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Research Report 183

Development of Statistical Methods for Multipollutant Research

Part 2. Development of Enhanced Statistical Methods for Assessing Health Effects Associated with an Unknown Number of Major Sources of Multiple Air Pollutants

E.S. Park et al.

Appendix A. Literature Review on Studies that Evaluated the Effects of Short-Term Exposures to Air Pollution ($PM_{2.5}$ or VOCs) on Mortality (or morbidity) from Specific Cardiovascular Diseases and Respiratory Diseases

Note: Appendices available only on the Web have been reviewed solely for spelling, grammar, and cross-references to the main text. They have not been formatted or fully edited by HEI.

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APPENDIX A: LITERATURE REVIEWS

Literature Review on Studies that Evaluated the Effects of Short-Term Exposures to Air Pollution ($PM_{2.5}$ or VOCs) on Mortality (or morbidity) from Specific Cardiovascular Diseases and Respiratory Diseases

A literature review was performed to identify studies that evaluated the effects of short-term exposures to air pollution ($PM_{2.5}$ or VOCs) on mortality (or morbidity) from specific cardiovascular diseases and respiratory diseases, as well as studies that examined associations between source-specific exposures and adverse health effects (presented in the Investigators' Report Introduction). See Table A.1 for a summary of studies that evaluated associations between short-term effects of particulate matter and specific cardiovascular or respiratory causes of mortality. A summary of studies that have evaluated associations between VOC exposures and adverse health effects appears in Table A.2.

Effects of Short-Term Exposures to Air Pollution on Mortality (or Morbidity) from Specific Cardiovascular Diseases and Respiratory Diseases

<u>Particulate Matter</u>

There is evidence of associations between increased daily mortality and ambient air pollution. The focus of much of this research has been on particulate matter (PM), although gaseous air pollutants such as nitrogen oxides and ozone have been implicated as well (Brook et al. 2004). Most studies have evaluated deaths from all causes (excluding deaths from accidental causes), deaths from cardiopulmonary diseases, or deaths from cardiovascular or respiratory diseases (for example, see the study by Samet and colleagues [2000]). There is, however, a growing literature that has begun to investigate effects of air pollution on specific cardiovascular or respiratory causes of mortality (see Table A.1).

For cardiovascular diseases, associations with PM have been investigated for myocardial infarction (Rossi et al. 1999; Braga et al. 2001; Sharovsky et al. 2004; Zeka et al. 2005, 2006; Ueda et al. 2009; Zanobetti and Schwartz 2009), ischemic heart diseases (Zeka et al. 2005; Schwartz et al. 1996; Klemm et al. 2000; Hoek et al. 2001; Wong et al. 2002; Klemm and Mason 2003; Forastiere et al. 2005; Ostro et al. 2006; Vichit-Vadakan et al. 2008; Revich and Shaposhnikov 2010; Tsai et al. 2010), heart failure (Rossi et al. 1999; Zeka et al. 2005; Ueda et al. 2009; Hoek et al. 2001), cardiac arrhythmia and conduction disorders (Zeka et al. 2005; Ueda et al. 2009; Hoek et al. 2001; Vichit-Vadakan et al. 2008; Fischer et al. 2003), embolism and thrombosis (Hoek et al. 2001) and stroke (Zeka et al. 2005, 2006; Zanobetti and Schwartz 2009; Wong et al. 2002; Vichit-Vadakan et al. 2008; Revich and Shaposhnikov 2010; Tsai et al. 2010; Hong et al. 2002a; Hong et al. 2002b; Kan et al. 2003; Franklin et al. 2007; Qian et al. 2007a; Qian et al. 2007b; Qian et al. 2010; Vidale et al. 2010). For respiratory diseases, associations between ambient air pollution have been investigated for chronic obstructive pulmonary disease (COPD) (Rossi et al. 1999; Braga et al. 2001; Zeka et al. 2005; Schwartz et al. 1996; Klemm et al. 2000; Wong et al. 2002; Klemm and Mason 2003; Vichit-Vadakan et al. 2008; Fischer et al. 2003; Schwartz and Dockery 1992; Xu et al. 1994; Wordley et al. 1997; Tellez-Rojo et al. 2000; Xu et al. 2000; Kan and Chen 2003; Wong et al. 2009), asthma (Vichit-Vadakan et al. 2008), pneumonia (Braga et al. 2001; Zeka et al. 2005; Schwartz et al. 1996; Klemm et al. 2000; Wong et al. 2002; Klemm and Mason 2003; Fischer et al. 2003; Schwartz and Dockery 1992; Wordley et al. 1997; Hoek et al. 2000), and influenza (Wong et al. 2002). There is also evidence of greater effects of air pollution among susceptible population groups, including elderly people and people with COPD (Fischer et al. 2003; Garcia-Aymerich et al. 2000; Sunyer et al. 2000).

To support the epidemiologic findings of adverse cardiovascular effects due to air pollution, pathophysiological pathways have been posited to explain the biological mechanisms that may explain the link between air pollutants (especially particulates) and cardiovascular diseases (Brook et al. 2004; Brook 2008; Pope and Dockery 2006). Two such mechanisms, for example, involve alteration of the autonomic nervous system that may affect heart rate rhythm and result in arrhythmia, or induce a plaque rupture and lead to thrombosis and myocardial infarction. Air pollutant risks of heart rhythm effects (Gold et al. 2000) and myocardial infarction (D'Ippoliti et al. 2003; Peters et al. 2001) have been reported in the epidemiologic literature as well. Several biological mechanisms have also been proposed for respiratory health effects due to exposure to ambient air pollutants and involve pro-inflammatory and cellular oxidative stress pathways (Kelly 2003; Seaton et al. 1995).

Volatile Organic Compounds (VOCs)

In contrast to the expanding literature that has investigated effects of PM, only one study (Tsai et al. 2010), to our knowledge, has evaluated VOCs and risks of mortality (and, in that study allcause mortality, as well as mortality from cardiovascular diseases, cerebrovascular diseases, ischemic heart diseases and stroke were investigated). Despite the paucity of mortality studies, investigations have been conducted to evaluate adverse health effects, primarily effects on the respiratory system, that are associated with short-term VOC exposures (see Table A.2). For example, a pair of studies conducted in Drammen, Norway evaluated associations with hospital admissions for respiratory diseases (Hagen et al. 2000; Oftedal et al. 2003). Additionally, Elliott and colleagues (2006) and Arif and Shah (2007) used data from the National Health and Nutrition Examination Survey (NHANES) to examine associations between VOCs and reduced pulmonary function and asthma, respectively. Additionally, a controlled chamber experiment evaluated VOC effects on lung function and neurobehavioral performance among adult women (Fiedler et al. 2005), and a panel study assessed the relationships between ambient air levels of VOCs and exacerbation of asthma symptoms among Hispanic children (Delfino et al. 2003ab).

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Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	**Location/Yrs**	**Specific Causes of Death**	**Deaths/day**	**Pollutants**	**Model**	**Confounders and Effect Modifiers**	**Measure of Association**	**Comments**
Braga et al. 2001	10 U.S. cities 1986–1993	Cardiovascular (CVD) (ICD-9: 390–429) Pneumonia (PN) (ICD-9: 480–487) Chronic Obstructive Pulmonary Disease (COPD) (ICD-9: 490–496) Myocardial Infarction (MI) (ICD-9: 410)	Range in daily means of deaths across cities Total: 6.0–133.4 deaths/day Pneumonia: 0.3–5.0 deaths/day COPD: 0.4–4.1 deaths/day CVD: 1.6–48.4 deaths/day MI: 0.5–15.2 deaths/day	PM_{10}	Generalized additive model (GAM) Poisson regression with lag 0, 2-day moving average (0- and 1-day lag), and 7-day distributed-lag model	LOESS smoother for time, temperature, relative humidity, barometric pressure on the same day, previous day's temperature, and the day-of-the-week.	% increase in mortality per 10 µg/m^3 increase of PM_{10} for distributed-lag model: PN: 2.7 (1.5–3.9) COPD: 1.7 (0.1–3.3) CVD: 1.0 (0.6–1.4) MI: 0.6 (0.0–1.2)	Results also reported using lag 0 and 2-day moving average
Fischer et al. 2003	The Netherlands 1986–1994	Total deaths Pneumonia (ICD-9: 480–486) Chronic obstructive lung diseases (ICD-9: 490–496) Cardiovascular diseases (ICD-9: 390–448)	330 deaths/day	PM_{10}, SO_2, CO, O_3, NO_2	GAM Poisson regression model	Long-term and seasonal trend, influenza epidemics, ambient temperature, ambient relative humidity, and indicator variables for day-of-the-week and holidays LOESS smoother was used EMM by age group	RR for differences between the 1st and 99th percentile (80 µg/m^3 for PM_{10}) (lag 0–6 days) CVD: < 45 yr: 0.906 (0.728–1.128) 45–64 yr: 1.023 (0.945–1.106) 65–74 yr: 1.002 (0.945–1.062) ≥ 75 yr: 1.016 (0.981–1.052) COPD: < 45 yr: 1.153 (0.587–	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	Location/Yrs	Specific Causes of Death	Deaths/day	Pollutants	Model	Confounders and Effect Modifiers	Measure of Association	Comments
							2.268) 45–64 yr: 1.139 (0.841–1.541) 65–74 yr: 1.166 (0.991–1.372) ≥ 75 yr: 1.066 (0.965–1.178) Pneumonia: < 45 yr: 1.427 (0.806–2.525) 45–64 yr: 1.712 (1.042–2.815) 65–74 yr: 1.240 (0.879–1.748) ≥ 75 yr: 1.123 (1.011–1.247)	
Forastiere et al. 2005	Rome, Italy 1998–2000	Ischemic Heart Disease (ICD-9: 410–414) (restricted to out-of hospital coronary deaths)		Particle number concentra-tion (PNC), PM_{10}, CO, NO_2, O_3	Case-crossover analysis	Time and meteorological variables	% increase in mortality per interquartile range (Lag 0 model) PNC (IQR = 27,790 particles/cm^3): 7.6 (2.0–13.6) PM_{10} (IQR = 29.7µg/m^3): 4.8 (0.1–9.8)	Results also reported for Lag 1, 2, 3, and 0–1 models
Franklin et al. 2007	27 U.S. communities 1997–2002	Nonaccidental causes (ICD-9 ≥ 800; ICD-10: V01–Y98) Respiratory	Range in % of all cause mortality across communities Respiratory: 6.9–12.0%	$PM_{2.5}$	Time-stratified case-crossover design in each community followed by a meta-analysis	Confounders: temperature, day-of-the-week	% increase per 10 µg/m^3 increase of $PM_{2.5}$ Lag 1 model	Results also reported for Lag 0, and Lag 0–1 models and stratified on the basis of age,

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	**Location/Yrs**	**Specific Causes of Death**	**Deaths/day**	**Pollutants**	**Model**	**Confounders and Effect Modifiers**	**Measure of Association**	**Comments**
		diseases (ICD-9: 460–519; ICD-10: J00–J99) Cardiovascular diseases (ICD-9: 390–429; ICD-10: I01–I52) Stroke (ICD-9: 430–438; ICD-10: I60–J69)	Cardiovascular: 26.1–38.0% Stroke: 4.0–9.0%		of effect estimates and their standard errors		Allcause: 1.21 (0.29–2.14) Respiratory: 1.78 (0.20–3.36) Cardiovascular: 0.94 (–0.14 to 2.02) Stroke: 1.03 (0.02–2.04)	sex, East vs. West, attainment of the NAAQS and prevalence of air conditioning prevalence
Goldberg et al. 2001	Montreal, Quebec, Canada 1984–1993	Coronary artery disease (ICD-9: 410–414) Diabetes (ICD-9: 250) Other specific causes of death (nonrespiratory or noncardiovascular)	Coronary artery disease: 9.4 deaths/day Diabetes: 1.0 death/day	$PM_{2.5}$, PM_{10}, Predicted $PM_{2.5}$ and fine sulfate particles TSP, Coefficient of Haze, extinction coefficient, total sulfate	Log-linear Poisson model	LOESS smoothers for day-of-the-week, and year, weather variables	Mean percentage change in daily mortality across the interquartile range (IQR) Lag 0 results for coronary artery disease TSP: (IQR = 28.57 µg/m^3): 2.58 (–1.09 to 6.38) PM_{10}: (IQR = 21.32 µg/m^3): 0.13 (–3.31 to 3.69) $PM_{2.5}$: (IQR = 12.51 µg/m^3): 0.85 (–2.61 to 3.96)	Results also reported for lag 1 and 3-day mean models

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	Location/Yrs	Specific Causes of Death	Deaths/day	Pollutants	Model	Confounders and Effect Modifiers	Measure of Association	Comments
							Lag 0 results for diabetes TSP: 0.99 (–9.31 to 12.45) PM_{10} and $PM_{2.5}$ – no change	
Goldberg et al. 2006	Montreal, Quebec, Canada 1984-1993	Diabetes Mellitus (ICD-9 code 250) among persons 65 yrs of age and older	Diabetes: 3,677 deaths	$S0_s$, NO_2, CO, O_3, Coefficient of Haze, Extinction, Predicted $PM_{2.5}$, Sulfate, Predicted sulfate from $PM_{2.5}$	Log-linear Poisson model with natural splines for continuous covariates	Confounders: Long-term temporal trends and daily weather conditions	% increase in daily mortality per interquartile range of predicted PM_{25} Lag 0 results: Predicted $PM_{2.5}$: 4.66 (–0.49 to 10.07)	Results also reported for lag 1- and 3-day mean models
Hoek et al. 2000	The Netherlands 1986–1994	Total deaths Pneumonia (ICD-9: 480–486) Chronic obstructive lung diseases (ICD-9: 490–496) Cardiovascular diseases (ICD-9: 390–448)	Median no. of deaths per day Total: 328 deaths/day CVD: 140 deaths/day COPD: 15 deaths/day Pneumonia: 9 deaths/day	PM_{10}, SO_2, CO, O_3, NO_2, Black Smoke (BS)	GAM Poisson regression model	Long-term and seasonal trend, influenza morbidity counts, ambient temperature, relative humidity, and indicator variables for day-of-the-week and holidays LOESS smoother was used	RR for differences between the 1st and 99th percentile (100 $\mu g/m^3$ for PM_{10}) Lag 1 results: Total: 1.018 (1.003–1.034) CVD: 1.015 (0.987–1.043) COPD: 1.096 (1.014–1.185)	Results for total mortality also reported for the 4 major cities, and Netherlands w/o major cities and by seasonal trend

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	Location/Yrs	Specific Causes of Death	Deaths/day	Pollutants	Model	Confounders and Effect Modifiers	Measure of Association	Comments
							Pneumonia: 1.167 (1.058–1.287) Weekly avg (Lag 0–6) Total: 1.023 (1.004–1.041) CVD: 1.015 (0.987–1.043) COPD: 1.096 (1.014–1.185) Pneumonia: 1.167 (1.058–1.287)	
Hoek et al. 2001	The Netherlands 1986–1994	Total CVD mortality (ICD-9: 390–448) Myocardial Infarction and other ischemic diseases (IHD) (ICD-9: 410–414) Cardiac arrhythmia (ICD-9: 427) Heart failure (HF) (ICD-9: 428) Cerebrovascular disease (ICD-9: 430–436)	Cardiovascular causes: 142 deaths/day IHD: 62.0 deaths/day Cardiac arrhythmia: 7.1 deaths/day HF: 13.8 deaths/day Cerebrovascular disease: 27.8 deaths/day Embolism and Thrombosis: 6.2 deaths/day	PM_{10}, CO, Black smoke, Ozone, SO_2, NO_2	GAM Poisson regression model	Adjustment for long-term and seasonal trends, influenza epidemics, ambient temperature and relative humidity, day-of-the-week, and holidays	Relative risks per 80 µg/m^3 for PM_{10} (7-day moving average) Total CVD: 1.012 (0.98–1.041) MI and other IHD: 1.005 (0.964–1.048) Cardiac arrhythmia: 1.041 (0.932–1.163) HF: 1.036 (0.960–1.118) Cerebrovascular disease: 1.031 (0.971–1.094)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	Location/Yrs	Specific Causes of Death	Deaths/day	Pollutants	Model	Confounders and Effect Modifiers	Measure of Association	Comments
		Embolism and Thrombosis (ICD-9: 415.1 433, 434, 444, 452, 453)					Embolism and Thrombosis: 1.010 (0.894–1.143)	
Hong et al. 2002b	Seoul, Korea 1991–1997	Hemorrhagic stroke (ICD-9: 431 and ICD-10: I61) Ischemic stroke (ICD-9: 434 and ICD-10: I63)	Hemorrhagic stroke: 4.6 deaths/day Ischemic stroke: 2.8 deaths/day	TSP, SO_2, NO_2, O_3, CO	GAM Poisson regression	Control tor time trends, day-of-the-week, same-day and previous-day temperature, relative humidity, atmospheric pressure; LOESS function of time; autoregressive terms in the model Lagged day exposures of up to 4 days were examined	RR for each interquartile range increase in TSP on the same day (51.69 $\mu g/m^3$) Ischemic stroke mortality: 1.03 (1.00–1.06) Hemorrhagic stroke: 1.04 (1.02–1.07)	Results reported for the adjusted models (adjusted for other pollutants, one at a time)
Hong et al. 2002a	Seoul, Korea 1995–1998	Stroke (ICD-10: code I60–I69)	Males – 7.3 deaths/day Females – 8.0 deaths/day	PM_{10}, SO_2, NO_2, O_3, CO	GAM Poisson regression	Control tor seasonal and long-term trends, day-of-the-week, same-day and previous-day temperature, relative humidity, barometric pressure; indicator variables for day-of-the-week; LOESS function of time; autoregressive terms in the model Pollutants added to the	% increase in stroke mortality per interquartile range increase in PM_{10} (same day) All: 1.5 (1.3–1.8) Males: –0.1 (–3.2 to 3.1) Females: 2.4 (–0.6 to 5.5) < 65 yr: –0.1 (–3.6 to 3.5)	Results reported for PM_{10}, stratified by other pollutants

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	Location/Yrs	Specific Causes of Death	Deaths/day	Pollutants	Model	Confounders and Effect Modifiers	Measure of Association	Comments
						model using a LOESS smoothing function (GOF using AIC) Lagged day exposures of up to 5 days were examined EMM by age (< 65, ≥ 65) and sex	≥ 65 yr: 2.1 (–0.6 to 4.9)	
Kan and Chen 2003	Shanghai, China 2000–2001	Total nonaccidental causes (ICD-9 < 800) Cardiovascular disease (ICD-9: 390–459) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–496)	Nonaccidental: 112.02 deaths/day Cardiovascular: 39.09 deaths/day COPD: 10.71 deaths/day	PM_{10}, SO_2, NO_2	GAM with log link and Poisson error	Smoothing terms for day, temperature, humidity, dew point, and dummy variables for days of the week	Relative Risks per 10 μg/m^3 increase of PM_{10} (lag 0 model) Total: 1.003 (1.001–1.005) Cardiovascular diseases: 1.003 (1.000–1.006) COPD: 1.005 (0.999–1.011)	Results also reported stratified by age (< 65, 65–75, > 75 yr)
Kan et al. 2003	Shanghai, China 2001–2002	Stroke (ICD-9: 430–438)	Stroke: 2,426 stroke deaths Stroke: 3.32 deaths/day	PM_{10}, SO_2, NO_2	GAM	Day-of-the-week Smoothing spline functions for trend, temp, relative humidity, dew point.	Relative risk per 10 μg/m^3 increase of PM_{10} 1.008 (1.000–1.016)	Results also reported for models adjusted for SO_2 or NO_2, or both
Klemm et al. 2000 Reanalysis of data reported by (Schwartz et al. 1996)	Watertown, MA; Kingston-Harriman, TN; St. Louis, MO; Steubenville,	Total nonaccidental mortality (ICD-9 < 800) Ischemic heart disease (IHD) (ICD-9: 410–414)	All causes: 3.0 deaths/day to 58.6 deaths/day COPD: 0.1 deaths/day to 1.7 deaths/day	$PM_{2.5}$, CM, PM_{15} or PM_{10}, SO_4	GAM Poisson regression	Loess smoothing for average daily temperature, average daily dew point temperature, and study date (time)	Increase in mortality per 10 μg/m^3 increase of PM (2-day mean) Combined estimate across cities	Results also reported separately by city

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Study	**Location/Yrs**	**Specific Causes of Death**	**Deaths/day**	**Pollutants**	**Model**	**Confounders and Effect Modifiers**	**Measure of Association**	**Comments**
	OH; Portage, WI; Topeka, KS 1979–late 1980's	Pneumonia (ICD-9: 480–486) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–496)	IHD: 1.0 deaths/day to 18.6 deaths/day Pneumonia: 0.1 deaths/day to 2.4 deaths/day				All-causes PM_{10}: 0.8% (0.5–1.0) $PM_{2.5}$: 1.3% (0.9–1.7) CM: 0.4% (–0.2 to 1.9) IHD PM_{10}: 1.1% (0.6–1.6) $PM_{2.5}$: 2.0% (1.3–2.7) CM: 0.6% (–0.3 to 1.6) COPD PM_{10}: 1.2% (–0.4 to 2.8) $PM_{2.5}$: 2.0% (–0.3 to 4.2) CM: 1.1% (–1.9 to 4.3) Pneumonia: PM_{10}: 2.5% (1.0–4.1) $PM_{2.5}$: 4.5%: (2.2–6.7) CM: 1.0% (–1.9 to 4.1)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Klemm and Mason, 2003 Reanalysis of (Schwartz et al. 1996) and (Klemm et al. 2000) using a more stringent convergence criteria (for LOESS smoothing models) and models with natural spline smoothers	Watertown, MA; Kingston-Harriman, TN; St. Louis, MO; Steubenville, OH; Portage, WI; Topeka, KS 1979–late 1980’s	Total nonaccidental mortality (ICD-9 < 800) Ischemic heart disease (IHD) (ICD-9: 410–414) Pneumonia (ICD-9: 480–486) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–496)		$PM_{2.5}$, CM, PM_{15} or PM_{10}, SO_4	GAM Poisson regression	Loess smoothing for average daily temperature, average daily dew point temperature, and study date (time) and Natural spline smoothers for long-term trends and weather	Increase in mortality per 10 μg/m^3 increase of PM (2-day mean) Combined estimate across cities All-causes PM_{10}: 0.7% (0.4–1.0) $PM_{2.5}$: 1.2% (0.8–1.6) CM: 0.3% (–0.2 to 1.9) $PM_{2.5}$ IHD: 1.8% (1.1–2.5) COPD: $PM_{2.5}$: 2.3% (0.1–4.5) Pneumonia: 4.1%: (1.9–6.2)	Results also reported separately by city Results also reported for 3 models with natural spline smoothers
Kwon et al. 2001	Seoul, Korea, 1994–1996 (cohort of 7,036 congestive heart failure patients)		2,874 deaths	PM_{10}, CO, NO_2, SO_2, O_3	Case-crossover design	Confounders: temperature, relative humidity, and barometric pressure	Per interquartile range increase of PM_{10} (42.1 μg/m^3) CVD: 1.102 (0.971–1.250) Cardiac deaths: 1.132 (0.978–1.310)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Moolgavkar, 2000	Cook County, IL; Los Angeles (LA) County, CA, Maricopa County, AZ 1987–1995	Cardiovascular deaths (ICD-10: I00–I99) Cardiac deaths (ICD-10: I20–I51)	Median deaths/day Cook Co. CVD: 43 deaths/day CrD: 9 deaths/day COPD: 4 deaths/day LA County: CVD: 57deaths/day CrD: 14deaths/day COPD: 6 deaths/day LA County: CVD: 57deaths/day CrD: 14 deaths/day COPD: 6 deaths/day	CO, NO_2, O_3, SO_2, PM_{10}, $PM_{2.5}$ (LA only)	GAM Poisson regression model	Indicator variables for day of week, spline smoother for temporal trends. Temperature and relative humidity included with lags that minimized deviance. Lags from 0 to 5 days were evaluated.	% excess deaths per 50 μg/m^3 of PM_{10}: Lag 0 Cook County: 1.16 (–1.25 to 3.57) Los Angeles County: 1.24 (–2.61 to 5.10) Maricopa County: 3.96 (–2.51 to 10.42)	Results also reported for Lags 1–5, and for copollutant model (PM_{10} and O_3)
Ostro et al. 2006	Nine CA counties 1999–2002	Respiratory disease (ICD-10: J00 to J98) Cardiovascular disease (ICD-10: I00–I99) Ischemic heart disease (ICD-10: I20–I25) Diabetes (ICD-10: E10–E14)	Range in the mean deaths across counties Cardiovascular disease: 4.9 to 67.0 deaths per day Ischemic heart disease: 3.1 to 42.6 deaths per day Respiratory disease: 1.4 to 15 deaths per day	$PM_{2.5}$	Poisson regression with both penalized and natural spline models with 2-day average of lags 0 and 1 and a single day lag of 2 days	EM by sex, race/ethnicity, educational level, deaths in and out of hospitals Confounders: CO, NO_2, ozone, day-of-the-week Smoothing splines of 1-day lags of average temperature and humidity (each with 3 *df*)	% change per 10 μg/m^3 increase in $PM_{2.5}$ using penalized splines All cause: 0.6 (0.2–1.0) Cardiovascular: 0.6 (0.0–1.1) Respiratory: 2.2 (0.6–3.9) Ischemic heart disease: 0.3 (–0.5 to 1.0) Diabetes: 2.4 (0.6–4.2)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Qian et al. 2007	Wuhan, China 2001–2004	Nonaccidental mortality (ICD-9: 1–799 or ICD-10: A00–R99) Cardiovascular (ICD-9: 390–459 or ICD-10: I00–I99) Stroke: (ICD-9: 430–438; ICD-10: I60–I69) Cardiac diseases: (ICD-9: 390–398, 410-429 or ICD-10: I00–I09, I20–I52) Respiratory diseases: (ICD-9: 460–519 or ICD-10: J00–J98) Cardiopulmonary (Cardiovascular and Respiratory) (ICD-9: 460–519 or ICD-10: J00–J98 and ICD-9: 390–459 or ICD-10: I00–I99)	Mean no. of deaths per day Nonaccidental: 61.0 deaths/day Cardiovascular: 27.8 deaths/day Stroke: 17.5 deaths/day Cardiac: 8.3 deaths/day Respiratory: 7.0 deaths/day Cardiopulmonary 34.9 deaths/day	PM_{10}, SO_2, NO_2, O_3	GAM Poisson regression model	EMM by age group (< 45 vs ≥ 45 and < 65 vs ≥ 65 yrs) Confounders: day-of-the-week, time trends, indicator variables for hot days, cold days, and humid days and natural or penalized splines for temperature, and humidity, respectively	% change per 10 μg/m^3 increase in PM_{10} (lag 0 model results) Nonaccidental: 0.36 (0.19–0.53) Cardiovascular: 0.51 (0.28–0.75) Stroke: 0.44 (0.16–0.72) Cardiac: 0.49 (0.08–0.89) Respiratory: 0.71 (0.20–1.23) Cardiopulmonary: 0.46 (0.23–0.69)	Results reported for Lag 0, Lag 1, 2-day mean, 5-day mean models Results also reported by age group

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Qian et al. 2008	Wuhan, China July, 2000–2004	Nonaccidental mortality (ICD-9: 1–799 or ICD-10: A00–R99) Cardiovascular (ICD-9: 390–459 or ICD-10: I00–I99) Stroke: (ICD-9: 430–438; ICD-10: I60–I69) Cardiac diseases: (ICD-9: 390–398 or ICD-10: 410–429) Respiratory diseases: (ICD-9: 460–519 or ICD-10: J00–J98) Cardiopulmonary diseases: (ICD-9: 390–459 and 460–519 or ICD-10: I00–I99 and J00–J98)	Nonaccidental: Normal temp: 59.82 deaths/day Low temp: 79.99 deaths/day High temp: 63.37 deaths/day Cardiovascular: Normal temp: 27.14 deaths/day Low temp: 38.56 deaths/day High temp: 29.10 deaths/day Stroke: Normal temp: 17.14 deaths/day Low temp: 23.47 deaths/day High temp: 17.81 deaths/day Cardiac: Normal temp: 8.09 deaths/day Low temp: 12.30 deaths/day High temp: 8.68 deaths/day Respiratory: Normal temp: 6.76 deaths/day Low temp: 12.25 deaths/day	PM_{10}, SO_2, NO_2, O_3	GAM Poisson regression model	Indicators for day-of-the-week, natural or penalized splines for time trends, factor variable for three periods (peaks of death; indicator variables for hot and cold days, and humid days	% change in daily mortality per 10 µg/m^3 increase in PM_{10} Nonaccidental: Normal: 0.36 (0.17–0.56) Low: 0.62 (–0.09 to 1.34) High: 2.20 (0.74–3.68) Cardiovascular: Normal: 0.39 (0.11–0.66) Low: 0.72 (–0.25 to 1.70) High: 3.28 (1.24–5.37) Stroke: Normal: 0.38 (0.06–0.70) Low: 0.67 (–0.50 to 1.85) High: 2.35 (–0.03 to 4.78) Cardiac: Normal: 0.32 (–0.14 to 0.79) Low: 0.50 (–1.10 to 2.13) High: 3.31 (–0.22 to 6.97) Respiratory: Normal: 0.80 (0.25–1.35)	Results also reported for other pollutants, and by age (< 65 and ≥ 65 yrs)

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

			High temp: 6.84 deaths/day Cardiopulmonary Normal temp: 33.90 deaths/day Low temp: 50.81 deaths/day High temp: 35.93 deaths/day				Low: 1.07 (–0.76 to 2.95) High: 1.15 (–3.54 to 6.07) Cardiopulmonary: Normal: 0.45 (0.19–0.70) Low: 0.69 (–0.22 to 1.61) High: 3.02 (1.03–5.04)	
Qian et al. 2010	Wuhan, China 2001–June, 2004	Nonaccidental mortality (ICD-9: 1–799 or ICD-10: A00–R99) Cardiovascular (ICD-9: 390–459 or ICD-10: I00–I99) Stroke: (ICD-9: 430–438; ICD-10: I60–I69) Respiratory diseases: (ICD-9: 460–519 or ICD-10: J00–J98)		PM_{10}, SO_2, NO_2, O_3	GAM Poisson regression model	EMM by season Confounders: day-of-the-week, two peaks of mortality, extreme cold weather, extreme hot weather, extreme humid weather, smoothers for time, daily mean temperature, daily mean relative humidity, and local smoothing over two peaks of mortality and remaining period, indicators for seasons	% change per 10 μg/m^3 increment in PM_{10} (lag 0–1 model) All-natural: Sp: 0.34 (0.00–0.69) Su: 0.45 (–0.13 to 1.04) Fall: –0.21 (–0.54 to 0.12) Winter: 0.69 (0.44–0.94) Cardiovascular: Sp: 0.29 (–0.2 to 0.77) Su: 0.59 (–0.21 to 1.4) Fall: –0.48 (–0.94 to –0.02) Winter: 0.85 (0.51–1.19) Stroke: Sp: 0.14 (–0.43 to 0.71) Su: 0.18 (–0.77 to 1.14) Fall: –0.54 (–1.07 to 0.00)	Results reported for Lag 0, Lag 1, 2-day mean, 5-day mean models Results also reported by age group

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

							Winter: 1.02 (0.60–1.43) Respiratory: Sp: 0.74 (–0.30 to 1.80) Su: 0.41 (–1.53 to 2.38) Fall: 0.46 (–0.57 to 1.51) Winter: 0.99 (0.32–1.66)	
Revich and Shaposhnikov 2010	Moscow, Russia 2003–2005	Nonaccidental causes (ICD-10: V00–Y98) Ischemic heart disease and angina pectoris (ICD-10: I20–I25) Cerebrovascular diseases (ICD-10: I60–I69)	Nonaccidental causes: 331.2 deaths/day Ischaemic heart disease: 114.5 deaths/day Cerebrovascular diseases: 68.8 deaths/day	PM_{10} and O_3	Generalize linear bivariate model	Daily air temperature and temporal trends	% change per 10 µg/m^3 increment in PM_{10} (same day) Nonaccidental causes: 0.33 (0.09–0.57) Ischemic heart disease: 0.66 (0.30–1.02) Cerebrovascular diseases: 0.48 (0.02–0.94)	Results also reported for persons ages 75+
Rossi et al. 1999	Milan, Italy 1980–1989	All causes day (ICD-9: 1–799) Myocardial infarction (ICD-9: 410) Heart failure (ICD-9: 428) Respiratory Infections (ICD-9: 480–486, 466)	All causes: 31.9 deaths/day Cardiac causes: 4 deaths/day	TSP, SO_2 NO_2	GAM Poisson regression model	LOESS function to model season, weather, and humidity; indicator variables for hot days Nonparametric smooth function of TSP concentration	% increase in mortality per increase of 100 µg/m^3 of TSP MI: 10% (3 to 18%) for mean TSP levels 3 and 4 days prior to death Heart failure: 7% (3 to 11%) on the concurrent day Respiratory Infections: 11% (5 to 17%) on the	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

		COPD (ICD-9: 490–496)					concurrent day COPD: 12% (6 to 17%) for mean TSP levels 3 and 4 days prior to death	
Schwartz and Dockery, 1992	Philadelphia, PA 1973–1980	Pneumonia (ICD-9: 480–486 plus 507; ICD-8 480–486) Chronic obstructive pulmonary disease (ICD-9: 490–496, ICD-8 490–493 plus 519.3) Cardiovascular disease (ICD-9: 390–448)	Cardiovascular disease: 22.1 deaths/day Cancer: 10.5 deaths/day Pneumonia: 1.44 deaths/day COPD: 0.89 deaths/day	TSP, SO_2	Poisson regression with GEE	Confounders: Indicator variable for Year, continuous time variable. 24-hr mean temperature, dew-point temperature, indicator variables for hot days, cold days, humid days, and hot and humid days, seasonal indicator variables and interaction terms between season and weather variables were considered as confounders.	Increase in mortality per 100 $\mu g/m^3$ increase in TSP (same day) COPD: 19 % (0–42%) Pneumonia: 11% (−3 to 27%) CVD: 10% (6–14%)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Schwartz et al. 1996	Watertown, MA; Kingston-Harriman, TN; St. Louis, MO; Steubenville, OH; Portage, WI; Topeka, KS 1979–late 1980’s	Total nonaccidental mortality (ICD-9 < 800) Ischemic heart disease (IHD) (ICD-9: 410–414) Pneumonia (ICD-9: 480–486) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–496)	All causes – 3.6 deaths/day to 60.2 deaths/day COPD: 0.1 deaths/day to 1.4 deaths/day IHD: 1.2 deaths/day to 17 deaths/day	PM_{10}, $PM_{2.5}$	GAM Poisson regression model	Confounders; time tends and weather variables	Increase in mortality per 10 µg/m^3 increase of PM (2-day mean) Combined estimate across cities PM_{10} All-cause: 0.8% (0.5–1.1%) $PM_{2.5}$ All cause: 0.4% (–0.1 to 1.0%) CM All cause: 1.5% (1.1–1.9%) $PM_{2.5}$ IHD: 2.1% (1.4–2.8%) COPD: 3.3% (1.0–5.7%) Pneumonia: 4.0% (1.8–6.2%)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Sharovsky et al. 2004	Sao Paulo, Brazil 1996–1998	Myocardial infarction (MI) (ICD-10: I21)	MI: 16.4 deaths/day	PM_{10}, SO_2, CO	GAM Poisson regression model	LOESS for seasonal trend and temperature, relative humidity, atmospheric pressure, day-of-the-week indicators	Regression coefficients and standard errors for PM_{10} ($\mu g/m^3 \times 100$): Single pollutant model: 0.1 (0.1) Multipollutant model: 0.04 (0.08)	
Tellez-Rojo et al. 2000	Mexico City 1994	Total respiratory diseases (ICD-9: 490–496 and ICD-9: 466, 480–487) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–496)	Respiratory diseases: 13.5 deaths/day COPD: 6.3 deaths/day	PM_{10}, O_3	GAM Poisson regression model	Cold or warm months, 1-day lagged minimum temperature EMM: Place of death (outside and inside medical unit)	RR for an increase of 10 $\mu g/m^3$ of PM_{10} Respiratory causes: Outside medical unit Lag 1: 1.0244 (1.0043–1.0448) Avg 3 days: 1.0377 (1.0141–1.0619) Inside medical unit Lag 1: 1.0157 (0.9971–1.0347) Avg 3 days: 1.0200 (1.0010–1.0422) COPD: Outside medical unit Lag 1: 1.0295 (1.0012–1.0585) Avg 3 days: 1.0525 (1.0189–1.0872) Inside medical unit Lag 1: 1.0189 (0.9907–1.0479)	Results also reported for Lags 2–5 and averages of 5 and 7 days

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

							Avg 3 days: 1.0304 (0.9973–1.0647)	
Tsai et al. 2010	Central Taiwan 1993–2006	All cause (ICD-9: 1–800) Cardiovascular (ICD-9: 410–411, 414, 430–437) Ischemic heart diseases (ICD-9: 410–411 and 414) Cerebrovascular diseases (ICD-9: 430–437) Strokes (ICD-9: 430–434)	All-causes: 13.0 deaths/day Cardiovascular: 1.5 deaths/day Ischemic heart disease: 0.5 deaths/day Cerebrovascular: 1.0 deaths/day Stroke: 0.5 deaths/day	NO_2, CO, PM_{10}	GAM Poisson regression model	LOESS for yearly trend, month and temperature	RRs per interquartile range increase of PM_{10} (46.4 µg/m^3) All-cause death Lag 0: 1.011 (1.002–1.020) Lag 1: 1.018 (1.009–1.027) Lag 2: 1.012 (0.9720–1.055) Cardiovascular Lag 0: 1.041(1.015–1.068) Lag 1: 1.036 (1.010–1.063) Lag 2: 1.017 (0.992–1.044) Ischemic heart disease Lag 0: 0.978 (0.934–1.025) Lag 1: 0.983 (0.937–1.030) Lag 2: 1.010 (0.964–1.059) Cerebrovascular disease Lag 0: 1.022 (0.991–1.053) Lag 1: 1.026 (0.995–1.058)	

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

							Lag 2: 1.019 (0.988–1.051) Strokes Lag 0: 1.021 (0.979–1.065) Lag 1: 1.021 (0.980–1.065) Lag 2: 1.012 (0.970–1.055	
Ueda et al. 2009	9 Japanese cities 2002–2004	All heart diseases (ICD-10: I01–I02, I05–I09, I20–I25, I30–I52) Acute MI (AMI) (ICD-10: I21–I22) Heart Failure (HF): (ICD-10: I50) Cardiac arrhythmia and conduction disorders CACD (ICD-10: I44–I49)	67,897 deaths from heart disease Daily mean number of cardiac deaths: range (across cities) from 0.8 to 8.7 deaths/day	$PM_{2.5}$	GAM Poisson regression model	EMM: Age group (0–64 and 65+ yrs) Confounders: ambient temperature, relative humidity, seasonality, and day-of-the-week	% increase in mortality per 10 μg/m^3 of $PM_{2.5}$ Lag 0 model: All heart disease: 1.27 (0.22–2.32) AMI: 1.32 (–0.82 to 3.50) HF: 2.27 (–1.34 to 6.01) CACD: 1.46 (–1.75 to 4.78)	Results reported for Lag 0, Lag 1, Lag 2, 2-day moving average of same day and prior day, moving average of same day, and 1 and 2 days prior
Vichit-Vadakan et al. 2008	Bangkok, Thailand 1999–2003	Cardiovascular (ICD-10: I00–I99) Respiratory (ICD-10: J00–J98) Ischemic Heart Diseases (ICD-10: I20–I25) Stroke (ICD-10:	Deaths/day ± SD Cardiovascular: 13.0 ± 4.3 Respiratory: 8.0 ± 3.1 Ischemic Heart Diseases: 4.0 ± 2.3	PM_{10}	Poisson regression with natural cubic spline models with smoothing for time and weather and control for time trend	EMM: Age (cardiovascular ≥ age 65, Respiratory < age 1, LRI < 5 years, Respiratory > 65) Confounders: time trend, seasonality, temperature, relative humidity, day of week, and public holidays	% excess Risk per 10 μg/m^3 of PM_{10} Cardiovascular: 1.9 (0.8–3.0) Ischemic Heart Disease: 1.5 (–0.4 to 3.5) Stroke: 2.3 (0.6–4.0)	Sensitivity analyses to assess different model specifications (different lags for PM_{10}, various sets of *df* for time and weather, different lags of

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

		I60–I69) Conduction Disorder (ICD-10: I44–I49) COPD (ICD-10: J40–J47) Asthma (ICD-10: J45–J46) Senility (ICD-10: R 54)	Stroke: 5.0 ± 2.5 Conduction Disorder: 1.0 ± 0.5 COPD: 2.0 ± 1.0 Asthma: 1.2 ± 0.4 Senility: 14.0 ± 4.2				Conduction disorders: –0.3 (–5.9 to 5.6) Respiratory: 1.0 (–0.4 to 2.4) COPD: 1.3 (–1.8 to 4.4) Asthma: 7.4 (1.1–14.1) Senility: 1.8 (0.7–2.8)	temperature and relative humidity, penalized splines for time and weather
Vidale et al. 2010	Como, Italy 2000–2003	Ischemic stroke (ICD-9: 433–434)	2.2 ischemic strokes/1000/yr with 23.6% yearly mortality rate	SO_2, NO_2, CO, O_3, PM_{10}	GAM Poisson regression model	Meteorological covariates (not specified)	Positive association between daily mortality and PM_{10} with 5-day delay (*P* < 0.05) (no other result reported)	
Wong et al. 2002	Hong Kong 1995–1998	Cardiovascular diseases (ICD-9: 390–459) Ischaemic Heart Disease (IHD) (ICD-9: 410–414) Cerebrovascular disease (ICD-9: 430–438) Respiratory diseases (ICD-9: 461–519)	All cardiovascular diseases: 23 deaths/day Ischaemic heart disease: 9 deaths/day Cerebrovascular disease: 9 deaths/day All respiratory diseases: 17 deaths/day	NO_2, SO_2, O_3, PM_{10}	Poisson regression model	Confounders: time trend, seasonal variation, temperature and humidity	RRs per 10 µg/m^3 increase of PM_{10} Respiratory diseases (lag 1): 1.008 (1.001–1.014) COPD (lag 0–3 days): 1.017 (1.002–1.033) Pneumonia and influenza (lag 2): 1.007 (0.999–1.015) Cardiovascular diseases (lag 2): 1.003 (0.998–1.008)	Results also reported for a 4 pollutant model

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

		Chronic Obstructive Pulmonary Disease (COPD) (ICD-9: 490–496) Pneumonia and influenza (ICD-9: 480–487)	COPD: 6 deaths/day Pneumonia and influenza: 10 deaths/day				Ischaemic heart disease (lag 0–3): 1.001–1.025) Cerebrovascular disease (lag 2): 1.007 (0.998–1.016)	
Wong et al. 2009	Hong Kong 1996–2002	Cardiovascular diseases (CVD) (ICD-9: 390–459; ICD-10: I00–I99) Respiratory diseases (RD) (ICD-9: 461–519; ICD-10: J00–J98) Chronic Obstructive Pulmonary Disease (COPD) (ICD-9: 490–496; ICD-10: J40–J47) Acute Respiratory Disease (ICD-9: 460–466, 480–487; ICD-10: J00–J05)	Mean deaths/day ± SD RD: 16.2 ± 5.2 COPD: 5.9 ± 2.9 CVD: 23.8 ± 6.5	NO_2, SO_2, PM_{10}, O_3	GAM Poisson regresson model	Indicator variables for day-of-the-week and public holidays, natural spline smoothing functions of daily mean temperature, relative humidity, time trend and seasonality	Excess risks per 10 μg/m^3 (average of lag 0 and lag 1) Baseline effect (assuming no influenza intensity) RD: 0.69 (–0.10 to 1.49) COPD: –0.05 (–1.36 to 1.28) CVD: 0.45 (–0.23 to 1.13)	Results also reported when influenza intensity changed from baseline to the mean level (10%), and when intensity was assumed equal to 10%

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Wordley et al. 1997	Birmingham, U.K. 1992–1994	Respiratory (ICD-9: 460–519) COPD (ICD-9: 490–496 excluding 493) Pneumonia (ICD-9: 480–486) (Also circulatory deaths included)	All respiratory: 3.5 deaths/day COPD: 1.4 deaths/day Pneumonia: 2 deaths per day	PM_{10}, SO_2, NO_2, O_3	Linear regression	Daily maximum temperature, relative humidity, and dummy variables for day-of-the-week & month. Linear trend included in some models.	Percent increase in daily events per 10 μg/m^3 of PM_{10} Same day effects: COPD: 5.0 (0.7–9.3)	Results also reported for lag 1
Xu et al. 1994	Beijing, China 1989	Cardiovascular disease (ICD-9: 390–414, 417–448) Pulmonary heart disease (ICD-9: 415–416) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–493) Cancer (CD-9 I40–208)	Total: 21.6 deaths/day COPD: 0.7 death/day Pulmonary heart disease: 2.0 deaths/day Cardiovascular disease 10.1 deaths/day Cancer: 4.7 deaths/day Others: 4.0 deaths/day	TSP, SO_2	Poisson regression	Temperature, humidity, indicator variable for Sunday, previous day's mortality count	% increase with a doubling of TSP (same day) All-cause: 4% (–2 to 11) COPD: 38% (4–72) Pulmonary heart disease: 8% (–9 to 26)	Results also reported stratified by season for one pollutant and copollutant models

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Xu et al. 2000	Shenyang, China 1992	Total nonaccidental (ICD-9 ≤ 800) Cardiovascular disease (ICD-9: 390–414, 417–448) Pulmonary heart disease (ICD-9: 415–416) Chronic obstructive pulmonary disease (COPD) (ICD-9: 490–493) Cancer (CD-9 I40–208)	Median deaths/day COPD: 5 deaths/day Pulmonary heart disease: 2.0 deaths/day Cardiovascular disease 19 deaths/day Cancer: 12 deaths/day Others: 8.0 deaths/day	TSP, SO_2	Poisson regression with a Markov approach	Indicator variables for quintiles of temperature and humidity, humidity, and Sunday	Estimated coefficients (SE) per 100 μg/m^3 and Relative risks All deaths: 0.173 (0.0055); RR = 1.017 COPD: 0.0257(0.0.0161); RR = 1.026 CVD: 0.0213 (0.0080); RR = 1.021 Cancer: 0.0087 (0.0103); RR = 1.009	Results also reported for a model with TSP and SO_2 analyzed together
Zanobetti and Schwartz 2009	U.S. 1999–2005	Respiratory disease (ICD-10: J00–J99) CVD (ICD-10: I01–I59) MI (ICD-10: I 21–I22) Stroke ICD-10: I60–I69) All-cause mortality (ICD-10: A00–R99)	5,609,349 total deaths; 1,787,078 for CVD, 397,894 for MI, 330,613 for stroke, and 547,660 for respiratory disease 0.5 to 67 CVD deaths per day (range by city)	$PM_{2.5}$ Course PM (> $PM_{2.5}$ and PM_{10})	Poisson regression models (stratified by season and city, and then pooled in a random-effects meta-analysis	Cubic regression spline with 1.5 *df* for each season for each year; day-of-the-week using indicator variables, and a natural cubic spline with 3 *df* for the same-day temperature and previous day temperature Single and copollutant models Stratified by seasons	% increase in mortality per 10 μg/m^3 for the mean of lags 0 and 1 (2-day mean) All cause mortality: 0.98% (0.75–1.22) CVD: 0.85 (0.46–1.24) MI: 1.18 (0.48–1.89) Stroke: 1.78 (0.96–2.62) Respiratory: 1.68 (1.04–2.33)	Results also reported by season

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Zeka et al. 2005	20 U.S. cities (not Houston), 1989–2000	All-cause mortality (ICD-10: V01–Y98) Heart disease (ICD-10: I01–I51) Ischaemic heart disease (ICD-10: I20–I25) Myocardial infarction (ICD-10: I21–I22) Dysrhythmias (ICD-10: I46–I49) Heart failure (ICD-10: I50) Stroke (ICD-10: I60–I69) Respiratory disease (ICD-10: J00–J99) Pneumonia (ICD-10: J12–J18) Chronic obstructive pulmonary disease (COPD) (ICD-10: J40–J44)	1,896,306 deaths (10% from any respiratory disease; 33% from heart disease; 7% from stroke)	PM_{10}	Case-crossover design (lag 0, lag 1, and lag 2 – single- and distributed-lag models)	Day-of-the-week as indicator variables, quadratic spline functions for apparent temperature EMM: city-level: prevalence of AC, population density, SMRs, proportion of elderly, daily minimum temperature in summer, daily maximum temperature in winter, percentage of primary PM_{10} from traffic sources	% increase in mortality per 10 μg/m^3 increase of PM_{10} (3-day cumulative averages) All-cause: 0.45 (0.25–0.65) All Resp disease: 0.87 (0.38–1.36) COPD: 0.43 (–0.35 to 1.21) Pneumonia: 1.24 (0.46–2.02) All Heart Disease 0.50 (0.25–0.75) IHD: 0.65 (0.32–0.98) MI: 0.36 (–0.25 to 0.97) HF: 0.60 (–0.50 to 1.70) Dysrhythmias: 0.20 (–1.03 to 1.43) Stroke: 0.46 (–0.13 to 1.05)	Results reported for single lag model (lag 0, lag 1 and lag 2); distributed-lag models, and 3-day cumulative estimates (results shown in this table)

Table A.1: Studies Evaluating Associations Between Short-term Effects of Particulate Matter and Specific Cardiovascular or Respiratory Causes of Mortality

Zeka et al. 2006	20 U.S. cities 1989–2000	All-cause mortality (ICD-10: V01–Y98) Heart disease (ICD-10: I01–I51) Myocardial infarction (ICD-10: I21–I22) Stroke (ICD-10: I60–I69) Respiratory disease (ICD-10: J00–J99)	1,896,306 deaths	PM_{10}	Case-crossover design (either average concentration on multiple days or a single day)	Day-of-the-week as indicator variables, quadratic spline functions for apparent temperature EMM: Sex, race, age, location of death, season, contributing causes of death	% increase in mortality per 10 $\mu g/m^3$ increase of PM_{10} No differences by race; differences by gender, education (inverse effect), location, season, and secondary diagnoses	Focus on modifiers of effects of PM on daily mortality

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Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

Study	**Location/Yrs**	**Outcome**	**Events/day or sample size**	**Pollutants**	**Model**	**Confounders and Effect Modifiers**	**Measure of Association**
Tsai, Wang, Chuang and Chan 2010	Taichung, Taiwan 2003–2006	All-cause mortality Cardiovascular mortality (ICD-9: 410–411, 414, 430–437) Cerebrovascular diseases (ICD-9, 430–437) Ischemic heart diseases (ICD-9, 410–411, 414) Stroke (ICD-9, 430–434)	Daily means of deaths All-causes: 13.0 deaths/day Cardiovascular: 1.5 deaths/day Ischemic Heart Disease: 0.5 deaths/day Cerebrovascular diseases: 1.0 death/day Strokes: 0.5 death/day	Propane Iso-butane Propylene Benzene m,p-xylene o-xylene	Generalized additive model (GAM) Poisson regression with lags 0, 1, and 2	Yearly trend, month and temperature LOESS smoother was used	RR for IQR increases in pollutant levels (presented graphically or commented on in the text) All-cause mortality – no significant associations Cardiovascular mortality – significant associations with propane and i-butane No associations with any of the VOCs and mortality from cerebrovascular diseases, ischemic heart diseases and stroke at any lag period
Oftedal, Nafstad, Magnus, Bjorkly and Skrondal 2003 (Follow-up of study by Hagen, Nafstad,	Drammen, Norway 1995–2000	Hospital admissions for respiratory diseases (ICD-9, 460–519; ICD-10, J00–J99)	Daily means of hospital admissions Respiratory diseases: 2.2/day (1994–1997); 2.3/day (1998–2000)	Benzene Formaldehyde Toluene	GAM Poisson regression model	Temperature, humidity, cubic spline smoother of time trend	RR for IQR increases in pollutant levels Benzene (10.47 μg/m^3): 1.14 (1.06–1.22) Formaldehyde (6.19 μg/m^3): 1.09 (1.01–1.18)

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

Study	**Location/Yrs**	**Outcome**	**Events/day or sample size**	**Pollutants**	**Model**	**Confounders and Effect Modifiers**	**Measure of Association**
Skrondal, Bjorkly and Magnus [2000]; study period 11/1994–1997)							Toluene (23.57 μg/m^3): 1.07 (1.02–1.13
Elliott, Longnecker, Kissling and London 2006	NHANES sample, 1988–1994	Pulmonary function measures FEV_1 (forced expiratory volume at 1 sec) FVC (forced vital capacity) PEFR (peak expiratory flow rate) MMEFR (maximum mid-expiratory flow rate)	953 adults)	VOC blood levels 1,1,1-TCE 1,4-dichlorobenzene (1,4 DCB) 2-Butanone Acetone Benzene Ethylbenzene *m,p*-Xylene *o*-Xylene Styrene Tetrachloroethene Toluene	Least-squares regression of natural log transformations of VOC blood concentrations	Race/ethnicity, sex, age, age-squared, standing height, body mass index, self-reported doctor diagnosis of emphysema, smoking status, no. of cigarettes smoked per day, years smoked, serum cotinine levels	Only 1,4-DCB was associated with reduced pulmonary function Note: 1,4-DCB is related to the use of air fresheners, toilet blow deodorants, and mothballs

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

Arif and Shah 2007	NHANES, 1999–2000	Self-reported physician-diagnosed asthma Self-reported wheezing in the previous 12 months (among those with physician-diagnosed asthma)	550 adults	Benzene Chloroform Ethylbenzene Tetrachloroethene (PCE) Toluene Trichloroethene *o*-Xylene *m,p*-Xylene 1,4-Dichlorobenzene Methyl tertiary butyl ether (MTBE) Personal exposure measurements (48–72 hr)	Exploratory factor analysis Logistic regression analyses (accounted for sample weights; no adjustment for variance estimates)	Age, sex, race/ethnicity, body mass index, atopy, smoking, ETS, poverty level, interaction terms for individual VOCs and race/ethnicity, VOCs and poverty level	7 of 10 VOCs loaded on 2 factors: aromatic compounds and chlorinated hydrocarbons OR for a 1 unit increase in exposure <u>Self-reported asthma</u> Factor 1: 1.63 (1.17–2.27) Factor 2: 0.93 (0.66–1.32) Benzene: 1.33 (1.13–1.56) Ethylbenzene: 1.34 (1.01–1.78) Toluene: 1.21 (0.93–1.58) o-xylene: 1.32 (1.04–1.67) m,p-xylene: 1.33 (1.08–1.64) Tetrachloroethene: 1.02 (0.90–1.15) Trichloroethene: 0.94 0.77–1.14)

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							Chloroform: 1.10 (0.89–1.35) 1,4-dichlorobenzene: 1.16 (1.03–1.30) MTBE: 1.19 (1.07–1.32) <u>1–2 attacks of wheezing</u> Factor 1: 1.68 (1.08–2.61) Factor 2: 1.50 (1.01–2.23) Benzene: 0.91 (0.66–1.26) Ethylbenzene: 1.76 (1.23–2.50) Toluene: 1.00 (0.82–1.22) o-xylene: 1.39 (1.05–1.84) m,p-xylene: 1.47 (1.06–2.04) Tetrachloroethene: 1.20 (0.85–1.70)

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							Trichloroethene: 1.29 (0.98–1.68) Chloroform: 2.65 (1.18–5.96) 1,4-dichlorobenzene: 0.90 (0.74–1.09) MTBE: 1.23 (1.05–1.43) 3 or more attacks of wheezing No associations were detected.
Fiedler, et al. 2005	Controlled chamber experiment	Neurobehavioral tests (composite score) Pulmonary function texts (FVC and FEV_1)	130 healthy women	Controlled exposures to 23 VOCs with and without ozone and psychological stress	Mixed linear models		No effects detected for lung function or neurobehavioral performance
Delfino, Gong, Linn, Pellizzari and Hu 2003 (Delfino, Gong, Linn, Hu and Pellizzari [2003] evaluated the	Los Angeles Nov. 1999–Jan 2000	Asthma symptoms (diaries)	22 Hispanic children	Benzene Ethylbenzene Formaldehyde Acetaldehyde Acetone	Regression modeling (GEE) for lags 0–4	Respiratory infections	ORs for interquartile increases in ambient VOC levels for symptom scores > 1 (results also reported for symptom scores > 2) Acetaldehyde (lag 0): 1.39 (0.80–2.41)

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

relationship between acute asthma symptoms and exhaled breath measure-ments of VOCs using data from the same panel study.)				1,3-Butadiene Tetrachloroethylene Toluene *m*,*p*-Xylene *o*-Xylene			Acetaldehyde (lag 1): 1.48 (1.16–1.87) Acetone (lag 0): 1.12 (0.72–1.74) Acetone (lag 1): 1.13 (0.80–1.60) Formaldehyde (lag 0): 1.09 (0.70–1.68) Formaldehyde (lag 1): 1.37 (1.04–1.80) Benzene (lag 0): 1.23 (1.02–1.48) Benzene (lag 1): 1.06 (0.83–1.36) 1,3-butadiene (lag 0): 1.16 (0.90–1.49) 1,3-butadiene (lag 1): 1.32 (0.97–1.80) Chloromethane (lag 0): 1.07 (0.92–1.23) Chloromethane (lag 1): 1.00 (0.79–1.26) *p*-Dichlorobenzene (lag 0): 1.18 (0.86–1.62)

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							p-Dichlorobenzene (lag 1): 1.20 (0.86–1.67) Ethlybenzene (lag 0): 1.38 (1.09–1.75) Ethlybenzene (lag 1): 1.18 (0.90–1.55) Methlylene chloride (lag 0): 1.09 (0.91–1.30) Methlylene chloride lag 1): 0.96 (0.82–1.14) Tetrachloroethylene (lag 0): 1.37 (1.09–1.71) Tetrachloroethylene (lag 1): 1.13 (0.81–1.57) Toluene (lag 0): 1.35 (0.99–1.84) Toluene (lag 1): 1.16 (0.86–1.58) *m,p*-Xylene (lag 0): 1.35 (1.01–1.80) *m,p*-Xylene (lag 1):

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							1.19 (0.89–1.58) *o*-Xylene (lag 0): 1.28 (1.00–1.66) *o*-Xylene (lag 1): 1.18 (0.90–1.53)
	Los Angeles Nov. 1999–Jan 2000	Asthma symptoms (diaries)	21 Hispanic children	Benzene Ethylbenzene Formaldehyde Acetaldehyde Acetone 1,3-Butadiene Tetrachloroethylene Toluene *m,p*-Xylene *o*-Xylene	Regression modeling (GEE) for lags 0–4	Respiratory infections	ORs for interquartile increases in ambient VOC levels for symptom scores > 1 (results also reported for symptom scores > 2) Acetaldehyde (lag 0): 1.39 (0.80–2.41) Acetaldehyde (lag 1): 1.48 (1.16–1.87) Acetone (lag 0): 1.12 (0.72–1.74) Acetone (lag 1): 1.13 (0.80–1.60) Formaldehyde (lag 0): 1.09 (0.70–1.68) Formaldehyde (lag 1): 1.37 (1.04–1.80) Benzene (lag 0): 1.23 (1.02–1.48) Benzene (lag 1): 1.06

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							(0.83–1.36) 1,3-butadiene (lag 0): 1.16 (0.90–1.49) 1,3-butadiene (lag 1): 1.32 (0.97–1.80) Chloromethane (lag 0): 1.07 (0.92–1.23) Chloromethane (lag 1): 1.00 (0.79–1.26) *p*-Dichlorobenzene (lag 0): 1.18 (0.86–1.62) *p*-Dichlorobenzene (lag 1): 1.20 (0.86–1.67) Ethlybenzene (lag 0): 1.38 (1.09–1.75) Ethlybenzene (lag 1): 1.18 (0.90–1.55) Methlylene chloride (lag 0): 1.09 (0.91–1.30) Methlylene chloride lag 1): 0.96 (0.82–1.14) Tetrachloroethylene

Table A.2: Studies Evaluating Associations Between Short-term Effects of VOCs and Adverse Health Effects

							(lag 0): 1.37 (1.09–1.71) Tetrachloroethylene (lag 1): 1.13 (0.81–1.57) Toluene (lag 0): 1.35 (0.99–1.84) Toluene (lag 1): 1.16 (0.86–1.58) *m*,*p*-Xylene (lag 0): 1.35 (1.01–1.80) *m*,*p*-Xylene (lag 1): 1.19 (0.89–1.58) *o*-Xylene (lag 0): 1.28 (1.00–1.66) *o*-Xylene (lag 1): 1.18 (0.90–1.53)

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