However, the time-stratified case-crossover design used in this study has been shown to effectively control for confounding by time trends in both exposure and outcomes.<sup>24</sup> In particular, this approach provides effective control for time trends that occur over periods longer than 1 calendar month. Additionally, studies directly examining this possibility suggest that respiratory epidemics are not important confounders of the association between particulate matter and all-cause or cardiovascular mortality.<sup>37</sup>

## Conclusions

In the current study, we found that a transient increase in ambient particles was associated with an increased risk of hospital admission for ischemic but not hemorrhagic stroke.



Although the relative increase in risk was small, given the large number of people simultaneously at risk for ischemic stroke and exposed to urban pollution, even a small relative risk may be of significant public health interest. Additional studies with more detailed data on the clinical characteristics of subjects and more accurate assessment of the timing of symptom onset are needed to confirm or refute these findings.

### Acknowledgments

This study was supported by grants ES013804, HL07374, and ES09825 from the National Institutes of Health and by US Environmental Protection Agency research award R827353 from the US Environmental Protection Agency.

### References

- Peters A, Dockery DW, Muller JE, Mittleman MA. Increased particulate air pollution and the triggering of myocardial infarction. *Circulation*. 2001;103:2810–2815.
- D'Ippoliti D, Forastiere F, Ancona C, Agabiti N, Fusco D, Michelozzi P, Perucci CA. Air pollution and myocardial infarction in rome: a case-crossover analysis. *Epidemiology*. 2003;14:528–535.
- Rich DQ, Schwartz J, Mittleman MA, Link M, Luttmann-Gibson H, Catalano PJ, Speizer FE, Dockery DW. Association of short-term ambient air pollution concentrations and ventricular arrhythmias. *Am J Epidemiol*. 2005;161:1123–1132.
- Wellenius GA, Bateson TF, Mittleman MA, Schwartz J. Particulate air pollution and the rate of hospitalization for congestive heart failure among medicare beneficiaries in pittsburgh, pennsylvania. *Am J Epidemiol*. 2005;161:130–136.
- Pope CA 3rd, Dockery DW, Kanner RE, Villegas GM, Schwartz J. Oxygen saturation, pulse rate, and particulate air pollution: A daily time-series panel study. *Am J Respir Crit Care Med*. 1999;159:365–372.
- Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, Gates KA, Hartley LH, Suh H, Gold DR. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation*. 2004;110:2184–2189.
- Ghio AJ, Kim C, Devlin RB. Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers. *Am J Respir Crit Care Med*. 2000;162:981–988.
- Schwartz J. Air pollution and blood markers of cardiovascular risk. *Environ Health Perspect*. 2001;109(Suppl III):405–409.
- Riediker M, Cascio WE, Griggs TR, Herbst MC, Bromberg PA, Neas L, Williams RW, Devlin RB. Particulate matter exposure in cars is associated with cardiovascular effects in healthy young men. *Am J Respir Crit Care Med*. 2004;169:934–940.
- Gold DR, Litonjua A, Schwartz J, Lovett E, Larson A, Nearing B, Allen G, Verrier M, Cherry R, Verrier R. Ambient pollution and heart rate variability. *Circulation*. 2000;101:1267–1273.
- Creason J, Neas L, Walsh D, Williams R, Sheldon L, Liao D, Shy C. Particulate matter and heart rate variability among elderly retirees: The Baltimore 1998 pm study. *J Expo Anal Environ Epidemiol*. 2001;11:116–122.
- Maheswaran R, Haining RP, Brindley P, Law J, Pearson T, Fryers PR, Wise S, Campbell MJ. Outdoor air pollution and stroke in sheffield, united kingdom: a small-area level geographical study. *Stroke*. 2005;36:239–243.
- Wordley J, Walters S, Ayres JG. Short term variations in hospital admissions and mortality and particulate air pollution. *Occup Environ Med*. 1997;54:108–116.
- Moolgavkar SH. Air pollution and hospital admissions for diseases of the circulatory system in three U.S. metropolitan areas. *J Air & Waste Manag Assoc*. 2000;50:1199–1206.
- Linn WS, Szlachet Y, Gong H Jr, Kinney PL, Berhane KT. Air pollution and daily hospital admissions in metropolitan los angeles. *Environ Health Perspect*. 2000;108:427–434.
- Tsai SS, Goggins WB, Chiu HF, Yang CY. Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. *Stroke*. 2003;34:2612–2616.
- Burnett RT, Smith-Doiron M, Stieb D, Cakmak S, Brook JR. Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. *Arch Environ Health*. 1999;54:130–139.
- Le Tertre A, Medina S, Samoli E, Forsberg B, Michelozzi P, Boumghar A, Vonk JM, Bellini A, Atkinson R, Ayres JG, Sunyer J, Schwartz J, Katsouyanni K. Short-term effects of particulate air pollution on cardiovascular diseases in eight European cities. *J Epidemiol Community Health*. 2002;56:773–779.
- Sunyer J, Ballester F, Tertre AL, Atkinson R, Ayres JG, Forastiere F, Forsberg B, Vonk JM, Bisanti L, Tenias JM, Medina S, Schwartz J, Katsouyanni K. The association of daily sulfur dioxide air pollution levels with hospital admissions for cardiovascular diseases in europe (the aphea-ii study). *Eur Heart J*. 2003;24:752–760.
- Hong YC, Lee JT, Kim H, Kwon HJ. Air pollution: a new risk factor in ischemic stroke mortality. *Stroke*. 2002;33:2165–2169.
- Department of Health and Human Services. *International Classification of Diseases, 9th Revision, Clinical Modification: ICD-9-CM*. 3rd ed. Washington, DC: US Government Printing Office; 1989.
- Zanobetti A, Schwartz J, Dockery DW. Airborne particles are a risk factor for hospital admissions for heart and lung disease. *Environ Health Perspect*. 2000;108:1071–1077.
- O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. *Am J Epidemiol*. 2003;157:1074–1082.
- Schwartz J, Zanobetti A, Bateson TF. Morbidity and mortality among elderly residents in cities with daily pm measurements. In: *Revised Analyses of Air Pollution and Health. Special Report*. Boston, Mass: Health Effects Institute; 2003:25–58.
- Levy D, Lumley T, Sheppard L, Kaufman J, Checkoway H. Referent selection in case-crossover analyses of acute health effects of air pollution. *Epidemiology*. 2001;12:186–192.
- Samet JM, Zeger SL, Dominici F, Currier F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. The national morbidity, mortality, and air pollution study. Part II: Morbidity and mortality from air pollution in the United States. *Res Rep Health Eff Inst*. 2000;94:5–79.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177–188.
- van Eeden SF, Hogg JC. Systemic inflammatory response induced by particulate matter air pollution: The importance of bone-marrow stimulation. *J Toxicol Environ Health A*. 2002;65:1597–1613.
- Nemmar A, Hoet PH, Dinsdale D, Vermeylen J, Hoylaerts MF, Nemery B. Diesel exhaust particles in lung acutely enhance experimental peripheral thrombosis. *Circulation*. 2003;107:1202–1208.
- Ito K, De Leon S, Thurston GD, Nadas A, Lippmann M. Monitor-to-monitor temporal correlation of air pollution in the contiguous us. *J Expo Anal Environ Epidemiol*. 2005;15:172–184.
- Janssen NA, Hoek G, Brunekreef B, Harssema H, Mensink I, Zuidhof A. Personal sampling of particles in adults: Relation among personal, indoor, and outdoor air concentrations. *Am J Epidemiol*. 1998;147:537–547.
- Sarnat JA, Brown KW, Schwartz J, Coull BA, Koutrakis P. Ambient gas concentrations and personal particulate matter exposures: Implications for studying the health effects of particles. *Epidemiology*. 2005;16:385–395.
- Ebelt ST, Wilson WE, Brauer M. Exposure to ambient and nonambient components of particulate matter: A comparison of health effects. *Epidemiology*. 2005;16:396–405.
- Goldstein LB. Accuracy of icd-9-cm coding for the identification of patients with acute ischemic stroke: Effect of modifier codes. *Stroke*. 1998;29:1602–1604.
- Broderick J, Brott T, Kothari R, Miller R, Khoury J, Pancioli A, Gebel J, Mills D, Minneci L, Shukla R. The greater Cincinnati/northern Kentucky stroke study: Preliminary first-ever and total incidence rates of stroke among blacks. *Stroke*. 1998;29:415–421.
- Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, Cohen A. Exposure measurement error in time-series studies of air pollution: Concepts and consequences. *Environ Health Perspect*. 2000;108:419–426.
- Touloumi G, Samoli E, Quenel P, Paldy A, Anderson RH, Zmirou D, Galan I, Forsberg B, Schindler C, Schwartz J, Katsouyanni K. Short-term effects of air pollution on total and cardiovascular mortality: The confounding effect of influenza epidemics. *Epidemiology*. 2005;16:49–57.