The following document was submitted "for the record" to the Intermodal Container Transfer Facility (ICTF) Joint Powers Authority (JPA) during the Notice of Preparation/Initial Study (NOP/IS) comment period for the ICTF Modernization and Expansion Project.

The document was submitted by:

Andrea M. Hricko
Assoc Prof Prev Med
Keck School of Med &
Director, Community Outreach and Education
Southern CA Env Health Sciences Ctr
1540 Alcazar Street CHP 236
L.A. CA 90033
323-442-3077

---------- End Page ----------

Relation of Heart Failure Hospitalization to Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD[a,*], Dale G. Renlund, MD[b,c], Abdallah G. Kfoury, MD[b,c], Heidi T. May, MSPH[b], and Benjamin D. Horne, PhD, MPH[b,c]

Cardiopulmonary disease has been associated with particulate matter (PM) air pollution. There is evidence that exposure to elevated PM concentrations increases risk of acute ischemic heart disease events, alters cardiac autonomic function, and increases risk of arrhythmias. It is plausible, therefore, that PM exposure may exacerbate heart failure (HF). A case-crossover study design was used to explore associations between fine PM ($PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm) and 2,628 HF hospitalizations. Patients lived on Utah's Wasatch Front and were drawn from those hospitalized at Intermountain Healthcare facilities with a primary diagnosis of HF. A 14-day lagged cumulative moving average of 10 $\mu g/m^3$ $PM_{2.5}$ was associated with a 13.1% (95% confidence interval 1.3 to 26.2) increase in HF admissions. The strongest $PM_{2.5}$–HF associations were for elderly patients who had previously been admitted for HF and who required only a short period of hospitalization. HF hospitalizations are associated with lagged cumulative exposure to $PM_{2.5}$ of approximately 2 weeks. In conclusion, particulate air pollution may play a role in precipitating acute cardiac decompensation in otherwise well-managed patients with HF, perhaps through effects of PM on myocardial ischemia, cardiac autonomic function, and/or arrhythmic effects. **(Am J Cardiol 2008;102:1230–1234)**

Exposure to elevated concentrations of ambient particulate matter (PM) air pollution has been associated with cardiopulmonary disease and mortality.[1–8] This study analyzes hospitalization data of patients with heart failure (HF) who lived in a well-defined area with long-term daily monitoring of particulate air pollution and with substantial temporal variability in PM concentrations due to densely populated mountain valley topography and frequent temperature inversions. It is hypothesized that elevated PM concentrations are associated with increased risk of HF hospitalization. Also, because hospitalization follows onset of symptoms, which likely follow a period of cumulative exposure, a distributed lag structure relating exposure to hospitalization of a few days or more is hypothesized.

Methods

More than 2 million people, approximately 80% of Utah's population, live on the Wasatch Front, a narrow area of land that is bordered on the east by the Wasatch Mountain range and on the west by the Great Salt Lake, Utah Lake, and smaller mountain ranges. This area is approximately 10 to 15 miles wide from east to west and approximately 80 miles long from north to south. It contains 3 nearly contiguous metropolitan areas, including the Ogden area to the North, the Salt Lake City area located in the center, and the Provo/Orem area to the south. Study participants included patients who were hospitalized with a primary discharge diagnosis of HF at Intermountain Healthcare. All patients had been admitted to Utah Valley Regional Medical Center, American Fork Hospital, Alta View Hospital, Cottonwood Hospital, LDS Hospital, or McKay-Dee Hospital for the years 1994 to 2006. These 6 hospitals accounted for approximately 60% of hospital admittances in the study area. Hospitalizations were identified by searching the Intermountain Healthcare electronic medical records data warehouse for HF International Classification of Diseases, ninth edition (ICD-9) diagnosis codes, as discussed elsewhere.[9] The study was approved by the Intermountain Healthcare Urban Central Region institutional review board. There were a total of 3,747 HF admissions including patients from throughout the state of Utah and from neighboring Western states. The present analysis includes the 2,618 admittances (including readmittances) of patients who lived in the Wasatch Front study area and who had their event on a date when air pollution and weather data were available. Individual patient variables included date and time of admission, date and time of discharge, age, gender, race, and zip code of residence.

Common weather patterns are shared across the Wasatch Front study area. PM concentrations are elevated during low-level temperature inversion episodes due to trapping of local emissions in a stagnant air mass near the valley floor. Daily weather data were collected from the National Weather Service (Salt Lake City International Airport station) for the time period January 1, 1993 through December 31, 2006. These data included temperature, dew point temperature, barometric pressure, and clearing index. The clear-

[a]Brigham Young University, Provo; [b]Cardiovascular Department, Intermountain Medical Center; and [c]University of Utah, Salt Lake City, Utah. Manuscript received April 23, 2008; revised manuscript received and accepted June 20, 2008.

This study was supported by Deseret Foundation, Salt Lake City, Utah, and funds from the Mary Lou Fulton Professorship, Brigham Young University, Provo, Utah.

*Corresponding author: Tel: 801-422-2157; fax: 801-422-0194.

E-mail address: cap3@byu.edu (C.A. Pope).

0002-9149/08/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjcard.2008.06.044

Table 1
Summary of pollution concentration data 1993 to 2006

Monitoring Sites		n (days)	Mean ($\mu g/m^3$)	SD	Max
Ogden	$PM_{2.5}$ monitored	1,005	10.6	9.9	108
Ogden	$PM_{2.5}$ monitored + imputed	5,108	10.7	9.3	108
SLC, Hawthorne	$PM_{2.5}$ monitored	3,007	11.1	11.2	94
SLC, Hawthorne	$PM_{2.5}$ monitored + imputed	5,109	11.9	11.8	104
Provo/Orem, Lindon	$PM_{2.5}$ monitored	3,021	10.1	9.3	82
Provo/Orem, Lindon	$PM_{2.5}$ monitored + imputed	5,113	10.6	10.7	142

$PM_{2.5}$ refers to particles with an aerodynamic diameter ≤2.5 micrometer cut point.

Table 2
Descriptive information regarding the hospitalized patients with HF

Number of Admissions	2,618
Age (yrs)	67 ± 15
Men	57%
Race (white)	90%
Readmissions	38%
Length of stay (days)	6 ± 9

Data presented as proportions (%) or averages (mean ± SD).

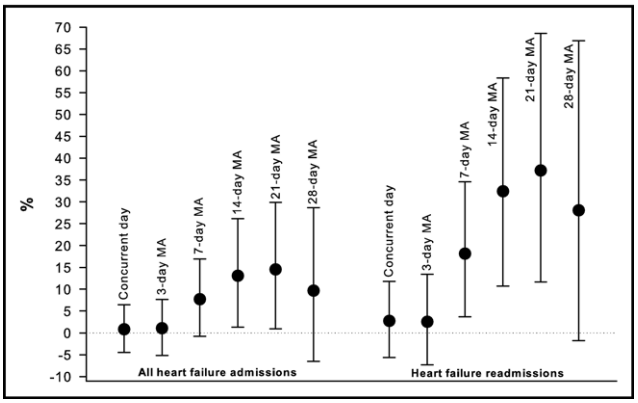

Figure 1. Percent increase in risk and 95% CIs of HF admissions and readmissions, associated with a 10 $\mu g/m^3$ of $PM_{2.5}$ for selected lagged moving average (MA) exposures 0 to 28 days.

ing index ranges from 0 to 1,050. Low index values reflect stagnant air conditions; high values reflect greater diffusion pollution potential.

Particulate air pollution data for PM_{10} (particles with an aerodynamic diameter ≤10 μm), and $PM_{2.5}$ (particles with an aerodynamic diameter ≤2.5) were obtained from the Utah Department of Environmental Quality, Division of Air Quality, Salt Lake City, Utah. Data from monitoring sites along the Wasatch Front from January 1, 1993 to December 31, 2006 were collected. Monitoring was conducted in accordance with the US Environmental Protection Agency federal reference method.[10] In Ogden and Provo/Orem, PM_{10} monitoring was conducted at a single community-based site with monitoring completeness of 83% and 93%, respectively. In Salt Lake City, the centrally located monitoring site, the Salt Lake City Air Monitoring Center (SLC AMC) was replaced by another site (SLC Hawthorne) with concurrent overlapping monitoring for over a year. Daily PM_{10} data were available from ≥1 of these 2 sites for 95% of the days. In addition, PM_{10} data were collected from another Salt Lake City monitoring site (SLC North). Daily PM_{10} concentrations between all of the Wasatch Front sites were highly correlated (r = 0.72 to 0.94). For $PM_{2.5}$, daily monitoring at the SLC Hawthorn and Lindon sites and every third day monitoring at the Ogden site began in January 1998. Missing values for $PM_{2.5}$ at specific monitors were estimated using available $PM_{2.5}$, PM_{10}, and clearing index data using a 2-stage statistical approach reported in more detail elsewhere.[8] First, PM_{10} concentration ratios between monitors were calculated and missing PM_{10} values were estimated based on these ratios and monitored PM_{10} data at the nearest monitoring site without missing data. Second, for each of the 3 Wasatch Front metropolitan areas, the $PM_{2.5}/PM_{10}$ ratios were estimated for 10 different air stagnation (clearing index ≤100; 101 to 200; 201 to 500; 501 to 999; 1,000 to 1,050) and seasonal periods (winter months December to February vs non-winter months) using regression models and missing $PM_{2.5}$ concentrations were estimated based on these ratios.

The analysis of HF hospitalizations and ambient $PM_{2.5}$ was based on the case-crossover design, which is an adaptation of the retrospective case-control design.[8,11,12] This approach matches exposures at the time of or shortly before the event of interest with ≥1 periods when the event did not occur (control or referent periods) and evaluates potential excess risk using conditional logistic regression. Details of the use of conditional logistic regression in case-crossover studies with application to air pollution exposure are given elsewhere.[13,14] Because patients with HF serve as their own controls, there is perfect matching on all participant-specific characteristics that do not vary over time; thus, this approach controls for participant-specific risk factors by design. By choosing matching referent periods close in time (before and after the event) and on the same day of the week, the analysis is structured such that time-dependent risk factors including day of week, seasonality, and long-term time trends are also controlled for by design. In this analysis, referent or control period exposures were matched on day of week in the same month and year as the HF hospitalization, resulting in ≤4 control periods per hospitalization event date. The details of this specific time-stratified referent selection approach, and a statistical exposition on why it allows for unbiased conditional logistic regression estimates and avoids bias that can occur due to time trends in air pollution exposure is presented elsewhere.[13,14]

Analyses using all hospitalizations and analyses stratified by gender, age, length of stay, and first HF admissions

Table 3
Percent increase in risk and 95% CIs of HF hospital admission associated with 10 $\mu g/m^3$ $PM_{2.5}$ lagged moving average of 14 days for all admissions, readmissions, and stratified by various subgroups

Variable	All HF Admissions		Readmissions	
	n	% Increase (95% CI)	n	% Increase (95% CI)
All	2,618	13.1 (1.3, 26.2)*	999	32.4 (10.7, 58.4)†
Men	1,495	13.4 (−1.7, 30.7)‡	570	29.2 (2.7, 62.6)*
Women	1,123	12.7 (−5.1, 33.9)	429	41.5 (5.4, 89.9)*
Age <65 yrs	977	3.5 (−13.5, 23.8)	376	−3.1 (−26.5, 27.8)
Age ≥65 yrs	1,641	19.6 (4.0, 37.5)*	623	64.1 (28.6, 109)†
Length of stay 0–2 days	682	24.4 (−0.8, 56.0)‡	244	68.9 (12.5, 154)*
Length of stay 3–7 days	1,395	10.8 (−4.6, 28.7)	528	35.7 (5.9, 73.9)*
Length of stay 8+ days	541	6.5 (−15.9, 34.8)	227	2.6 (−28.5, 47.1)
First HF admissions	1,619	2.1 (−11.3, 17.5)	—	—
Subsequent HF admits	999	32.4 (10.7, 58.4)†	—	—

* p <0.05.
† p <0.01.
‡ p <0.10.

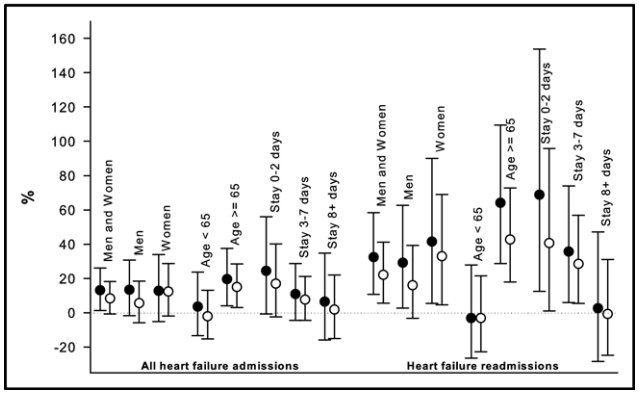

Figure 2. Percent increase in risk and 95% CIs of HF admissions and readmissions associated with 10 $\mu g/m^3$ of $PM_{2.5}$ lagged moving average of 14 days stratified by gender, age, and length of hospital stay. Closed and open circles are estimates from models including and excluding weather variables, respectively.

versus readmissions were conducted. $PM_{2.5}$ concentrations for different lag structures, including concurrent day and lagged moving average concentrations ≤28 days (including the concurrent day), were evaluated. To control for weather variables, the 14-day lagged moving average (including concurrent day and previous 13 days) of temperature, dew point temperature, and barometric pressure (as both linear and quadratic terms) were included in the conditional logistic regression models.

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

Results

A summary of the $PM_{2.5}$ concentration data and basic descriptive information regarding the HF hospitalizations is provided in Tables 1 and 2, respectively. Figure 1 presents risk estimates of $PM_{2.5}$ for different lag structures. The strongest associations were with 14-day or 21-day lagged moving average $PM_{2.5}$ concentrations. Although the 21-day lagged moving average has slightly larger point estimates of the risk effect estimates, the 14-day lagged moving average had the strongest statistical associations based on largest effect estimate relative to standard error of the estimate and lowest p value. Increased risk was not significantly associated with concurrent-day or previous-day concentrations of $PM_{2.5}$.

Table 3 lists the percent increased risk and 95% CI of HF hospital admission associated with 10 $\mu g/m^3$ $PM_{2.5}$ lagged moving average of 14 days for all admissions and admissions stratified by various subgroups. When all admissions were included in the analysis, statistically significant associations between $PM_{2.5}$ and HF admissions were observed. The $PM_{2.5}$ effect estimates were not significantly different for men versus women. The effect estimates were larger for those >65 years of age versus younger patents, and larger PM effects were observed for those that required shorter hospitalization. Furthermore, the $PM_{2.5}$ effects were seen primarily in patients who had previously been hospitalized for HF. Approximately 38% of the admissions were readmissions. Table 3 also lists the results from analyses that included only admissions of patients who had previously been admitted. Again, in this subset of readmissions, the strongest $PM_{2.5}$ associations were for elderly patients, who required a relatively short period of hospitalization.

Figure 2 presents the $PM_{2.5}$ hospitalization risk estimates and 95% CI from models that included 14-day lagged moving averages for both $PM_{2.5}$ and the weather variables (temperature, dew point temperature, and barometric pressure, as linear and quadratic terms) and from models that did not include the weather variables. The $PM_{2.5}$ risk effect estimates were not highly sensitive to controlling for weather variables in the models but, in general, the inclusion of weather variables resulted in somewhat larger pollution effect estimates.

Discussion

This study indicates that lagged cumulative exposures to $PM_{2.5}$ of 1 to several weeks are significantly associated with increased risk of HF exacerbations, as represented by hospitalization with a primary discharge diagnosis of HF. This

study has both limitations and strengths. Although the study area had a relatively reliable long-term network of PM monitoring sites, missing $PM_{2.5}$ concentration data required some imputation based on existing $PM_{2.5}$, PM_{10}, and air stagnation data. A primary limitation of the case-crossover design used in this study is that it only allows for analysis of relatively short-term $PM_{2.5}$ exposure and its potential to exacerbate existing HF. Nevertheless, this study design provides effect estimates that are not likely due to confounding by age, gender, smoking, or other subject-level characteristics because subjects serve as their own controls and subject-level characteristics are controlled for by design. Similarly, long-term time trends, seasonality, day of week and long-term changes in patient characteristics between multiple events for the same patient are controlled for by matching. Furthermore, it has been demonstrated that the time-stratified referent selection strategy used in this analysis allows for unbiased conditional logistic regression estimates and avoids bias that can occur due to time trends in air pollution exposure.[13,14]

HF associations with PM were also observed in a large daily time-series analysis of $PM_{2.5}$ and cardiovascular and respiratory hospitalizations using a national database constructed from United States Medicare files.[15] A 10 $\mu g/m^3$ increase in concurrent-day $PM_{2.5}$ was associated with a 1.28% (95% CI 0.78 to 1.78) increase in HF admissions. An analysis of PM air pollution and HF hospital admissions for Medicare recipients in 7 cities found a 10 $\mu g/m^3$ increase in concurrent-day PM_{10} associated with a 0.72% (95% CI 0.35 to 1.10) increase in HF admissions.[16] In our analysis, similar effect sizes for concurrent-day $PM_{2.5}$ associations were observed (0.81% and 2.74% increase in all HF admissions and readmissions, respectively), but due to sample size considerations these estimates had much larger CIs (Figure 1) and were not statistically significant. In our analysis, substantially larger $PM_{2.5}$ effects were observed for lagged cumulative exposures of approximately 2 weeks.

The distributed lag structure of approximately 14 days may reflect the importance of cumulative $PM_{2.5}$ exposure and that the onset of symptoms may follow elevated exposure with hospitalization after onset of symptoms related to HF exacerbation. The peaking of the size of the effect estimate at 2 or 3 weeks and then the decline in the estimated effect suggests a trade-off between the importance of cumulative exposure and the proximity in time of exposure. In a previous case-crossover study, we found that short-term exposure to $PM_{2.5}$ was associated with the triggering of acute ischemic heart disease events, especially in patients with underlying coronary artery disease.[8] A much shorter lag structure of approximately 1 to 4 days was observed, suggesting that proximity in time may be more important than long-term cumulative exposure in triggering ischemic events in persons with existing coronary artery disease. Several time-series studies, however, have explored the effects of PM on risk of mortality using longer time scales or extended distributed lags of $\leq$40 days.[17–19] PM mortality effect estimates were larger when time scales longer than a few days were used. A more comprehensive review of the mortality effects of longer term exposures to PM concludes that adverse effects of PM exposure are dependent on both exposure concentrations and length of exposure and longer-term exposures have larger, more persistent cumulative effects than short-term exposures.[19]

An analysis of the American Cancer Society (ACS) prospective cohort, a study of long-term exposure and mortality, reported similar air pollution associations with HF related mortality risk as observed in the present study.[3] Long-term elevated exposure of 10 $\mu g/m^3$ $PM_{2.5}$ was associated with a 13% (95% CI 5 to 21) increased risk of mortality from the cause-of-death grouping that included dysrhythmias, HF, and cardiac arrest. Although they did not focus on HF specifically, the Harvard Six Cities[1,5] and the Women's Health Initiative[7] studies reported larger associations between long-term $PM_{2.5}$ exposure and the risk of cardiovascular disease. The Harvard Six Cities study[5] reported that long-term elevated exposure of 10 $\mu g/m^3$ $PM_{2.5}$ was associated with a 28% (95% CI 13 to 44) increased risk of cardiovascular mortality and the Women's Health Initiative study[7] reported that long-term elevated exposure of 10 $\mu g/m^3$ $PM_{2.5}$ was associated with a 24% (95% CI 9 to 41) increased risk of first cardiovascular event and a 76% (95% CI 25 to 147) increased risk of death from cardiovascular causes.

The mechanisms underlying the link between PM exposure and exacerbation of HF are not fully elucidated. Previous research results linking short-term PM exposures to acute ischemic heart disease events,[8,20] ischemic stroke,[21] electrocardiographic ST-segment depression,[22] increased plasma viscosity,[23] increased circulating markers of inflammation,[24–26] changes in cardiac autonomic function as indicated by various measures of heart rate variability,[26–28] and increased risk of arrhythmias[29,30] are suggestive of potential impacts of PM on HF. More detailed discussions of the pathophysiological or mechanistic pathways that plausibly link PM exposure and cardiopulmonary disease and death are provided elsewhere.[3,4,6] These results, however, suggest that exposure to air pollution may exacerbate HF by triggering decompensation through effects of PM on myocardial ischemia, cardiac autonomic function, and/or arrhythmic effects.

1. Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG, Speizer FE. An association between air pollution and mortality in six US cities. *N Engl J Med* 1993;329:1753–1759.
2. Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002;287:1132–1141.
3. Pope CA III, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D, Godleski JJ. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. *Circulation* 2004;109:71–77.
4. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, Luepker R, Mittleman M, Samet J, Smith SC, Tager I. Air pollution and cardiovascular disease: a statement for healthcare professionals from the expert panel on population and prevention science of the American Heart Association. *Circulation* 2004;109:2655–2671.
5. Laden F, Schwartz J, Speizer FE, Dockery DW. Reduction in fine particulate air pollution and mortality: extended follow-up of the Harvard Six Cities Study. *Am J Respir Crit Care Med* 2006;173:667–672.
6. Pope CA III, Dockery DW. Health effects of fine particulate air pollution: lines that connect. *J Air Waste Manage Assoc* 2006;56:709–742.
7. Miller KA, Sisovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD. Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med* 2007;5:447–458.

8. Pope CA III, Muhlestein JB, May HT, Renlund DG, Anderson JL, Horne BD. Ischemic heart disease events triggered by short-term exposure to fine particulate air pollution. *Circulation* 2006;114:2443–2448.
9. Kfoury AG, French TK, Horne BD, Rasmusson KD, Lappé DL, Rimmasch HL, Roberts CA, Evans RS, Muhlestein JB, Anderson JL, Renlund DG. Incremental survival benefit with better institutional adherence to standardized HF core measures: a performance evaluation study of 2,958 patients. *J Card Fail* 2008;14:95–102.
10. US Environmental Protection Agency. Revised requirements for the designation of reference and equivalent methods for $PM_{2.5}$ and ambient air quality surveillance for particulate matter; final rule. *Fed Reg* 1997;62:5725–5726.
11. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991;133: 144–153.
12. Maclure M, Mittleman MA. Should we use a case-crossover design? *Annu Rev Public Health* 2000;21:193–221.
13. Janes H, Sheppard L, Lumley T. Overlap bias in the case-crossover design, with application to air pollution exposures. *Statist Med* 2005; 24:285–300.
14. Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiology* 2005;16:717–726.
15. 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 disease. *JAMA* 2006;295:1127–1134.
16. Wellenius GA, Schwartz J, Mittleman MA. Particulate air pollution and hospital admissions for congestive heart failure in seven United States cities. *Am J Cardiol* 2006;97:404–408.
17. Dominici F, McDermott A, Zeger SL, Samet JM. Airborne particulate matter and mortality: timescale effects in four U.S. cities. *Am J Epidemiol* 2003;157:1055–1065.
18. Zanobetti A, Schwartz J, Samoli E, Gryparis A, Touloumi G, Peacock J, Anderson RH, LeTertre A, Bobros J, Celko M, Goren A, Forsberg B, et al. The temporal pattern of respiratory and heart disease mortality in response to air pollution. *Environ Health Perspect* 2003;111:1188–1193.
19. Pope CA III. Mortality effects of longer term exposures to fine particulate air pollution: review of recent epidemiological evidence. *Inhalation Toxicology* 2007;19(Suppl 1): 33–38.
20. Zanobetti A, Schwartz J. The effect of particulate air pollution on emergency admissions for myocardial infarction: a multicity case-crossover analysis. *Environ Health Perspect* 2005;113:978–982.
21. Wellenius GA, Schwartz J, Mittleman MA. Air pollution and hospital admissions for ischemic and hemorrhagic stroke in medicare beneficiaries. *Stroke* 2005;36:2549–2553.
22. Gold DR, Litonjua AA, Zanobetti A, Coull BA, Schwartz J, MacCallum G, Verrier RL, Nearing BD, Canner MJ, Suh H, Stone PH. Air pollution and ST-segment depression in elderly subjects. *Environ Health Perspect* 2005;113:883–887.
23. Peters A, Doring A, Wichmann H-E, Koenig W. Increase plasma viscosity during an air pollution episode: a link to mortality? *Lancet* 1997;349:1582–1587.
24. 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.
25. Rückerl R, Ibald-Mulli A, Koenig W, Schneider A, Woelke G, Cyrys J, Heinrich J, Marder V, Frampton M, Wichmann HE, Peters A. Air pollution and markers of inflammation and coagulation in patients with coronary heart disease. *Am J Respir Crit Care Med* 2006;173:432–441.
26. Pope CA, Hansen ML, Long RW, Nielsen KR, Eatough NL, Wilson WE, Eatough DJ. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. *Environ Health Perspect* 2004;112:339–345.
27. Liao D, Duan Y, Whitsel EA, Zheng Z, Heiss G, Chinchilli VM, Lin H-M. Association of higher levels of ambient criteria pollutants with impaired cardiac autonomic control: a population-based study. *Am J Epidemiol* 2004;159:768–777.
28. Schwartz J, Park SK, O'Neill MS, Vokonas PS, Sparrow D, Weiss ST, Kelsey K. Glutathione-S-Transferase M1, obesity, statins, and autonomic effects of particles. *Am J Respir Crit Care Med* 2005;172: 1529–1533.
29. Peters A, Liu E, Verrier RL, Schwartz J, Gold DR, Mittleman M, Baliff J, Oh JA, Allen G, Monahan K, Dockery DW. Air pollution and incidence of cardiac arrhythmia. *Epidemiol* 2000;11:11–17.
30. Dockery DW, Luttmann-Gibson H, Rich DQ, Link MS, Mittleman MA, Gold DR, Koutrakis P, Schwartz JD, Verrier RL. Association of air pollution with increased incidence of ventricular tachyarrhythmias recorded by implanted cardioverter defibrillators. *Environ Health Perspect* 2005;113:670–674.