A Systematic Review of Relation between Long-term Exposure to Ambient Air Pollution and Chronic Disease: On-line Appendix

Hong Chen, MSc[1]

Mark S. Goldberg, PhD[1,2,3]

Paul J. Villeneuve, PhD[4,5]

1 Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec

2 Department of Medicine, McGill University, Montreal, Quebec

3 Division of Clinical Epidemiology McGill University Health Center, Montreal, Quebec

4 Population Studies Division, Health Canada, Ottawa, Ontario

5 Department of Public Health Sciences, University of Toronto, Toronto, Ontario

Address for correspondence:
Mark Goldberg, PhD
Division of Clinical Epidemiology
McGill University Health Center – RVH
687 Pine Avenue West, R4.29
Montreal, Quebec H3A 1A1
Tel: (514) 934-1934, ext 36917
Fax: (514) 843-1493
Email: mark.goldberg@mcgill.ca

TABLE A. Estimates of relationship between **all-cause mortality** and long-term exposure to ambient air pollution in published epidemiological studies, according to studies and exposures

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR (95% CI)			Stat. analysis	Covariates
ALL NATURAL CAUSES								
Adventist Health Study on the Health Effects of Smog (ASHMOG)								
Abbey 1993 /48/	US	Cohort	NO_2: 5 pphm‡ NO_2: sum of hr/yr in excess of 5, 15, 20, and 25 pphm	NS/NR‡			Cox	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, presently live with smoker in 1987
Abbey 1999 /49/	US	Cohort			Men	Women	Cox	Age, education, ex-smoking, history of high blood pressure, ETS‡, physical exercise, BMI‡, and alcohol use
			PM_{10}‡: 10 μg/m^3	PM_{10}:	1.04 (0.99-1.10)	0.97 (0.93-1.02)		
			PM_{10}: 43d/yr above 100 μg/m^3	PM_{10}:	1.12 (1.01-1.24)	0.94 (0.86-1.03)		
			O_3: 10 μg/m^3	O_3:	1.04 (0.98-1.10)	0.98 (0.93-1.03)		
			O_3: 551.1 h/yr above 100 ppb	O_3:	1.14 (0.98-1.32)	0.90 (0.80-1.02)		
			SO_2, NO_2, SO_4: 10 μg/m^3	SO_2:	1.05 (0.94-1.18)	1.00 (0.91-1.10)		
				NO_2:	1.01 (0.97-1.04)	1.00 (0.97-1.03)		
				SO_4:	1.18 (0.84-1.65)	0.81 (0.61-1.08)		
McDonnell 2000 /58/	US	Cohort	$PM_{2.5}$‡, PM_{10}, $PM_{2.5-10}$: 10 μg/m^3		Men	Women	Cox	Age, education, ex-smoking, history of high blood pressure, ETS, physical exercise, BMI, and alcohol use
				$PM_{2.5}$:	1.09 (0.98-1.21)	NS/NR		
				PM_{10}:	1.05 (0.98-1.12)	NS/NR		
				$PM_{2.5-10}$:	1.05 (0.92-1.21)	NS/NR		
American Cancer Society (ACS) study								
Pope 2002 /61/	US	Cohort	$PM_{2.5}$, PM_{10}, $PM_{15-2.5}$‡, TSP, SO_4, SO_2, CO, NO_2, O_3: 10 μg/m^3	Men and women:			Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol consumption, occupational exposure, and diet
				$PM_{2.5}$:	1.06 (1.02-1.11)			
				PM_{10}:	1.01 (0.98-1.03)			
				$PM_{15-2.5}$:	1.00 (0.98-1.03)			
				TSP:	1.00 (0.99-1.01)			
				SO_4:	1.09 (1.06-1.13)			
				SO_2:	1.06 (1.03-1.08)			
				NO_2:	1.00 (0.98-1.01)			
				CO:	0.70 (0.50-0.97)			
				O_3:	1.00 (0.98-1.02)			
Jerrett 2005 /54/ (Los Angeles)	US	Cohort	$PM_{2.5}$, O_3: 10 μg/m^3 Distance to freeways: <500 vs. ≥500m	$PM_{2.5}$:	1.11 (0.99–1.25)		Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables (i.e. %unemployed, total population, etc)
				O_3:	0.98 (0.96–1.01)			
				Distance to freeways:	0.99 (0.88–1.11)			
Cohort of Norwegian Men								

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR (95% CI)	Stat. analysis	Covariates
Nafstad 2004 /60/	Norway	Cohort	NOx, SO_2: 10 μg/m^3	NOx: 1.08 (1.06–1.11) SO_2: 0.98 (0.96–1.01)	Cox	Education, occupation, smoking, leisure-time physical activity, risk group of cardiovascular diseases, and age at inclusion
French PAARC study						
Filleul 2005 /51/	France	Cohort	TSP‡, SO_2, Black smoke, NO_2, NO: 10 μg/m^3	TSP: 1.00 (0.99-1.01) SO_2: 1.01 (0.99-1.03) Black smoke: 0.99 (0.98-1.01) NO_2: 0.96 (0.93-1.00) NO: 0.99 (0.98-1.00)	Cox	Age, sex, BMI, smoking, occupation, and education
Harvard Six Cities Study						
Krewski 2005 /55/	US	Cohort	$PM_{2.5}$: most polluted vs. least polluted city (equivalent to per 18.6 μg/m^3 increase)	1.28 (1.10-1.48)	Cox	Age, sex, smoking, BMI, education, occupational exposure to dust, gases, or fumes, and diabetes
Laden 2006 /56/	US	Cohort	$PM_{2.5}$: 10 μg/m^3	1.16 (1.07–1.26)	Cox	Age, sex, smoking, less than high school education, and BMI
Ontario Cohort Study (retrospective)						
Finkelstein 2003 /52/	Canada	Cohort	TSP, SO_2: above vs. below median pollution level	Subjects with below-median income TSP: 1.14 (1.07-1.20) SO_2: 1.18 (1.11-1.26) Subjects with above-median income TSP: 1.33 (1.12-1.57) SO_2: 1.35 (1.05-1.73)	Cox	Age, sex, baseline pulmonary function, BMI, previous diagnosis of chronic pulmonary disease, chronic ischemic heart disease, and diabetes
Netherlands Cohort Study on Diet and Cancer (NLCS)						
Beelen 2008 /47/	Nether.	Cohort	NO_2 (background and local traffic): 10 μg/m^3 Black smoke (background and local traffic): 10 μg/m^3 SO_2 (background): 10 μg/m^3 $PM_{2.5}$ (background and local traffic): 10 μg/m^3 Local traffic exposure (adjusting for background conc. of black smoke): (1) traffic intensity on the nearest road: a change of the 95th and 5th percentile, (2) sum of traffic intensity in a buffer of 100m: a change of the 95th and 5th percentile, (3) living near a major road: <100m from motorway or <50m from a local road vs. otherwise	NO_2: 1.03 (1.00–1.05) Black smoke: 1.05 (1.00–1.11) SO_2: 0.98 (0.95–1.02) $PM_{2.5}$: 1.06 (0.97–1.16) Traffic intensity on nearest road: 1.03 (1.00–1.08) Traffic intensity in a 100-m buffer: 1.02 (0.97–1.07) Living near a major road: 1.05 (0.97–1.12)	Cox	Age, sex, smoking, and area-level income (e.g. % of persons with a low and with a high income at the neighborhood scale and the COROP area scale)

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR (95% CI)	Stat. analysis	Covariates
ALL CAUSES§						
California Cancer Prevention Study (CA CPS I)						
Enstrom 2005 /50/	US	Cohort	$PM_{2.5}$: 10 μg/m^3	1.04 (1.01-1.07)	Cox	Age, sex, smoking, race, education, marital status, BMI‡, male occupational exposure, physical exercise, fruit/juice consumption
German Women's Health Study in North Rhine-Westphalia (retrospective)						
Gehring 2006 /53/	Germany	Cohort	NO_2, PM_{10}: 10 μg/m^3 Distance of home to a major road: <50 vs. ≥50 m	NO_2: 1.11 (1.01-1.23) PM_{10}: 1.19 (0.98-1.45) Distance to road: 1.29 (0.93-1.78)	Cox	Age, sex, smoking, SES, occupational exposure, baseline health status, BMI
Pennsylvania Cohort						
Morris 1976 /59/	US	Cohort	Contrast between regions of residence: Seward vs. New Florence	NR‡	Ratio of SMR‡	Age, sex, smoking (three categories: heavy, intermediate, and never smoked)
USEPRI-Washington University Veterans' Cohort Mortality Study						
Lipfert 2006 /57/	US	Cohort	∑$PM_{2.5}$ components: 10 μg/m^3 $PM_{2.5}$ (TEOM and gravimetric measurements): 10 μg/m^3 O_3, NO_2, CO, SO_2: 10 μg/m^3 Traffic density: annual vehicle-miles traveled per unit of land area (in log scale)	∑$PM_{2.5}$ components: 1.00 (0.86-1.16) $PM_{2.5}$ (TEOM and gravimetric measurements): 1.00 (0.86-1.16) O_3: 1.00 (0.97-1.03) NO_2: 1.00 (0.97-1.03) CO: 1.00 (1.00-1.00) SO_2: 1.00 (0.98-1.02) ln (Traffic density): 1.06 (1.02-1.09)	Cox	Age, sex, Zip code- and county-level SES, smoking (ever or at recruitment), BMI, blood pressure

‡ pphm, part per hundred million; NS/NR: the estimates of association were reported as not significant, but no quantitative results were provided; PM_{10}, particulate matter less than 10 microns in diameter; $PM_{2.5}$, particulate matter less than 2.5 microns in diameter; $PM_{15-2.5}$, particulate matter between 15 and 2.5 microns in diameter; ETS, environment tobacco smoking; BMI, body mass index; TSP, total suspended particulate; NR, not reported; SES, socioeconomic status; SMR, standardized mortality ratio

§ These studies did not explicitly report exclusion of accidental deaths; hence, accidental deaths may potentially be tallied in the outcomes

TABLE B. Estimates of relationship between risk of developing and/or dying from **lung cancers** and long-term exposure to ambient air pollution in published cohort studies, according to exposures and methods of assessment

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
INCIDENCE						
Adventist Health Study on the Health Effects of Smog (ASHMOG)						
Mills 1991 /65/	US	Cohort	TSP: (1) sum of hr/yr in excess of 200 µg/m3 with increment of 1000 h/yr, (2) annual mean: per µg/m^3 increase O_3: sum of hr/yr in excess of 10 pphm‡ with increase of 500 h/hr	TSP (1000 h/yr): 1.72 (0.81-3.65) TSP (mean conc.): NS/NR‡ O_3 (500 h/hr): 2.25 (0.96-5.31)	Cox	Age, sex, education, ex-smoking, ETS‡, and occupational exposure
Beeson 1998 /62/	US	Cohort	PM_{10}‡: (1) 10 µg/m^3, (2) sum of days/year above 100 µg/m^3: per 43 d/yr increase O_3: (1) 10 µg/m^3 (daily 8 hr avg.), (2) sum of hours/year above 100 ppb SO_2: 10 µg/m^3 NO_2: 10 µg/m^3	Men / Women PM_{10} (10 µg/m^3) 1.99 (1.32-3.00) / NS/NR PM_{10} (43 days/yr) 2.95 (1.71-5.09) / NS/NR O_3 (10 µg/m^3) 6.87 (0.56-83.99) / NS/NR O_3 (556 hr/yr) 3.56 (1.35-9.42) / 0.94 (0.41-2.16) SO_2: 4.07 (1.99-8.32) / 2.98 (1.55-5.71) NO_2: 2.71 (0.34-21.47) / NS/NR	Cox	Age, sex, education, ex-smoking, ETS, physical exercise, BMI‡, diet, and alcohol use
Cohort of Norwegian Men						
Nafstad 2003 /67/	Norway	Cohort	NOx, SO_2: 10 µg/m^3	Men and women: NOx: 1.08 (1.02-1.15) SO_2: 1.01 (0.94-1.08)	Cox	Age, education, occupation, smoking habits, leisure-time physical activity, and baseline cardiovascular diseases
Danish Cohort Study on Lung Cancer, Smoking, and Environment						
Engholm 1996 /64/	Denmark	Cohort	Contrast between regions of residence: capital, suburbs, town, vs. rural	Men / Women Capital vs. rural: 1.1 (1.02-1.20) / 1.71 (CI: NR) Suburbs vs. rural: 1.0 (0.91-1.09) / NR‡ Towns vs. rural: 1.12 (1.05-1.16) / NR	Poisson regression	Age, sex, smoking, occupation, dwelling, and marital status
GenAir study						

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
Vineis 2006 /68/	Ten European countries	Cohort	PM_{10}, NO_2, SO_2: 10 μg/m^3 Proximity of residence to major streets: exposed vs. unexposed	Men and women: PM_{10}: 0.91 (0.70-1.18) NO_2: 1.14 (0.78-1.67) SO_2: 1.08 (0.89-1.30) Residence in the major roads: 1.31 (0.82-2.09)	Cond. logistic	Age, BMI, education, intake of fruit and vegetables, intake of meat, intake of alcohol, physical activity, gender, smoking habits, time since recruitment, country, occupational index, and cotinine
MORTALITY						
Adventist Health Study on the Health Effects of Smog (ASHMOG)						
Mills 1991 /65/	US	Cohort	TSP: (1) annual mean concentration (per μg/m^3), (2) exceedance frequency (1000 hr/yr above 200 ug/m^3) O_3: (1) cumulative annual mean concentration (pphm: part per hundred million), (2) exceedance frequency (500 hr/yr above 10 pphm)	O_3 (mean concentration): NS/NR O_3 (exceedance frequency): 2.25 (0.96-5.31) TSP (mean concentration): NS/NR TSP (exceedance frequency): 1.72 (0.81-3.65)	Cox	Age, sex, education, ex-smoking, ETS, and occupational exposure
Abbey 1999 /49/	US	Cohort	PM_{10}: 10 μg/m^3 PM_{10}: 43d/yr above 100 μg/m^3 O_3: 10 μg/m^3 O_3: 551.1 h/yr above 100 ppb SO_2, NO_2, SO_4: 10 μg/m^3	Men / Women: PM_{10}: 1.65 (1.21-2.27) / 1.13 (0.81-1.57) PM_{10}: 2.38 (1.42-3.97) / 1.08 (0.55-2.13) O_3: 1.37 (1.00-1.88) / 0.90 (0.66-1.22) O_3: 4.19 (1.81-9.69) / 1.39 (0.52-3.67) SO_2: 2.03 (1.25-3.29) / 3.10 (1.91-5.03) NO_2: 1.17 (0.98-1.41) / 1.32 (1.04-1.68) SO_4: Not studied / Not studied	Cox	Age, sex, education, ex-smoking, ETS, physical exercise, BMI, diet, and alcohol use
McDonnell 2000 /58/	US	Cohort	PM_{10}, $PM_{2.5}$, $PM_{2.5\text{-}10}$‡: 10 μg/m^3	Men / Women: PM_{10}: 1.23 (0.84-1.80) / NS/NR $PM_{2.5}$: 1.39 (0.79-2.46) / NS/NR $PM_{2.5\text{-}10}$: 1.25 (0.62-2.56) / NS/NR	Cox	Age, sex, education, ex-smoking, history of high blood pressure, ETS, physical exercise, BMI, and alcohol use
American Cancer Society (ACS) study						
Pope 2002 /61/	US	Cohort	$PM_{2.5}$‡, PM_{10}, $PM_{15\text{-}2.5}$‡, TSP, SO_4, SO_2, NO_2, CO, O_3: 10 μg/m^3	Men and women: $PM_{2.5}$: 1.14 (1.04-1.23) PM_{10}: 1.01 (0.96-1.05) $PM_{15\text{-}2.5}$: 1.00 (0.95-1.05) TSP: 1.00 (0.98-1.02) SO_4: 1.15 (1.06-1.24) SO_2: 1.03 (0.98-1.08) NO_2: 0.99 (0.96-1.02) CO: 0.36 (0.18-0.71) O_3: 0.98 (0.95-1.02)	Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol consumption, occupational exposure, and diet

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
Jerrett 2005 /54/ (Los Angeles)	US	Cohort	$PM_{2.5}$, O_3: 10 μg/m^3 Distance to freeways: <500m vs. ≥500m	$PM_{2.5}$: 1.20 (0.79-1.82) O_3: 0.99 (0.91-1.07) Distance to freeways: 1.44 (0.94-2.21)	Cox	Age, sex, race, education, smoking, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables (i.e. % unemployed, total pop.)
American Legion Study Population						
Buell 1967 /63/	US	Cohort	Lived ≥10 years in Los Angeles County vs. in other counties of California Lived ≥10 years vs. <10 years in Los Angeles County	Los Angeles County vs. other counties: 1.21 (0.88-1.67) ≥10 yr vs. < 10 yr in Los Angeles County: 1.26 (0.81-1.95)	Direct Standard-ization	Age, sex, smoking, and size of birthplace
Cohort of Norwegian Men						
Nafstad 2004 /60/	Norway	Cohort	NOx, SO_2: 10 μg/m^3	NOx: 1.11 (1.03–1.19) SO_2: 1.00 (0.93–1.08)	Cox	Age, education, occupation, smoking habits, leisure-time physical activity, and baseline cardiovascular diseases
French PAARC study						
Filleul 2005 /51/	France	Cohort	TSP, black smoke, NO, NO_2, SO_2: 10 μg/m^3	TSP: 0.97 (0.94-1.01) Black smoke: 0.97 (0.93-1.01) NO: 0.97 (0.94-1.01) NO_2: 0.97 (0.85-1.10) SO_2: 0.99 (0.92-1.07)	Cox	Age, sex, BMI, smoking habit, occupational exp, and education
Harvard Six Cities Study						
Krewski 2005 /55/	US	Cohort	$PM_{2.5}$: most polluted vs. least polluted city (equivalent to per 18.6 μg/m^3 increase)	1.43 (0.85-2.41)	Cox	Age, sex, smoking, BMI, education, occupational exposure to dust, gases, or fumes, and diabetes
Laden 2006 /56/	US	Cohort	$PM_{2.5}$: 10 μg/m^3	1.27 (0.96-1.69)	Cox	Age, sex, current smoker, current pack-years of smoking, former smoker, former pack-years of smoking, less than high school education, and linear and quadratic terms for body mass index.
Netherlands Cohort Study on Diet and Cancer (NLCS)						
Beelen 2008 /47/	Nether.	Cohort	NO_2 (background and local traffic): 10 μg/m^3 Black smoke (background and local traffic): 10 μg/m^3 SO_2 (background): 10 μg/m^3 $PM_{2.5}$ (background and local traffic): 10 μg/m^3 Local traffic exposure (adjusting for background conc. of black smoke): (1) traffic intensity on the nearest road: a change of the 95th and 5th percentile, (2)	NO_2: 0.97 (0.90–1.05) Black smoke: 1.03 (0.88–1.20) SO_2: 1.00 (0.89–1.12) $PM_{2.5}$: 1.06 (0.82–1.38) Traffic intensity on nearest road: 1.07 (0.96–1.19) Traffic intensity in a 100-m buffer: 1.07 (0.93–1.23) Living near a major road: 1.20 (0.98–1.47)	Cox	Age, sex, smoking, and area-level income

First author, year (ref)	Location	Study design	Pollutants and increment of exposure	RR / OR (95% CI)		Stat. analysis	Covariates
			sum of traffic intensity in a buffer of 100m: a change of the 95th and 5th percentile, (3) living near a major road: <100m from motorway or <50m from a local road vs. otherwise				
Oslo Cohort Study (retrospective)							
Naess 2007 /66/	Norway	Cohort	$PM_{2.5}$, PM_{10}, NO_2: quartile increase		Men	Women	Cox	Age, sex, occupational class, and education
				Aged (51-70)				
				$PM_{2.5}$	1.07 (0.97-1.18)	1.27 (1.13-1.43)		
				PM_{10}	1.07 (0.97-1.18)	1.27 (1.13-1.43)		
				NO_2	1.07 (0.97-1.18)	1.23 (1.10-1.38)		
				Aged (71-90)				
				$PM_{2.5}$	1.07 (0.97-1.18)	1.16 (1.02-1.32)		
				PM_{10}	1.08 (0.98-1.20)	1.17 (1.03-1.33)		
				NO_2	1.09 (0.98-1.20)	1.12 (0.98-1.27)		

‡ M-H, Mantel-Haenszel estimation; NR, not reported; NS/NR: the estimates of association were reported as not significant, but no quantitative results were provided; PM_{10}, particulate matter less than 10 microns in diameter; $PM_{2.5}$, particulate matter less than 2.5 microns in diameter; $PM_{15-2.5}$, particulate matter between 15 and 2.5 microns in diameter; $PM_{2.5-10}$, particulate matter between 10 and 2.5 microns in diameter; ETS, environment tobacco smoking; BMI, body mass index; TSP, total suspended particulate; SES, socioeconomic status; pphm, part per hundred million

TABLE C. Estimates of relationship between risk of developing and/or dying from **other site cancers** and long-term exposure to ambient air pollution in published cohort studies, according to exposures and methods of assessment

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)		Stat. analysis	Covariates
Adventist Health Study on the Health Effects of Smog (ASHMOG)								
Mills 1991 /65/	US	Cohort	Incidence and mortality: all malignant neoplasm colorectal cervix leukemia/lymphoma	O_3: mean concentration (NR‡) O_3: exceedance frequency (500 hr/yr above 10 pphm) TSP‡: mean concentration (100 ug/m^3) TSP: exceedance frequency (1000 hr/yr above 200 ug/m^3)	INCIDENCE *All malignant neoplasm:* O_3: TSP: mean concentration TSP: exceedance frequency *Breast cancer:* TSP: mean concentration TSP: exceedance frequency *Cervix cancer:* TSP: mean concentration TSP: exceedance frequency *Colorectal cancer:* TSP: mean concentration TSP: exceedance frequency *Leukemia/lymphoma:* TSP: mean concentration TSP: exceedance frequency	Men NS/NR‡ NS/NR‡ NS/NR NS/NR NS/NR NA‡ NA NS/NR NS/NR NS/NR NS/NR NS/NR NS/NR	Women NS/NR NS/NR 1.37 (1.05-1.80) NS/NR 1.51 (0.92-2.47) NS/NR 0.64 (0.05-7.55) NS/NR 1.08 (0.55-2.11) NS/NR 1.05 (0.33-3.37)	Cox	Age, sex, education, ex-smoking, ETS‡, and occupational exposure
					MORTALITY TSP, O_3: NS/NR			
Abbey 1993 /48/	US	Cohort	Incidence: all cancers	NO_2: Per 5 pphm‡ increase, Sum of hr/yr in excess of 5, 15, 20, and 25 pphm	Men and women: NS/NR		Cox	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, presently live with smoker in 1987

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
American Cancer Society (ACS) study							
Jerrett 2005 /54/ (Los Angeles)	US	Cohort	Mortality: digestive cancer	$PM_{2.5}$, O_3 (expected peak daily concentration): 10 $\mu g/m^3$ Distance to freeways: <500m vs. ≥500m	Men and women: $PM_{2.5}$: 1.14 (0.74–1.74) O_3: 1.01 (0.93–1.09) Distance to freeways: 0.84 (0.53–1.35)	Cox	Age, sex, race, smoking, education, marital status, BMI‡, alcohol consumption, occupational exposure, diet, and other ecological variables (i.e. %unemployed, total population, etc)

‡ TSP, total suspended particulate; NS/NR: the estimates of association were reported as not significant, but no quantitative results were provided; NA: not applicable; NR: not reported; BMI: body mass index; ETS: environmental tobacco smoking; pphm, part per hundred million

TABLE D. Estimates of relationship between risk of developing and/or dying from **cardiovascular diseases** and long-term exposure to ambient air pollution in published cohort studies, according to exposures and methods of assessment

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
Adventist Health Study on the Health Effects of Smog (ASHMOG)							
Abbey 1993 /48/	US	Cohort	Incidence: MI‡	NO_2: Per 5 pphm increase, Sum of hr/yr in excess of 5, 15, 20, and 25 pphm	NS/NR‡	Cox	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, presently live with smoker in 1987
Abbey 1999 /49/	US	Cohort	Mortality: cardiopulmonary	PM_{10}‡: 10 μg/m^3 PM_{10}: 43d/yr above 100 μg/m^3 O_3: 10 μg/m^3 O_3: 551.1 h/yr above 100 ppb SO_2, NO_2, SO_4: 10 μg/m^3	Men / Women PM_{10}: 1.04 (0.97-1.11) / 0.97 (0.91-1.02) PM_{10}: 1.09 (0.95-1.24) / 0.90 (0.80-1.01) O_3: 1.03 (0.96-1.11) / 0.99 (0.93-1.05) O_3: 1.06 (0.88-1.29) / 0.88 (0.75-1.02) SO_2: 1.01 (0.86-1.18) / 1.02 (0.90-1.16) NO_2: 1.00 (0.96-1.05) / 1.01 (0.94-1.08) SO_4: 1.08 (0.01-101.06) / 0.90 (0.63-1.30)	Cox	Age, education, ex-smoking, history of high blood pressure, ETS‡, physical exercise, BMI‡, and alcohol use
Chen 2005 /69/	US	Cohort	Mortality: coronary heart disease	PM_{10}, $PM_{2.5}$‡, O_3, NO_2, SO_2: 10 μg/m^3	Men / Women PM_{10}: 0.94 (0.82–1.08) / 1.22 (1.01–1.47) $PM_{2.5}$: 0.90 (0.76–1.05) / 1.42 (1.06–1.90) O_3: 0.94 (0.77–1.15) / 0.98 (0.82–1.18) NO_2: 1.08 (0.94–1.23) / 1.08 (0.99–1.19) SO_2: 1.08 (0.79–1.48) / 0.79 (0.46–1.37)	Cox	Past smoking, education, BMI, water consumption, meat and nuts consumption, ETS, baseline total physical activity, exposure to occupational dust/fumes, hours outdoors, HRT (for woman only), calendar time
American Cancer Society (ACS) study							
Pope 2002 /61/	US	Cohort	Mortality: cardiopulmonary	$PM_{2.5}$, PM_{10}, $PM_{15-2.5}$, TSP, SO_4, SO_2, NO_2, CO, O_3: 10 μg/m^3	Men and women: $PM_{2.5}$: 1.09 (1.03-1.16) PM_{10}: 1.03 (1.00-1.07) $PM_{15-2.5}$: 1.02 (0.99-1.05) TSP: 1.01 (1.00-1.02) SO_4: 1.08 (1.02-1.14) SO_2: 1.06 (1.03-1.10) NO_2: 1.00 (0.98-1.02) CO: 0.56 (0.35-0.90) O_3: 1.01 (0.98-1.04)	Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol consumption, occupational exposure, and diet
Pope 2004 /72/	US	Cohort	Mortality: all cardiovascular diseases plus diabetes,	$PM_{2.5}$: 10 μg/m^3 (average of two periods, 1979-83 and 1999-00)	All cardiovascular plus diabetes: 1.12 (1.08-1.15) IHD: 1.18 (1.14-1.23)	Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol, occupation, diet

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
			ischemic heart disease (IHD), cerebrovascular disease		Cerebrovascular disease 1.02 (0.95-1.10)		
Jerrett 2005 /54/ (Los Angeles)	US	Cohort	Mortality: ischemic heart disease (IHD), cardiopulmonary	$PM_{2.5}$, , O_3 (expected peak daily): 10 μg/m^3 Distance to freeways: <500m vs. ≥500m	IHD / Cardiopulmonary $PM_{2.5}$ 1.25 (0.99-1.59) / 1.07 (0.91-1.26) O_3 0.97 (0.93-1.02) / 0.97 (0.94-0.99) Distance to freeways 0.90 (0.71-1.14) / 0.92 (0.77-1.08)	Cox	Age, sex, race, education, smoking, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables (i.e. % unemployed, total pop.)
Cohort of Norwegian Men							
Nafstad 2004 /60/	Norway	Cohort	Mortality: ischemic heart disease (including sudden death), cerebrovascular disease	NOx, SO_2: 10 μg/m^3	IHD / Cerebrovascular NOx: 1.08 (1.03–1.12) / 1.04 (0.94–1.15) SO_2: 0.95 (0.91–0.99) / 1.02 (0.93–1.12)	Cox	Education, occupation, smoking, leisure-time physical activity, risk group of cardiovascular diseases, and age at inclusion
French PAARC study							
Filleul 2005 /51/	France	Cohort	Mortality: cardiopulmonary	TSP‡, black smoke, NO, NO_2, SO_2: 10 μg/m^3	TSP: 1.01 (0.99-1.03) Black smoke: 1.00 (0.97-1.02) NO: 1.00 (0.98-1.02) NO_2: 1.01 (0.94-1.08) SO_2: 0.97 (0.92-1.02)	Cox	Age, sex, BMI, smoking, occupation, and education
Harvard Six Cities Study							
Krewski 2005 /55/	US	Cohort	Mortality: cardiopulmonary	$PM_{2.5}$: most polluted vs. least polluted city (equivalent to per 18.6 μg/m^3 increase)	1.38 (1.12-1.69)	Cox	Age, sex, smoking, BMI, education, occupational exposure to dust, gases, or fumes, and diabetes
Laden 2006 /56/	US	Cohort	Mortality: cardiovascular	$PM_{2.5}$: 10 μg/m^3	1.28 (1.13–1.44)	Cox	Age, sex, smoking, less than high school education, and BMI
Netherlands Cohort Study on Diet and Cancer (NLCS)							
Beelen 2008 /47/	Nether.	Cohort	Mortality: cardiovascular, cardiopulmonary	NO_2 (background and local traffic): 10 μg/m^3 Black smoke (background and local traffic): 10 μg/m^3 SO_2 (background): 10 μg/m^3 $PM_{2.5}$ (background and local traffic): 10 μg/m^3 Local traffic exposure (adjusting for background conc. of black smoke): (1) traffic intensity on the nearest road: a change of the 95th and	*Cardiovascular* NO_2: 1.02 (0.98–1.07) Black smoke: 1.04 (0.95–1.13) SO_2: 0.97 (0.91–1.03) $PM_{2.5}$: 1.04 (0.90–1.21) Traffic intensity on nearest road: 1.05 (0.99–1.12) Traffic intensity in a 100-m buffer: 1.00 (0.92–1.08) Living near a major road: 1.05 (0.93–1.18)	Cox	Age, sex, smoking, and area-level income

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
				5th percentile, (2) sum of traffic intensity in a buffer of 100m: a change of the 95th and 5th percentile, (3) living near a major road: <100m from motorway or <50m from a local road vs. otherwise	*Cardiopulmonary* Black smoke: 1.07 (0.98–1.15) Traffic intensity on nearest road: 1.06 (1.00–1.12)		
German Women's Health Study in North Rhine-Westphalia (retrospective)							
Gehring 2006 /53/	Germany	Cohort	Mortality: cardiopulmonary	NO_2, PM_{10}: 10 μg/m^3 Distance of home to a major road: >50 vs. ≤50m	NO_2: 1.41 (1.18–1.70) PM_{10}: 1.94 (1.35–2.78) Distance to road: 1.70 (1.02–2.81)	Cox	Age, sex, smoking, SES, occupational exposure, baseline health status, BMI
Ontario Cohort Study (retrospective)							
Finkelstein 2003 /52/	Canada	Cohort	Mortality: cardiopulmonary	TSP, SO_2: above vs. below median pollution level	Subjects with below-median income TSP: 1.47 (1.31-1.70) SO_2: 1.64 (1.46-1.83) Subjects with above-median income TSP: 1.14 (0.86-1.51) SO_2: 1.54 (1.13-2.10)	Cox	Age, sex, baseline pulmonary function, BMI, previous diagnosis of chronic pulmonary disease, chronic ischemic heart disease, and diabetes
Finkelstein 2005 /70/	Canada	Cohort	Mortality: cardiovascular, cerebrovascular	Pollution index: per unit increase Traffic indicator: binary classification (lived near or not near a major road/ highway)	Cardiovascular / Cerebrovascular Pollution index: 1.04 (0.97-1.11) / 0.97 (0.85-1.12) Traffic indicator: 1.37 (1.05-1.79) / 1.79 (1.06-3.04)	Cox	Age, sex, baseline pulmonary function, BMI, social deprivation index, and the diagnosis of obstructive lung disease, chronic ischemic heart disease, and diabetes
Oslo Cohort Study (retrospective)							
Naess 2007 /66/	Norway	Cohort	Mortality: cardiovascular	$PM_{2.5}$, PM_{10}, NO_2: every quartile increase	Men / Women Aged between 51-70 $PM_{2.5}$: 1.10 (1.05-1.16) / 1.14 (1.06-1.21) PM_{10}: 1.09 (1.04-1.15) / 1.11 (1.04-1.19) NO_2: 1.08 (1.04-1.13) / 1.07 (1.00-1.14) Aged between 71-90 $PM_{2.5}$: 1.05 (1.01-1.08) / 1.03 (1.00-1.05) PM_{10}: 1.04 (1.01-1.08) / 1.01 (0.99-1.04) NO_2: 1.02 (0.99-1.05) / 1.01 (0.99-1.04)	Cox	Age, sex, occupational class, and education
Women's Health Initiative Study							

First author, year (ref)	Location	Study design	Specific outcome(s)	Pollutants and increment of exposure	RR / OR (95% CI)	Stat. analysis	Covariates
Miller 2007 /71/	US	Cohort	Incidence (fatal and non-fatal): myocardial infarction, coronary revascularization, stroke Mortality: coronary heart or cerebrovascular disease	$PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, O_3: 10 μg/m^3	Women: Myocardial infarction (Incidence): $PM_{2.5}$: 1.06 (0.85–1.34) Coronary revascularization (incidence): $PM_{2.5}$: 1.20 (1.00–1.43) Stroke (incidence): $PM_{2.5}$: 1.28 (1.02–1.61) Any cardiovascular event (incidence and mortality): $PM_{2.5}$: 1.24 (1.09-1.41) PM_{10}: 1.04 (0.97-1.10) SO_2: 1.16 (0.95-1.40) NO_2: 1.04 (0.96-1.12) CO: 1.00 (0.81-1.22) O_3: 1.05 (0.99-1.11) Coronary heart disease (incidence and mortality): $PM_{2.5}$: 1.21 (1.04–1.42) Cerebrovascular disease (incidence and mortality): $PM_{2.5}$: 1.35 (1.08–1.68) Coronary heart disease and cerebrovascular disease (mortality): $PM_{2.5}$: 1.76 (1.25-2.47) Definite coronary heart disease (mortality): $PM_{2.5}$: 2.21 (1.17-4.16) Cerebrovascular disease (mortality): $PM_{2.5}$: 1.83 (1.11-3.00)	Cox	Age, race, education, household income, smoking, systolic blood pressure, BMI, and presence of diabetes, hypertension, or hypercholesterolemia, ETS, occupation, physical activity, diet, alcohol consumption, medical history, medication, and family history

‡ NS/NR: the estimates of association were reported as not significant, but no quantitative results were provided; NR, not reported; PM_{10}, particulate matter less than 10 microns in diameter; $PM_{2.5}$, particulate matter less than 2.5 microns in diameter; $PM_{15\text{-}2.5}$, particulate matter between 15 and 2.5 microns in diameter; $PM_{2.5\text{-}10}$, particulate matter between 10 and 2.5 microns in diameter; ETS, environment tobacco smoking; BMI, body mass index; TSP, total suspended particulate; SES, socioeconomic status; MI, myocardial infarction; IHD, ischemic heart disease

TABLE E. Estimates of relationship between risk of developing and/or dying from **chronic respiratory diseases** and long-term exposure to ambient air pollution in published cohort studies, according to exposures and methods of assessment

First author, year (ref)	Location	Study design	Outcomes	Pollutants and increment of exposure	RR (95% CI)	Stat. analysis	Covariates
Adventist Health Study on the Health Effects of Smog (ASHMOG)							
Abbey 1993 /95/	US	Cohort	Incidence: obstructive airway disease chronic bronchitis symptoms asthma	SO_4: Monthly mean concentration (10 $\mu g/m^3$ increase), Exceedence frequency: sum of hr/yr in excess of 6, 9, 12, 15 $\mu g/m^3$	Obstructive airway disease: NS/NR‡ Chronic bronchitis symptoms: NS/NR Asthma: SO_4 (monthly concentration): 4.51 (1.09-18.71) SO_4 (exceedance frequency): NS/NR	Uncond. Logistic	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, and presently live with smoker in 1987
Abbey 1993 /48/	US	Cohort	Incidence: obstructive airway disease chronic bronchitis symptoms asthma	NO_2: Monthly mean concentration: per 5 pphm‡ Exceedance frequency: sum of hr/yr in excess of 5, 15, 20, 25 pphm	Obstructive airway disease: NO_2 (monthly concentration): 1.26 (0.58-4.33) NO_2 (exceedance frequency): NS/NR Chronic bronchitis symptoms: NS/NR Asthma: NS/NR	Uncond. Logistic	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, and presently live with smoker in 1987
Greer 1993 /96/	US	Cohort	Incidence: asthma	TSP‡: per $\mu g/m^3$increase O_3: 1 pphm	TSP: NS/NR O_3 (monthly concentration): 1.31 (0.96-1.78) O_3 (exceedance frequency): Men 3.12 (1.61-5.85) women 0.94 (0.65-1.34)	Uncond. Logistic	Age, sex, education, history of COPD before age 16, and ETS at work
Abbey 1995 /98/	US	Cohort	Incidence: obstructive airway disease chronic bronchitis symptom asthma	$PM_{2.5}$: Monthly mean concentration (10 $\mu g/m^3$ increase) Exceedance frequency: sum of hr/yr in excess of 20, 30, and 40 $\mu g/m^3$	Obstructive airway disease: $PM_{2.5}$ (mean concentration): 1.09 (0.97-1.23) $PM_{2.5}$ (exceedance frequency): NS/NR Chronic bronchitis symptoms: $PM_{2.5}$ (mean concentration): 1.14 (1.00-1.30) $PM_{2.5}$ (exceedance frequency): NS/NR Asthma: $PM_{2.5}$ (mean concentration): 1.08 (0.85-1.37) $PM_{2.5}$ (exceedance frequency): NS/NR	Uncond. Logistic	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, and presently live with smoker in 1987
Abbey 1995 /97/	US	Cohort	Incidence: obstructive airway disease chronic bronchitis symptom asthma	PM_{10}: Monthly mean concentration (10 $\mu g/m^3$ increase) Exceedance frequency: 1000 hr/year increase above 100$\mu g/m^3$	Obstructive airway disease: PM_{10} (mean concentration): NS/NR PM_{10} (exceedance frequency): 1.17 (1.02-1.33) Chronic bronchitis symptom: PM_{10} (mean concentration): NS/NR PM_{10} (exceedance frequency): 1.17 (1.01-1.35) Asthma: PM_{10} (mean concentration): NS/NR PM_{10} (exceedance frequency): 1.30 (0.97-1.73)	Uncond. Logistic	Possible symptoms in 1977, childhood respiratory disease, childhood cold, age, gender, education, years of smoked in past, years of worked and lived with smoker, years of dust exposure, presently live with smoker in 1987

First author, year (ref)	Location	Study design	Outcomes	Pollutants and increment of exposure	RR (95% CI)		Stat. analysis	Covariates
Abbey 1999 /49/	US	Cohort	Mortality: any mention of nonmalignant respiratory disease	PM_{10}‡: 10 μg/m^3 PM_{10}: per 43d/yr above 100 μg/m^3 O_3: 10 μg/m^3 O_3: 551.1 h/yr above 100 ppb SO_2, NO_2, SO_4: 10 μg/m^3	Men PM_{10}: 1.09 (0.97-1.22) PM_{10}: 1.28 (1.03-1.57) O_3: 1.05 (0.93-1.18) O_3: 1.20 (0.88-1.64) SO_2: 0.87 (0.67-1.11) NO_2: 0.96 (0.90-1.03) SO_4: 1.18 (0.84-1.65)	Women 1.04 (0.94-1.15) 1.10 (0.91-1.33) 1.00 (0.89-1.13) 1.01 (0.77-1.33) 0.98 (0.78-1.23) 0.99 (0.93-1.06) 0.81 (0.61-1.08)	Cox	Age, education, ex-smoking, history of high blood pressure, ETS‡, physical exercise, BMI‡, and alcohol use
McDonnell 1999 /99/	US	Cohort	Incidence: asthma	O_3: Monthly average concentration (10 μg/m^3) Monthly 8-hr mean concentration: 10 μg/m^3 Exceedance frequency: per 907 hr/year increase above 60 ppb	Men Mean concentration: 2.16 (1.24-3.75) Mean 8-hr concentration: 1.15 (1.01-1.31) Exceedance frequency: 1.90 (0.99-3.64)	Women NS/NR 0.97 (0.90-1.05) NS/NR	Uncond. Logistic	Age, sex, education, smoking, and history of pneumonia or bronchitis before age 16, ever smoking, years lived or worked with a smoker, childhood code, and exposure to fumes or dust
McDonnell 2000 /58/	US	Cohort	Mortality: any mention of nonmalignant respiratory disease	PM_{10}, $PM_{2.5}$, $PM_{2.5-10}$: 10 μg/m^3	Men PM_{10}: 1.14 (0.98-1.34) $PM_{2.5}$: 1.23 (0.97-1.55) $PM_{2.5-10}$: 1.20 (0.87-1.64)	Women NS/NR NS/NR NS/NR	Cox	Age, education, ex-smoking, history of high blood pressure, ETS‡, physical exercise, BMI‡, and alcohol use
American Cancer Society (ACS) study								
Pope 2004 /72/	US	Cohort	Mortality: all respiratory disease, COPD and allied conditions	$PM_{2.5}$: 10 μg/m^3	Men and women: All respiratory diseases: 0.92 (0.86-0.98) COPD and allied conditions: 0.84 (0.77-0.93)		Cox	Age, sex, race, smoking, education, marital status, BMI, alcohol consumption, occupational exposure, and diet
Cohort of Norwegian Men								
Nafstad 2004 /60/	Norway	Cohort	Mortality: respiratory disease	NOx, SO_2: 10 μg/m^3	NOx: 1.16 (1.06–1.26) SO_2: 1.03 (0.93–1.14)		Cox	Education, occupation, smoking, leisure-time physical activity, risk group of cardiovascular diseases, and age at inclusion
Harvard Six Cities Study								
Laden 2006 /56/	US	Cohort	Mortality: respiratory disease	$PM_{2.5}$: 10 μg/m^3	1.08 (0.79–1.49)		Cox	Age, sex, smoking, less than high school education, and BMI
Netherlands Cohort Study on Diet and Cancer (NLCS)								
Beelen 2008 /47/	Nether.	Cohort	Mortality: respiratory disease	NO_2 (background and local traffic): 10 μg/m^3 Black smoke (background and local traffic): 10 μg/m^3 SO_2 (background): 10 μg/m^3 $PM_{2.5}$ (background and local	NO_2: 1.11 (1.00–1.23) Black smoke: 1.22 (0.99–1.50) SO_2: 0.94 (0.80–1.10) $PM_{2.5}$: 1.07 (0.75–1.52) Traffic intensity on nearest road: 1.10 (0.95–1.26)		Cox	Age, sex, smoking, and area-level income

First author, year (ref)	Location	Study design	Outcomes	Pollutants and increment of exposure	RR (95% CI)	Stat. analysis	Covariates
				traffic): 10 μg/m^3 Local traffic exposure (adjusting for background conc. of black smoke): (1) traffic intensity on the nearest road: a change of the 95th and 5th percentile, (2) sum of traffic intensity in a buffer of 100m: a change of the 95th and 5th percentile, (3) living near a major road: <100m from motorway or <50m from a local road vs. otherwise	Traffic intensity in a 100-m buffer: 1.21 (1.02–1.44) Living near a major road: 1.19 (0.91–1.56)		
Ontario Cohort Study (retrospective)							
Finkelstein 2005 /70/	Canada	Cohort	Mortality: respiratory disease	Pollution index: per unit increase Traffic indicator: binary classification (lived near or not near a major road/ highway)	Pollution index: 0.97 (0.88-1.05) Traffic indicator: 0.94 (0.71-1.25)	Cox	Age, sex, baseline pulmonary function, BMI, social deprivation index, and the diagnosis of obstructive lung disease, chronic ischemic heart disease, and diabetes
Oslo Cohort Study (retrospective)							
Naess 2007 /66/	Canada	Cohort	Mortality: COPD	$PM_{2.5}$, PM_{10}, NO_2: quartile increase	Men / Women Aged between 51-70 $PM_{2.5}$: 1.27 (1.11-1.47) / 1.09 (0.94-1.25) PM_{10}: 1.29 (1.12-1.48) / 1.06 (0.92-1.22) NO_2: 1.21 (1.05-1.39) / 1.06 (0.92-1.21) Aged between 71-90 $PM_{2.5}$: 1.10 (1.00-1.21) / 1.05 (0.96-1.16) PM_{10}: 1.08 (0.98-1.18) / 1.08 (0.98-1.19) NO_2: 1.04 (0.95-1.14) / 1.07 (0.97-1.17)	Cox	Age, sex, occupational class, and education
Residents of Lancaster and Glendora in California							
Detels 1987 /94/	US	Cohort	Lung function: FEV_1‡ $FEV_{25-75\%}$‡ V_{50}‡ V_{75}‡ $\Delta N_{2\ 750-1250}$‡ Incidence: symptoms of cough, wheezing, physician-diagnosed asthma, bronchitis and emphysema	Contrast between two cities: Lancaster and Glendora	Men and women: Lung function (only p-value provided): Men / Women FEV_1 >0.05 / 0.002 $FEV_{25-75\%}$ 0.004 / <0.001 $FEV_{25-75\%}$ <0.001 / <0.001 Incidence: NS/NR	Paired-t test	Age, sex, and smoking

‡ NS/NR: the estimates of association were reported as not significant, but no quantitative results were provided; TSP: total suspended particles; ETS: environmental tobacco smoking; BMI: body mass index; PM_{10}, particulate matter less than 10 microns in diameter; $PM_{2.5}$, particulate matter less than 2.5 microns in diameter; $PM_{15-2.5}$, particulate matter between 15 and 2.5 microns in diameter; $PM_{2.5-10}$, particulate matter between 10 and 2.5 microns in diameter; FEV_1, forced expiratory volume in one second; $FEV_{25-75\%}$, forced expiratory flow 25% to 75%; $\Delta_N 2_{750-1250}$, change in the percentage of nitrogen in the expired air at 750 and 1250 ml of expirate

TABLE F. Subgroup analysis of estimates for **all-cause mortality** associated with long-term exposure to **$PM_{2.5}$, NO_2,** and **SO_2**

Subgroup analysis	Number of studies	Summary RR (95% CI)	Measure of heterogeneity			*p*-value Meta-regression¶
			Q-value	*p*-value	I^2	
		$PM_{2.5}$				
All studies	6	1.06 (1.03-1.10)	6.95	0.224	28.1%	N/A
Location						
North America	5	1.07 (1.03-1.10)	6.94	0.139	42.4%	0.942
Europe	1	1.06 (0.97-1.16)	N/A *	N/A	N/A	Ref.*
Gender						
Both men and women	4	1.06 (1.03-1.11)	6.18	0.103	51.5%	0.840
Men only	2	1.06 (0.97-1.15)	0.77	0.380	0%	Ref.
Exposure assessment						
Intraurban comparison	3 ‡	1.08 (1.02-1.15)	0.39	0.824	0%	0.460
Interurban comparison	4	1.06 (1.02-1.11)	6.65	0.084	54.9%	Ref.
Completeness of follow up (%)						
≥ 90%	5	1.05 (1.03-1.07)	1.42	0.841	0%	0.019
Not reported	1	1.16 (1.07-1.26)	N/A	N/A	N/A	Ref.
Duration of follow up						
≥ 10 years	5	1.07 (1.03-1.10)	6.45	0.168	38.0%	0.428
< 10 years	1	1.00 (0.86-1.16)	N/A	N/A	N/A	Ref.
Exclusion of studies						
- Laden 2006 /56/	5	1.05 (1.03-1.07)	1.42	0.841	0%	N/A
- Lipfert 2006 /57/	4	1.05 (1.03-1.07)	1.03	0.793	0%	N/A
		NO_2				
All studies	6	1.00 (0.99-1.02)	13.08	0.023	61.8%	N/A
Location						
North America	3	1.00 (0.99-1.01)	0.02	0.989	0%	0.564
Europe	3	1.02 (0.96-1.08)	12.58	0.002	84.1%	Ref.
Gender						
Both men and women	4	1.00 (0.98-1.02)	8.93	0.03	66.4%	0.046
Men only	1	1.00 (0.97-1.03)	N/A	N/A	N/A	0.055
Women only	1	1.11 (1.01-1.23)	N/A	NA	N/A	Ref.
Exposure assessment						
Intraurban comparison	4	1.01 (0.99-1.04)	1.96	0.161	49.1%	0.656
Interurban comparison	2	1.00 (0.97-1.03)	8.92	0.030	66%	Ref.
Completeness of follow up (%)						
≥ 90%	5	1.00 (0.99-1.02)	7.14	0.129	44.0%	0.016
< 90%	1	0.96 (0.93-1.00)	N/A	N/A	N/A	Ref.
Duration of follow up						
≥ 10 years	5	1.00 (0.98-1.03)	13.05	0.011	69.3%	0.864
< 10 years	1	1.00 (0.97-1.03)	N/A	N/A	N/A	Ref.
Exclusion of studies						
- Filleul 2005 /51/	5	1.00 (0.99-1.02)	7.14	0.129	44.0%	N/A
- Gehring 2006 /53/	4	1.01 (0.99-1.02)	3.28	0.351	8.5%	N/A
- Lipfert 2006 /57/	3	1.01 (0.99-1.02)	3.16	0.206	36.7%	N/A
		SO_2 **				
All studies	6	1.01 (0.98-1.03)	24.06	<0.001	79.2%	N/A

Subgroup analysis	Number of studies	Summary RR (95% CI)	Measure of heterogeneity			*p*-value Meta-regression¶
			Q-value	*p*-value	I^2	
Location						
North America	3	1.03 (0.98-1.08)	13.57	0.001	85.3%	0.130
Europe	3	0.99 (0.97-1.02)	3.79	0.15	47.2%	Ref.
Gender						
Both men and women	4	1.02 (0.99-1.06)	13.95	0.003	78.5%	0.210
Men only	2	0.99 (0.97-1.01)	1.50	0.221	33.0%	Ref.
Exposure assessment						
Intraurban comparison	4	0.98 (0.96-1.01)	4.18	0.243	28.2%	0.169
Interurban comparison	2	1.03 (0.97-1.09)	13.56	<0.001	92.6%	Ref.
Completeness of follow up (%)						
≥ 90%	5	1.01 (0.98-1.04)	24.06	<0.001	83.4%	0.962
< 90%	1	1.01 (0.99-1.03)	N/A	N/A	N/A	Ref.
Duration of follow up						
≥ 10 years	5	1.01 (0.98-1.04)	22.77	<0.001	82.4%	0.760
< 10 years	1	1.00 (0.98-1.02)	N/A	N/A	N/A	Ref.
Exclusion of studies						
- Lipfert 2006 /57/	5	1.01 (0.98-1.04)	22.77	<0.001	82.4%	N/A

* N/A, not available because only 1 study; Ref., reference group

** Excluded Finkelstein 2003 /52/ because the reported effect estimates could not be converted to per 10 $\mu g/m^3$ increase

‡ Included Jerrett 2005 /54/ for subgroup analysis

¶ This meta-regression analysis used the method of reml (restricted maximum likelihood using an iterative procedure) to estimate the additive between studies variance tau^2.

TABLE G. Subgroup analysis of estimates for **mortality of lung cancer** associated with long-term exposure to **NO_2**

Subgroup analysis	Number of studies	Summary RR (95% CI)	Measure of heterogeneity			*p*-value Meta-regression¶
			Q-value	*p*-value	I^2	
		NO_2 **				
All studies	4	1.01 (0.94-1.09)	8.65	0.034	65.3%	N/A
Location						
North America	2	1.09 (0.88-1.34)	8.00	0.005	87.5%	0.605
Europe	2	0.97 (0.91-1.04)	0.00	0.990	0%	Ref.
Exposure assessment						
Intraurban comparison	3	1.04 (0.91-1.19)	8.32	0.016	76.0%	0.561
Interurban comparison	1	0.99 (0.96-1.02)	N/A	N/A	N/A	Ref.
Completeness of follow up						
≥ 90%	3	1.02 (0.94-1.13)	8.51	0.014	76.5%	0.704
< 90%	1	0.97 (0.85-1.10)	N/A	N/A	N/A	Ref.
Exclusion of studies						
- Filleul 2005 /51/	3	1.02 (0.94-1.13)	8.51	0.014	76.5%	N/A

* N/A, not available because only 1 study; Ref., reference group

** Excluded Naess 2007 /66/ because the reported effect estimates could not be converted to a 10 $\mu g/m^3$ increase

¶ This meta-regression analysis used the method of reml (restricted maximum likelihood using an iterative procedure) to estimate the additive between studies variance tau^2.

TABLE H. Subgroup analysis of estimates for the associations between **SO_2** and **cardiopulmonary mortality**

Subgroup analysis	Number of studies	Summary RR (95% CI)	Measure of heterogeneity			*p*-value Meta-regression¶
			Q-value	*p*-value	I^2	
		Mortality of cardiopulmonary diseases *				
All studies	3	1.02 (0.95-1.09)	8.19	0.017	75.6%	N/A
Location						
North America	2	1.06 (1.02-1.09)	0.65	0.420	0%	N/A
Europe	1	0.97 (0.92-1.02)	N/A **	N/A	N/A	N/A
Exposure assessment						
Intraurban comparison	2	0.98 (0.94-1.03)	0.68	0.411	0%	N/A
Interurban comparison	1	1.06 (1.03-1.10)	N/A	N/A	N/A	N/A
Completeness of follow up						
≥ 90%	2	1.06 (1.02-1.09)	0.65	0.420	0%	N/A
< 90%	1	0.97 (0.92-1.02)	N/A	N/A	N/A	N/A
Exclusion of studies						
- Filleul 2005 /51/	2	1.06 (1.02-1.09)	0.65	0.420	0%	N/A

* Excluded Finkelstein 2003 /52/ due to inconvertible increment of exposure in the RRs

** N/A, not available because only 1 study; Ref., reference group

¶ This meta-regression analysis used the method of reml (restricted maximum likelihood using an iterative procedure) to estimate the additive between studies variance tau^2.

APPENDIX: Search Strategies

1. Search MEDLINE database (Date: March 15, 2008)

Search	Most Recent Queries	Time	Result
#55	Search **(#46) NOT Review [PT]**	14:26:04	983
#46	Search **(#45) AND (risk* [Title/Abstract] OR risk* [MeSH:noexp] OR cohort studies[MeSH Terms] OR case-control studies [MeSH Terms])** Limits: **Publication Date from 1950/01/01 to 2007/12/31, Humans, All Adult: 19+ years**	13:16:04	1009
#45	Search **("Air Pollution"[Mesh] OR "Air Pollutants"[Mesh] OR "Ozone"[Mesh] OR "Nitrogen Dioxide"[Mesh] OR "Nitric Oxide"[Mesh] OR "Nitrogen Oxides"[Mesh] OR "Particulate Matter"[Mesh] OR "Sulfur Dioxide"[Mesh] OR "Carbon Monoxide"[Mesh] OR "Benzene"[Mesh] OR "Total Suspended Particle"[Text Word] OR "NO2"[Text Word] OR "NO"[Text Word] OR "NOx"[Text Word] OR "O3"[Text Word] OR "PM10"[Text Word] OR "PM2.5"[Text Word] OR "black smoke"[Text Word] OR "SO2"[Text Word] OR "TSP"[Text Word] OR "CO"[Text Word] OR "Hydrocarbons"[Text Word]) AND ("Urban" [Text Word] OR "Outdoor" [Text Word] OR "Ambient" [Text Word] OR "Traffic"[Text Word] OR "Mobile Source"[Text Word] OR "Gaseous"[Text Word] OR "Particulate"[Text Word] OR "Traffic Exposure"[Text Word] OR "Automobile Exhaust" [Text Word] OR "Proximity"[Text Word] OR "Near"[Text Word]) AND ("Chronic disease"[Text Word] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Infarction"[Mesh] OR "Myocardial Ischemia" [Mesh] OR "Stroke"[Text Word] OR "Neoplasms"[Mesh] OR "Lung Neoplasms"[Mesh] OR "Lung Cancer"[Text Word] OR "Respiratory Tract Diseases" [Mesh] OR "Bronchial Diseases"[Mesh] OR "Lung Diseases"[Mesh] OR "Chronic Obstructive Pulmonary Disease"[Text Word] OR "COPD"[Text Word] OR "Asthma" [Mesh] OR "Mortality"[Mesh] OR "Death"[Mesh])** Limits: **Publication Date from 1950/01/01 to 2007/12/31, Humans, All Adult: 19+ years**	13:15:47	1851

2. Search EMBASE database (Date: March 15, 2008)

#	Search History	Results	Display
1	air pollution/ or air pollutant/	26213	DISPLAY
2	Ozone/	11165	DISPLAY
3	Carbon Monoxide/ or Nitrogen Dioxide/ or Sulfur Dioxide/	21024	DISPLAY
4	Hydrocarbon/	7364	DISPLAY
5	Particulate Matter/	12625	DISPLAY
6	Suspended Particulate Matter/	3510	DISPLAY
7	1 or 2 or 3 or 4 or 5 or 6	67436	DISPLAY
8	urban area/	16379	DISPLAY
9	outdoor.mp.	5325	DISPLAY
10	outside.mp.	47018	DISPLAY
11	ambient air/	6755	DISPLAY
12	traffic/	3045	DISPLAY
13	motor vehicle/	2205	DISPLAY
14	Volatile Organic Compound/	4265	DISPLAY
15	Exhaust Gas/	7054	DISPLAY
16	exhaust exposure.mp.	88	DISPLAY
17	proximity.mp.	16172	DISPLAY
18	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	101124	DISPLAY
19	CHRONIC OBSTRUCTIVE LUNG DISEASE/ or LUNG NON SMALL CELL CANCER/ or LUNG CARCINOMA/ or LUNG	125335	DISPLAY

	SMALL CELL CANCER/ or LUNG METASTASIS/ or LUNG CANCER/ or LUNG SQUAMOUS CELL CARCINOMA/ or LUNG DISEASE/ or CHRONIC LUNG DISEASE/		
20	HEART DISEASE/ or HEART DEATH/ or HEART CANCER/	30380	DISPLAY
21	cardiovascular disease/ or cardiovascular inflammation/ or cardiovascular system tumor/ or heart disease/ or hypertension/ or vascular disease/	233568	DISPLAY
22	Chronic Disease/	30384	DISPLAY
23	mortality/	145497	DISPLAY
24	DEATH/ or "CAUSE OF DEATH"/	56614	DISPLAY
25	19 or 20 or 21 or 22 or 23 or 24	543906	DISPLAY
26	7 and 18 and 25	963	DISPLAY
27	limit 26 to (adult <18 to 64 years> or aged <65+ years>)	236	DISPLAY
28	limit 27 to human	232	DISPLAY
29	limit 28 to "causation-etiology (optimized)"	159	DISPLAY
30	29 not review.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name	159	DISPLAY

3. Search RISK ABSTRACT database (Date: March 16, 2008)

1) Query 1:

(((AB=(**traffic** or **proximity** or (**mobile source***))) or (AB=(**urban** or **outdoor** or **ambient**))) and ((AB=((**air pollut***) or **particulate*** or (**total suspended particle**))) or (AB=(**sulfate** or **nitrogen*** or **hydrocarbon***)))) and (AB=(**cohort** or (**case control**) or (**case cohort**)))

Results: 25 (note: same articles as those identified through PubMed or EMbase)

** Note that AB refers to abstract

2) Query 2:

((AB=((air pollut*) or particulate* or (total suspended particle))) or (AB=(sulfate or nitrogen* or hydrocarbon*))) and (AB=(cohort* or (case control) or (case cohort)))

Results: 92 (note: same articles as those identified through PubMed or EMbase)

** Note that AB refers to abstract