Annex A. Atmospheric Science

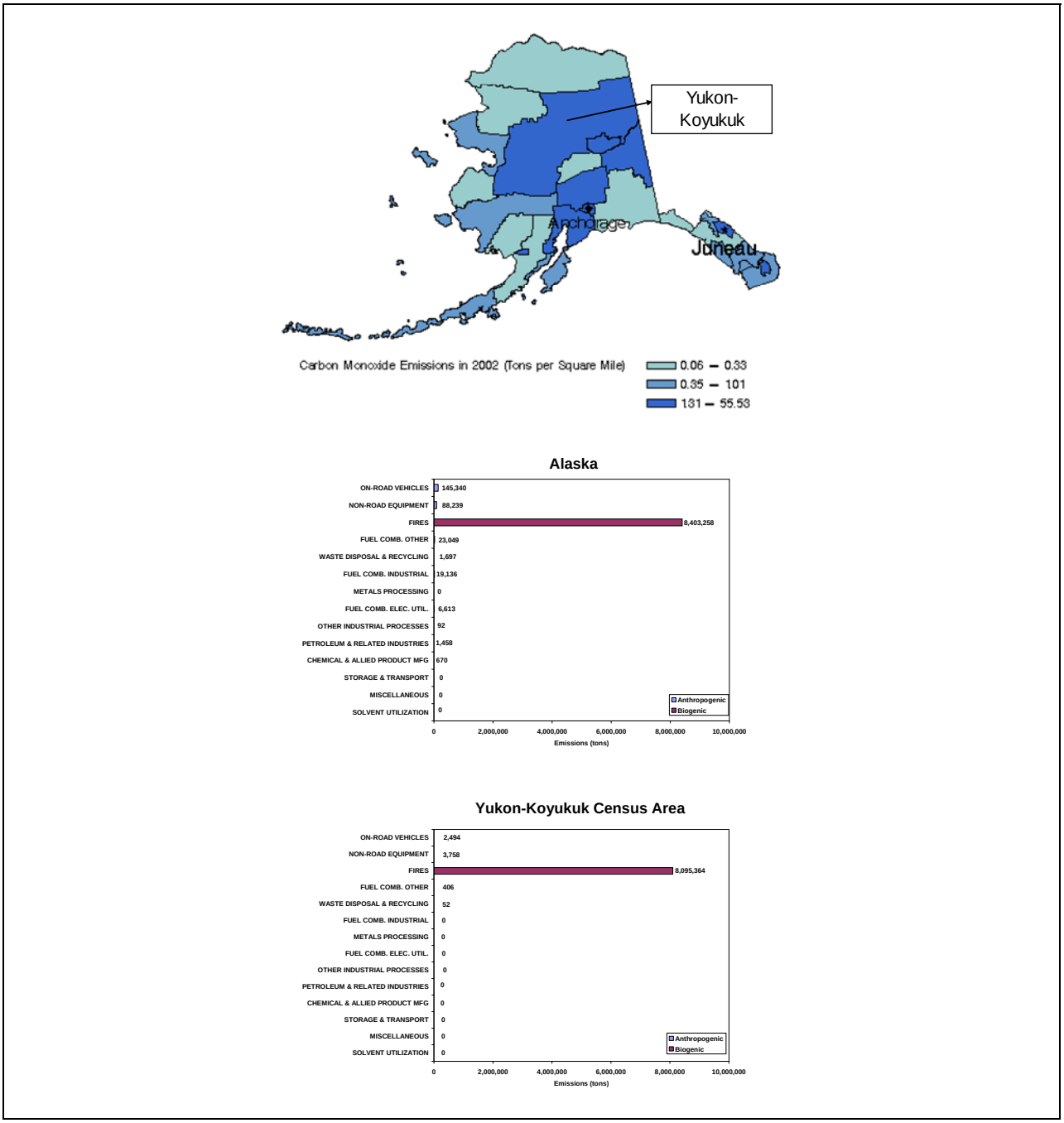


Figure A-1. CO emissions density map and distribution for the state of Alaska and for Yukon-Koyukuk County in Alaska.

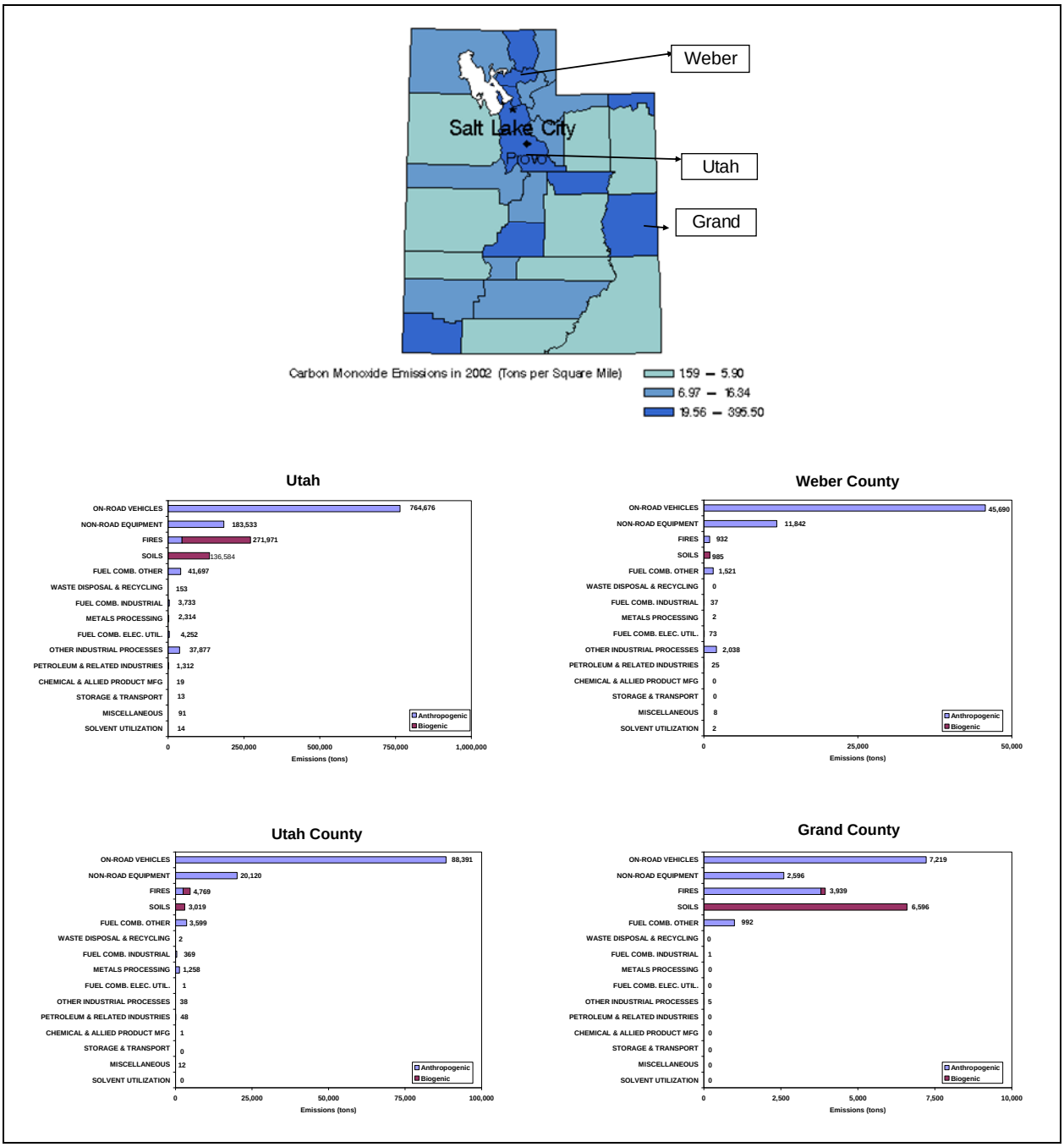


Figure A-2. CO emissions density map and distribution for the state of Utah and for selected counties in Utah.

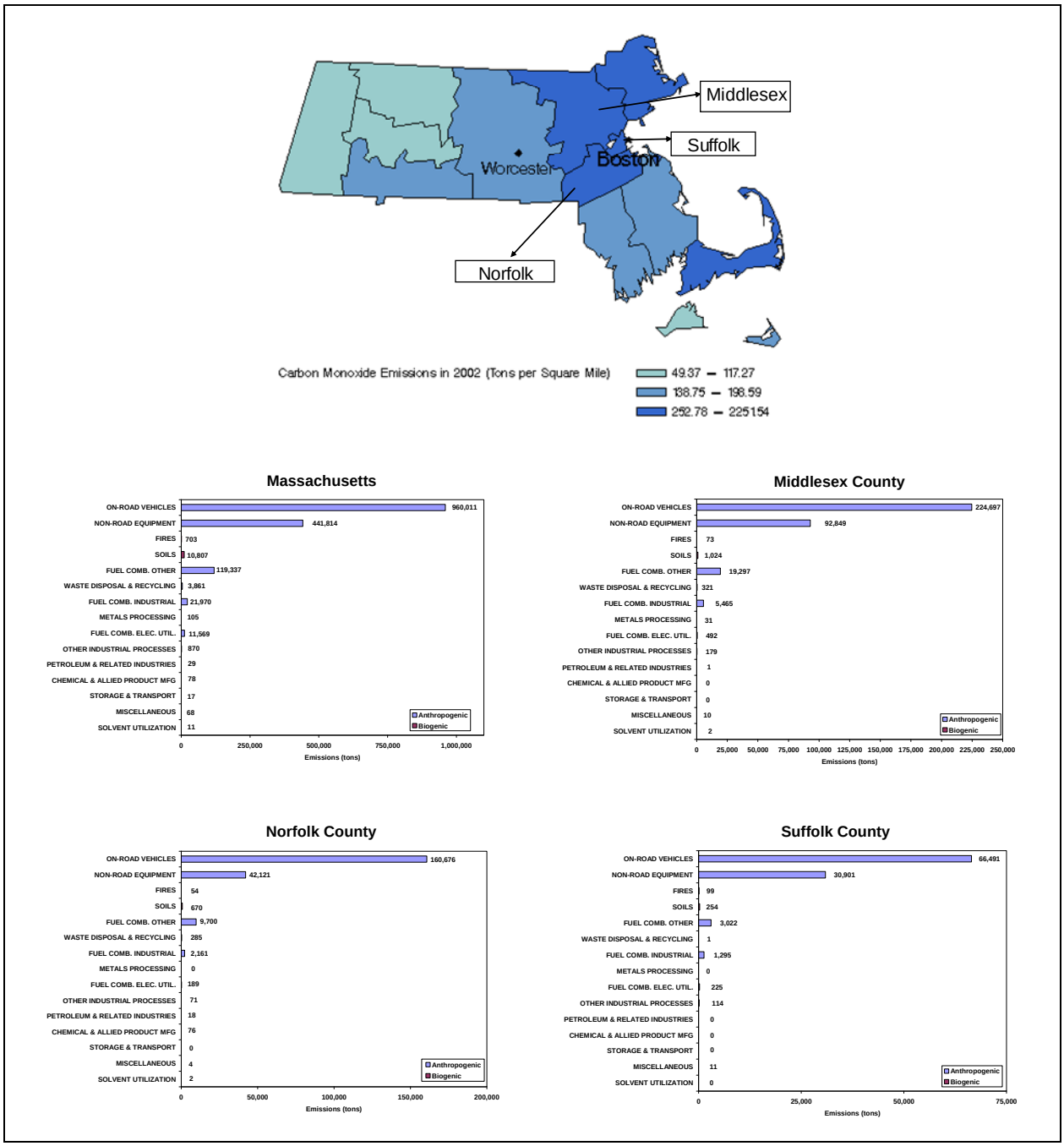


Figure A-3. CO emissions density map and distribution for the state of Massachusetts and for selected counties in Massachusetts.

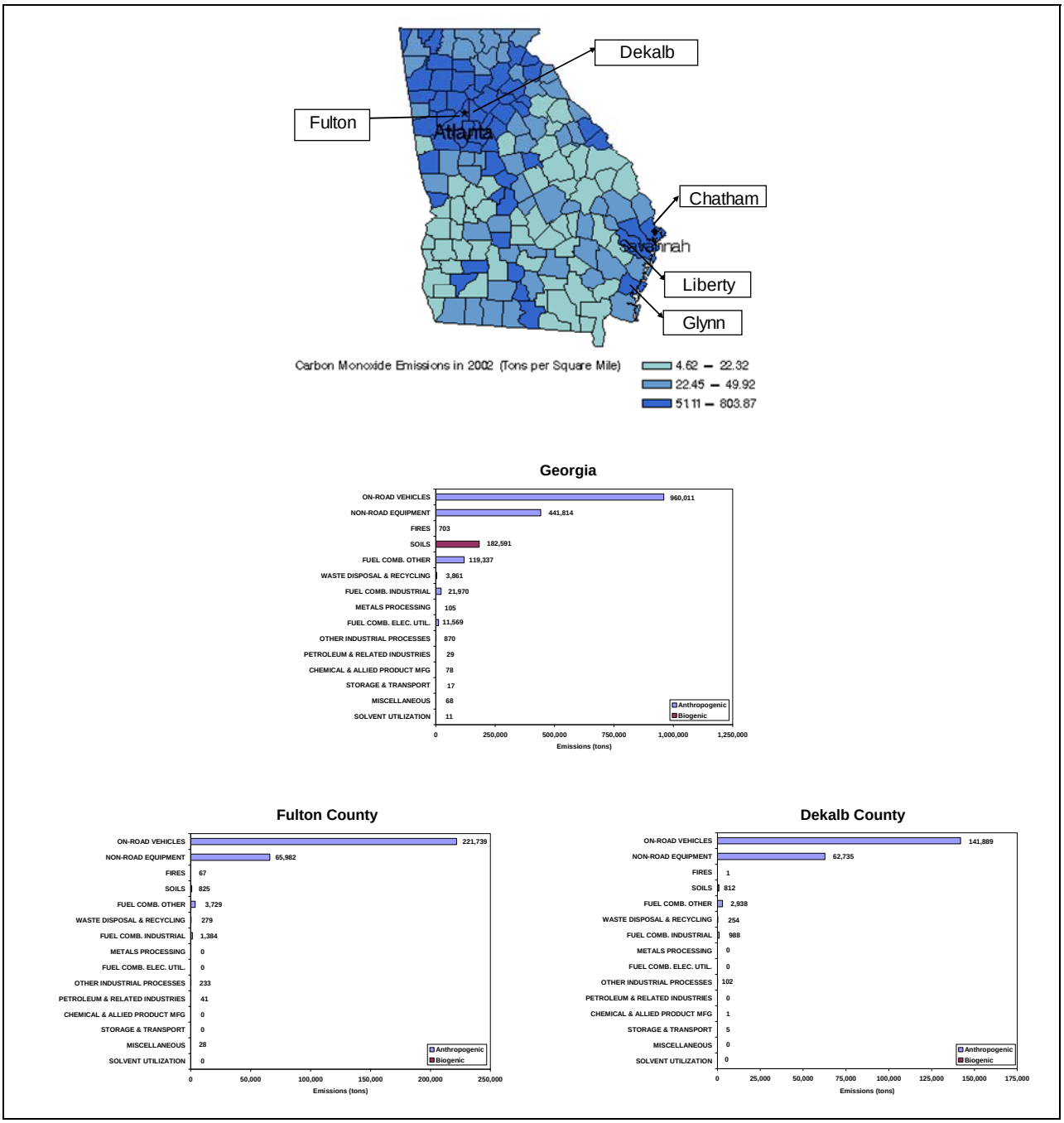


Figure A-4. CO emissions density map and distribution for the state of Georgia and for selected counties in Georgia (Figure 1 of 2).

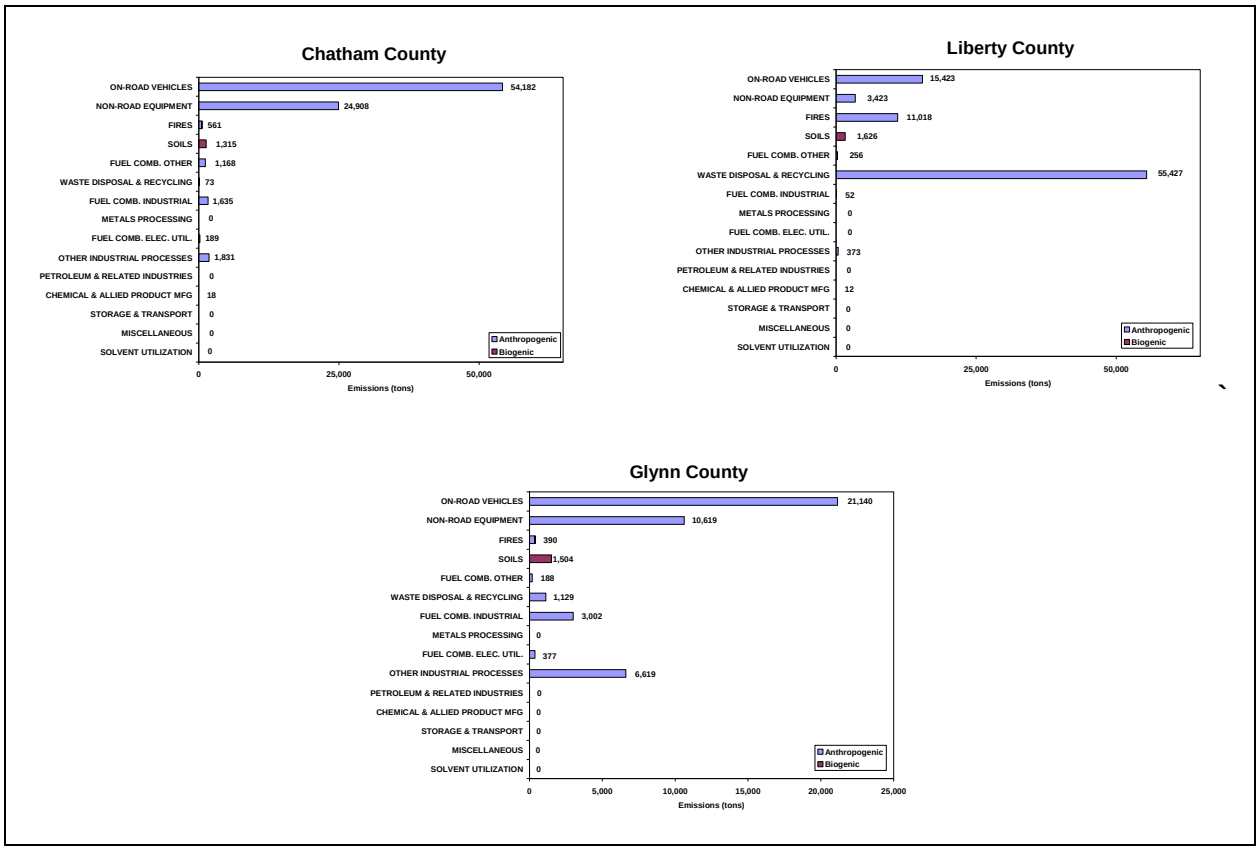


Figure A-5. CO emissions distribution for selected counties in Georgia (Figure 2 of 2).

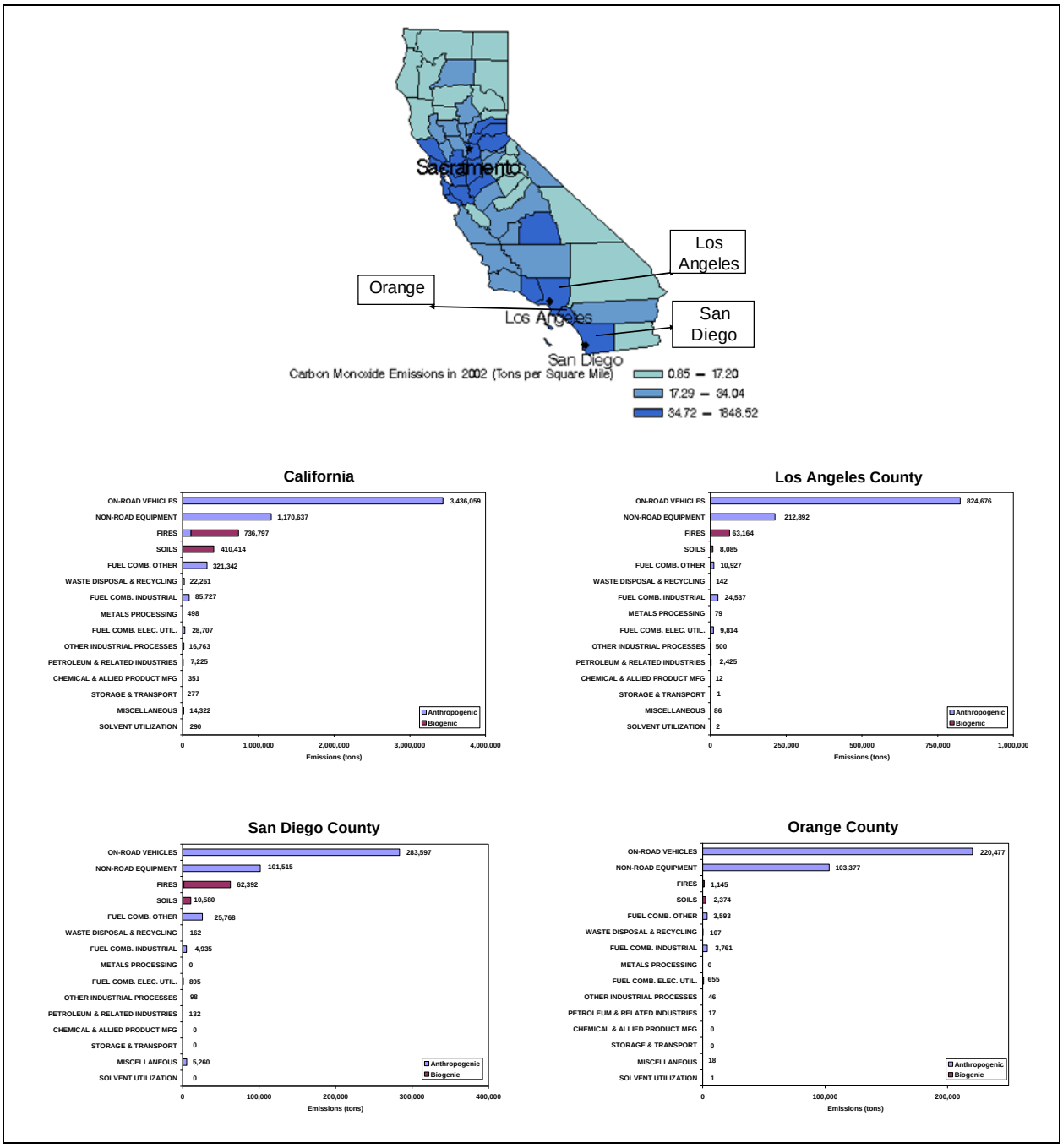
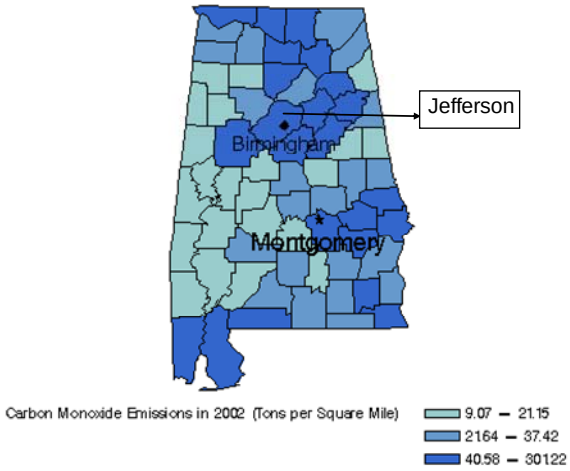
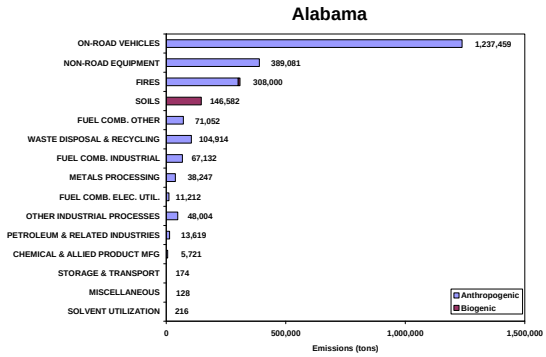


Figure A-6. CO emissions density map and distribution for the state of California and for selected counties in California.





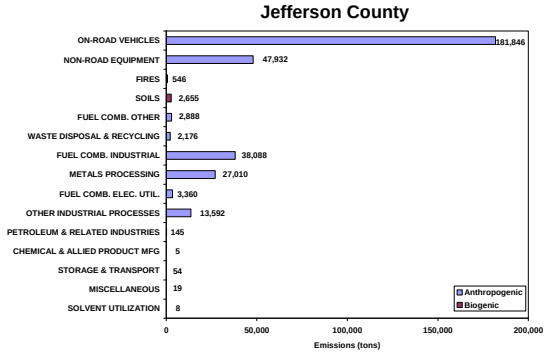


Figure A-7. CO emissions density map and distribution for the state of Alabama and for Jefferson County in Alabama.

Table A-1. Listing of all CO monitors currently in use, along with their limits of detection.

Method Code	Method Description	Reference Method Id	Fed MDL (ppm)
008	BENDIX 8501-5CA	RFCA-0276-008	0.50000
012	BECKMAN 866	RFCA-0876-012	0.50000
018	MSA 202S	RFCA-0177-018	0.50000
033	HORIBA AQM-10--11--12	RFCA-1278-033	0.50000
041	MONITOR LABS 8310	RFCA-0979-041	0.50000
048	HORIBA 300E/300SE	RFCA-1180-048	0.50000
050	MASS-CO 1 (MASSACHUSETTS)	RFCA-1280-050	0.50000
051	DASIBI 3003	RFCA-0381-051	0.50000
054	THERMO ELECTRON 48, 48C	RFCA-0981-054	0.50000
055	Gas Filter Correlation Thermo Electron 48C-TL	N/A	0.04000
066	MONITOR LABS 8830	RFCA-0388-066	0.50000
067	DASIBI 3008	RFCA-0488-067	0.50000
088	LEAR SIEGLER MODEL ML 9830	RFCA-0992-088	0.50000
093	API MODEL 300 GAS FILTER	RFCA-1093-093	0.50000
106	HORIBA INSTR. MODEL APMA-360	RFCA-0895-106	0.50000
108	ENVIRONMENT SA MODEL CO11M	RFCA-0995-108	0.50000
147	Environnement S.A. Model CO12M Co Analyzer	RFCA-0206-147	0.50000
158	HORIBA INSTR. MODEL APMA-370	RFCA-0506-158	0.50000
167	DKK-TOA Cork Mode GFC-311E	RFCA-0907-167	0.50000
172	SIR S.A. Model S5006	RFCA-0708-172	0.50000
554	Gas Filter Correlation Thermo Electron 48C-TLE	N/A	0.04000
588	Ecotech EC9830T	RFCA-0992-088	0.04000
593	API Model 300 EU	RFCA-1093-093	0.04000

Table A-2. Microscale monitors meeting 75% completeness criteria, 2005-2007.

Monitor Code	State Name	City Name	Traffic Count	Road Type
02-090-0002-42101-1	Alaska	Fairbanks	NR	NR
04-013-0016-42101-1	Arizona	Phoenix	50,000	ARTERIAL
04-019-1014-42101-1	Arizona	Tucson	41,200	MAJ ST OR HY
06-065-1003-42101-1	California	Riverside	40,000	FREEWAY
06-073-0007-42101-1	California	San Diego	6,000	THRU ST OR HY
08-013-0009-42101-1	Colorado	Longmont	20,000	MAJ ST OR HY
08-031-0002-42101-2	Colorado	Denver	17,200	MAJ ST OR HY
08-031-0019-42101-1	Colorado	Denver	500	MAJ ST OR HY
08-041-0015-42101-1	Colorado	Colorado Springs	44,200	MAJ ST OR HY
08-077-0018-42101-1	Colorado	Grand Junction	13,525	THRU ST OR HY
09-003-0017-42101-1	Connecticut	Hartford	10,000	THRU ST OR HY
11-001-023-42101-1	District Of Columbia	Washington	30,000	THRU ST OR HY
12-057-1070-42101-1	Florida	Tampa	133,855	ARTERIAL
12-086-4002-42101-1	Florida	Miami	5,000	LOCAL ST OR HY
12-095-1005-42101-1	Florida	Orlando	30,000	MAJ ST OR HY
12-103-0024-42101-1	Florida	Saint Petersburg	35,000	MAJ ST OR HY
12-103-2008-42101-1	Florida	Clearwater	67,751	MAJ ST OR HY
12-115-1004-42101-1	Florida	Sarasota	31,000	MAJ ST OR HY
13-121-0099-42101-1	Georgia	Atlanta	44,000	MAJ ST OR HY
17-031-0063-42101-1	Illinois	Chicago	5,000	LOCAL ST OR HY
17-031-6004-42101-1	Illinois	Maywood	NR	NR
17-143-0036-42101-1	Illinois	Peoria	18,500	ARTERIAL
17-167-0008-42101-1	Illinois	Springfield	16,400	MAJ ST OR HY
17-201-0011-42101-1	Illinois	Rockford	11,400	ARTERIAL
18-003-0011-42101-1	Indiana	Fort Wayne	30430	MAJ ST OR HY
18-089-0015-42101-1	Indiana	East Chicago	NR	NR
18-097-0072-42101-1	Indiana	Indianapolis	21,237	MAJ ST OR HY
18-163-0019-42101-1	Indiana	Evansville	24,498	LOCAL ST OR HY
21-111-1019-42101-1	Kentucky	Louisville	22,000	MAJ ST OR HY
27-053-0954-42101-1	Minnesota	Minneapolis	29,352	MAJ ST OR HY
27-123-0050-42101-1	Minnesota	St. Paul	NR	NR
27-137-0018-42101-1	Minnesota	Duluth	12,000	MAJ ST OR HY
27-145-3048-42101-1	Minnesota	St. Cloud	NR	NR
30-029-0010-42101-1	Montana	Kalispell	NR	THRU ST OR HY
30-031-0013-42101-1	Montana	Not in a city	2,000	THRU ST OR HY
33-011-1009-42101-1	New Hampshire	Nashua	40,000	MAJ ST OR HY
34-005-1001-42101-1	New Jersey	Burlington	8,000	THRU ST OR HY
34-017-1002-42101-1	New Jersey	Jersey City	25,000	THRU ST OR HY
37-067-0023-42101-1	North Carolina	Winston-Salem	22,000	MAJ ST OR HY
39-035-0048-42101-1	Ohio	Cleveland	24,300	THRU ST OR HY

Monitor Code	State Name	City Name	Traffic Count	Road Type
39-035-0051-42101-1	Ohio	Cleveland	16,150	MAJ ST OR HY
39-035-0053-42101-1	Ohio	Cleveland	19,550	MAJ ST OR HY
39-049-0036-42101-1	Ohio	Columbus	16,800	MAJ ST OR HY
39-061-0021-42101-1	Ohio	Cincinnati	17,250	LOCAL ST OR HY
39-085-0006-42101-1	Ohio	Mentor	25,240	MAJ ST OR HY
39-113-0034-42101-1	Ohio	Dayton	7,100	THRU ST OR HY
39-153-0022-42101-1	Ohio	Akron	13,150	MAJ ST OR HY
41-029-0018-42101-1	Oregon	Medford	NR	NR
41-039-0013-42101-1	Oregon	Eugene	17,500	MAJ ST OR HY
41-051-0087-42101-1	Oregon	Portland	4,150	LOCAL ST OR HY
45-079-0020-42101-1	South Carolina	Columbia	31,500	MAJ ST OR HY
47-037-0021-42101-1	Tennessee	Nashville	15,000	MAJ ST OR HY
47-157-0036-42101-1	Tennessee	Memphis	25,000	THRU ST OR HY
48-029-0046-42101-1	Texas	San Antonio	5,820	MAJ ST OR HY
48-201-0075-42101-1	Texas	Houston	6,576	LOCAL ST OR HY
53-033-0019-42101-1	Washington	Bellevue	100,000	MAJ ST OR HY
53-063-0049-42101-1	Washington	Spokane	10,000	MAJ ST OR HY

"NR" denotes that the value was not reported.

Table A-3. Middle scale monitors meeting 75% completeness criteria, 2005-2007.

Monitor Code	State Name	City Name	Traffic Count	Road Type
04-013-3010-42101-1	Arizona	Phoenix	18,500	ARTERIAL
06-029-0010-42101-1	California	Bakersfield	30,300	ARTERIAL
06-037-1301-42101-1	California	Lynwood	35,000	ARTERIAL
06-037-9033-42101-1	California	Lancaster	2,320	LOCAL ST OR HY
06-059-1003-42101-1	California	Costa Mesa	1,000	LOCAL ST OR HY
06-071-9004-42101-1	California	San Bernardino	21,900	THRU ST OR HY
06-085-0005-42101-1	California	San Jose	NR	LOCAL ST OR HY
12-0011-0010-42101-1	Florida	Fort Lauderdale	1,000	LOCAL ST OR HY
12-031-0080-42101-1	Florida	Jacksonville	1,000	LOCAL ST OR HY
12-031-0084-42101-1	Florida	Jacksonville	500	LOCAL ST OR HY
12-099-1004-42101-1	Florida	Palm Beach	30,000	MAJ ST OR HY
12-103-2006-42101-1	Florida	Clearwater	23,400	MAJ ST OR HY
17-031-3103-42101-1	Illinois	Schiller Park	47,900	ARTERIAL
20-209-0021-42101-1	Kansas	Kansas City	7,720	MAJ ST OR HY
24-510-0040-42101-1	Maryland	Baltimore	15,300	THRU ST OR HY
32-031-0022-42101-1	Nevada	Reno	NR	NR
34-003-0004-42101-1	New Jersey	Fort Lee	250,000	ARTERIAL
36-061-0056-42101-1	New York	New York	45,000	MAJ ST OR HY
39-049-0005-42101-1	Ohio	Columbus	36,600	FREEWAY
39-081-1001-42101-1	Ohio	Mingo Junction	2,500	LOCAL ST OR HY
39-151-0020-42101-1	Ohio	Canton	11,000	MAJ ST OR HY
40-143-0191-42101-1	Oklahoma	Tulsa	50,800	FREEWAY
42-003-0038-42101-1	Pennsylvania	Pittsburgh	15,000	MAJ ST OR HY
42-101-0047-42101-1	Pennsylvania	Philadelphia	NR	NR
45-019-0046-42101-1	South Carolina	Not in a city	NR	LOCAL ST OR HY
45-045-0008-42101-1	South Carolina	Greenville	NR	LOCAL ST OR HY
45-045-0009-42101-1	South Carolina	Taylors	9,500	LOCAL ST OR HY
47-163-0007-42101-1	Tennessee	Kingsport	NR	NR
48-439-1002-42101-1	Texas	Fort Worth	100	LOCAL ST OR HY
50-007-0014-42101-1	Vermont	Burlington	NR	MAJ ST OR HY
72-127-0003-42101-1	Puerto Rico	San Juan	64,000	MAJ ST OR HY

"NR" denotes that the value was not reported.

Table A-4. Neighborhood scale monitors meeting 75% completeness criteria, 2005-2007.

Monitor Code	State Name	City Name	Traffic Count	Road Type
01-073-1003-42101-1	Alabama	Fairfield	5,000	LOCAL ST OR HY
01-073-6004-42101-1	Alabama	Birmingham	NR	NR
02-020-0018-42101-1	Alaska	Anchorage	NR	NR
02-020-0048-42101-1	Alaska	Anchorage	5,000	LOCAL ST OR HY
02-090-0020-42101-1	Alaska	Fairbanks	NR	NR
04-013-0019-42101-1	Arizona	Phoenix	NR	LOCAL ST OR HY
04-013-3002-42101-1	Arizona	Phoenix	24,000	ARTERIAL
04-019-0002-42101-1	Arizona	Tucson	37,400	MAJ ST OR HY
04-019-1011-42101-1	Arizona	Tucson	47,000	MAJ ST OR HY
04-019-1028-42101-1	Arizona	Tucson	52,900	MAJ ST OR HY
06-001-1001-42101-1	California	Fremont (Centerville)	500	LOCAL ST OR HY
06-013-0002-42101-1	California	Concord	41,218	MAJ ST OR HY
06-037-5005-42101-1	California	Los Angeles	1,252	LOCAL ST OR HY
06-053-1003-42101-1	California	Salinas	33,193	THRU ST OR HY
06-065-9001-42101-1	California	Lake Elsinore	NR	NR
06-067-0007-42101-1	California	Sacramento	20,000	THRU ST OR HY
06-073-0001-42101-1	California	Chula Vista	5,000	LOCAL ST OR HY
06-073-1002-42101-1	California	Escondido	NR	NR
06-073-2007-42101-1	California	Otay Mesa	18,000	LOCAL ST OR HY
06-083-1025-42101-1	California	Capitan	NR	NR
06-083-2004-42101-1	California	Lompoc	NR	NR
06-083-2011-42101-1	California	Goleta	5,000	THRU ST OR HY
06-083-4003-42101-1	California	Vandenberg Air Force Base	NR	NR
08-01-3001-42101-1	Colorado	Welby	500	EXPRESSWAY
08-067-7001-42101-1	Colorado	Not in a city	2,436	LOCAL ST OR HY
08-069-1004-42101-1	Colorado	Fort Collins	5,000	THRU ST OR HY
08-123-0010-42101-1	Colorado	Greeley	6,650	THRU ST OR HY
11-001-0041-42101-1	District Of Columbia	Washington	540	LOCAL ST OR HY
12-011-2004-42101-1	Florida	Pompano Beach	1,000	LOCAL ST OR HY
12-011-3002-42101-1	Florida	Hollywood	1,000	LOCAL ST OR HY
12-031-0083-42101-1	Florida	Jacksonville	10,000	LOCAL ST OR HY
12-086-0031-42101-1	Florida	Miami	62,000	MAJ ST OR HY
12-086-1019-42101-1	Florida	Miami	8,000	MAJ ST OR HY
12-095-2002-42101-1	Florida	Winter Park	7,000	MAJ ST OR HY
12-103-0018-42101-1	Florida	Saint Petersburg	2,000	MAJ ST OR HY
17-031-4002-42101-1	Illinois	Cicero	NR	NR
17-163-0010-42101-1	Illinois	East Saint Louis	8,900	LOCAL ST OR HY
18-097-0073-42101-1	Indiana	Indianapolis (Remainder)	11,261	THRU ST OR HY
20-173-0010-42101-1	Kansas	Wichita	6,884	LOCAL ST OR HY
21-111-0046-42101-1	Kentucky	Louisville	6,500	THRU ST OR HY

Monitor Code	State Name	City Name	Traffic Count	Road Type
22-033-0009-42101-1	Louisiana	Baton Rouge	5,000	LOCAL ST OR HY
25-013-0016-42101-1	Massachusetts	Springfield	5,000	LOCAL ST OR HY
25-017-0007-42101-1	Massachusetts	Lowell	15,000	THRU ST OR HY
25-025-0042-42101-1	Massachusetts	Boston	12,785	LOCAL ST OR HY
27-03-0600-42101-1	Minnesota	Fridley	1,400	LOCAL ST OR HY
27-037-0020-42101-1	Minnesota	Rosemount	NR	NR
27-037-0423-42101-1	Minnesota	Inver Grove Heights (RR name Inver Grove)	NR	NR
29-510-0086-42101-1	Missouri	St. Louis	81,850	MAJ ST OR HY
30-111-0085-42101-1	Montana	Billings	5,700	THRU ST OR HY
31-055-0035-42101-1	Nebraska	Omaha	2,900	LOCAL ST OR HY
32-003-0538-42101-1	Nevada	Las Vegas	20,000	LOCAL ST OR HY
32-003-0539-42101-1	Nevada	Las Vegas	21,000	MAJ ST OR HY
32-003-0561-42101-1	Nevada	Las Vegas	28,400	MAJ ST OR HY
32-003-1021-42101-1	Nevada	Las Vegas	NR	NR
32-003-2002-42101-1	Nevada	Las Vegas	6,750	THRU ST OR HY
32-031-0016-42101-1	Nevada	Reno	22,700	LOCAL ST OR HY
32-031-0020-42101-1	Nevada	Reno	NR	NR
32-031-0025-42101-1	Nevada	Reno	NR	NR
32-031-1005-42101-1	Nevada	Sparks	2,600	LOCAL ST OR HY
32-031-2009-42101-1	Nevada	Lemmon Valley-Golden Valley	NR	NR
32-510-0004-42101-1	Nevada	Carson City	1	LOCAL ST OR HY
33-011-0020-42101-1	New Hampshire	Manchester	500	LOCAL ST OR HY
34-003-5001-42101-1	New Jersey	Hackensack	15,000	THRU ST OR HY
34-007-0003-42101-1	New Jersey	Camden	45,000	MAJ ST OR HY
35-001-019-42101-1	New Mexico	Albuquerque	1	ARTERIAL
35-001-0023-42101-1	New Mexico	Albuquerque	41,200	MAJ ST OR HY
35-001-0024-42101-1	New Mexico	Albuquerque	15,500	MAJ ST OR HY
35-001-0028-42101-1	New Mexico	Albuquerque	2,0600	THRU ST OR HY
35-001-1014-42101-1	New Mexico	Albuquerque	8,000	THRU ST OR HY
35-043-9004-42101-1	New Mexico	Not in a city	100	LOCAL ST OR HY
36-063-2008-42101-1	New York	Niagara Falls	5,000	LOCAL ST OR HY
37-119-0041-42101-1	North Carolina	Charlotte	16,400	MAJ ST OR HY
37-119-0041-42101-3	North Carolina	Charlotte	16,400	MAJ ST OR HY
39-035-0070-42101-1	Ohio	Cleveland	100	LOCAL ST OR HY
39-113-0028-42101-1	Ohio	Dayton	5,100	LOCAL ST OR HY
39-153-0020-42101-1	Ohio	Akron	200	LOCAL ST OR HY
40-021-9002-42101-1	Oklahoma	Park Hill	10,300	LOCAL ST OR HY
40-071-9010-42101-1	Oklahoma	Not in a city	300	LOCAL ST OR HY
40-109-0047-42101-1	Oklahoma	Oklahoma City	27,000	MAJ ST OR HY
41-051-0080-42101-1	Oregon	Portland	5,000	LOCAL ST OR HY
42-003-0031-42101-1	Pennsylvania	Pittsburgh	4,562	THRU ST OR HY
42-013-0801-42101-1	Pennsylvania	Altoona	100	LOCAL ST OR HY

Monitor Code	State Name	City Name	Traffic Count	Road Type
42-017-0012-42101-1	Pennsylvania	Bristol	500	LOCAL ST OR HY
42-021-0011-42101-1	Pennsylvania	Johnstown	6,000	LOCAL ST OR HY
42-049-0003-42101-1	Pennsylvania	Erie	1,000	LOCAL ST OR HY
42-071-0007-42101-1	Pennsylvania	Lancaster	2,000	THRU ST OR HY
42-073-0015-42101-1	Pennsylvania	New Castle	4,500	LOCAL ST OR HY
42-091-0013-42101-1	Pennsylvania	Norristown	8,500	MAJ ST OR HY
42-095-0025-42101-1	Pennsylvania	Freemansburg	100	LOCAL ST OR HY
42-101-0004-42101-1	Pennsylvania	Philadelphia	13800	MAJ ST OR HY
42-101-0027-42101-1	Pennsylvania	Philadelphia	46000	MAJ ST OR HY
42-107-0003-42101-1	Pennsylvania	Shenandoah	100	LOCAL ST OR HY
42-125-0005-42101-1	Pennsylvania	Charleroi	NR	NR
44-007-1010-42101-1	Rhode Island	East Providence	100,000	FREEWAY
48-061-0006-42101-1	Texas	Brownsville	30	LOCAL ST OR HY
48-113-0069-42101-2	Texas	Dallas	1,000	LOCAL ST OR HY
48-141-0002-42101-1	Texas	El Paso	7,270	THRU ST OR HY
48-141-0029-42101-1	Texas	El Paso	2,790	LOCAL ST OR HY
48-141-0037-42101-1	Texas	El Paso	5,000	LOCAL ST OR HY
48-141-0044-42101-1	Texas	El Paso	15,200	ARTERIAL
48-141-0053-42101-1	Texas	El Paso	1,992	FREEWAY
48-141-0057-42101-1	Texas	Socorro	500	LOCAL ST OR HY
48-141-0058-42101-1	Texas	El Paso	1,080	LOCAL ST OR HY
48-201-0024-42101-1	Texas	Not in a city	5,300	MAJ ST OR HY
48-201-0047-42101-1	Texas	Houston	5,860	MAJ ST OR HY
48-201-1035-42101-1	Texas	Houston	13,440	MAJ ST OR HY
48-201-1039-42101-1	Texas	Deer Park	16010	MAJ ST OR HY
48-439-3011-42101-1	Texas	Arlington	10,573	LOCAL ST OR HY
48-453-0014-42101-1	Texas	Austin	3,420	LOCAL ST OR HY
48-479-0017-42101-1	Texas	Laredo	30,380	ARTERIAL
49-035-0003-42101-1	Utah	Not in a city	16,500	THRU ST OR HY
50-021-0002-42101-1	Vermont	Rutland	NR	NR
51-059-0005-42101-1	Virginia	Not in a city	25	LOCAL ST OR HY
51-650-0004-42101-2	Virginia	Hampton	2,000	LOCAL ST OR HY
51-760-0024-42101-1	Virginia	Richmond	7,591	THRU ST OR HY
51-770-0015-42101-1	Virginia	Roanoke	NR	NR
54-009-0011-42101-1	West Virginia	Weirton	NR	NR
54-029-0009-42101-1	West Virginia	Weirton	NR	NR
54-029-1004-42101-1	West Virginia	Weirton	50	LOCAL ST OR HY

"NR" denotes that the value was not reported.

Table A-5. Urban scale monitors meeting 75% completeness criteria, 2005-2007.

Monitor Code	State Name	City Name	Traffic Count	Road Type
06-059-0007-42101-1	California	Anaheim	1,000	LOCAL ST OR HY
13-089-0002-42101-1	Georgia	Decatur	9,250	LOCAL ST OR HY
13-223-0003-42101-1	Georgia	Not in a city	6	LOCAL ST OR HY
25-027-0023-42101-1	Massachusetts	Worcester	NR	LOCAL ST OR HY
34-007-1001-42101-1	New Jersey	Not in a city	4,000	THRU ST OR HY
42-003-0010-42101-1	Pennsylvania	Pittsburgh	1,000	MAJ ST OR HY
42-007-0014-42101-1	Pennsylvania	Beaver Falls	NR	NR
42-129-0008-42101-1	Pennsylvania	Greensburg	100	THRU ST OR HY
42-133-0008-42101-1	Pennsylvania	York	8,400	THRU ST OR HY
48-141-0055-42101-1	Texas	El Paso	2450	LOCAL ST OR HY
51-059-0030-42101-1	Virginia	Franconia	200	LOCAL ST OR HY

"NR" denotes that the value was not reported.

Table A-6. Regional scale monitors meeting 75% completeness criteria, 2005-2007.

Monitor Code	State Name	City Name	Traffic Count	Road Type
23-009-0103-42101-1	Maine	Not in a city	3,500	LOCAL ST OR HY
35-001-0029-42101-1	New Mexico	South Valley	8,800	LOCAL ST OR HY

"NR" denotes that the value was not reported.

Table A-7. Monitors meeting 75% completeness criteria, 2005-2007 with no scale delared.

Monitor Code	State Name	City Name	Traffic Count	Road Type
04-013-9997-42101-1	Arizona	Phoenix	250	LOCAL ST OR HY
06-001-0007-42101-1	California	Livermore	2,400	LOCAL ST OR HY
06-007-0002-42101-1	California	Chico	44,000	LOCAL ST OR HY
06-013-1002-42101-1	California	Bethel Island	NR	NR
06-013-1004-42101-1	California	San Pablo	NR	THRU ST OR HY
06-013-3001-42101-1	California	Pittsburg	9,600	THRU ST OR HY
06-019-0007-42101-1	California	Fresno	500	LOCAL ST OR HY
06-019-0008-42101-1	California	Fresno	20,000	MAJ ST OR HY
06-019-0242-42101-1	California	Fresno	500	LOCAL ST OR HY
06-019-5001-42101-1	California	Clovis	16,461	THRU ST OR HY
06-025-0005-42101-1	California	Calexico	7,000	LOCAL ST OR HY
06-025-0006-42101-1	California	Calexico	10	THRU ST OR HY
06-025-1003-42101-1	California	El Centro	NR	NR
06-037-0002-42101-1	California	Azusa	600	THRU ST OR HY
06-037-0113-42101-1	California	West Los Angeles	NR	NR
06-037-1002-42101-1	California	Burbank	2,400	LOCAL ST OR HY
06-037-1103-42101-1	California	Los Angeles	9,000	THRU ST OR HY
06-037-1201-42101-1	California	Reseda	NR	NR
06-037-1701-42101-1	California	Pomona	NR	NR
06-037-2005-42101-1	California	Pasadena	18,000	THRU ST OR HY
06-037-4002-42101-1	California	Long Beach	24,000	LOCAL ST OR HY
06-037-6012-42101-1	California	Santa Clarita	4,395	LOCAL ST OR HY
06-041-0001-42101-1	California	San Rafael	15,000	MAJ ST OR HY
06-045-0008-42101-1	California	Ukiah	12,000	LOCAL ST OR HY
06-045-0009-42101-1	California	Willits	18,000	MAJ ST OR HY
06-055-0003-42101-1	California	Napa	NR	NR
06-059-2022-42101-1	California	Mission Viejo	42,400	MAJ ST OR HY
06-059-5001-42101-1	California	La Habra	NR	NR
06-065-5001-42101-1	California	Palm Springs	NR	NR
06-065-8001-42101-1	California	Rubidoux (West Riverside)	18,000	THRU ST OR HY
06-067-0002-42101-1	California	North Highlands	NR	NR
06-067-0006-42101-1	California	Sacramento	10,000	LOCAL ST OR HY
06-067-0013-42101-1	California	Sacramento	100	LOCAL ST OR HY
06-071-0001-42101-1	California	Barstow	NR	NR
06-071-0306-42101-1	California	Victorville	454	LOCAL ST OR HY
06-071-1004-42101-1	California	Upland	15,000	THRU ST OR HY
06-075-0005-42101-1	California	San Francisco	240,700	FREEWAY
06-077-1002-42101-1	California	Stockton	6,000	LOCAL ST OR HY
06-081-1001-42101-1	California	Redwood City	1,000	LOCAL ST OR HY
06-087-0003-42101-1	California	Davenport	NR	NR

Monitor Code	State Name	City Name	Traffic Count	Road Type
06-095-0004-42101-1	California	Vallejo	9,350	THRU ST OR HY
06-097-0003-42101-1	California	Santa Rosa	2,608	THRU ST OR HY
06-099-0005-42101-1	California	Modesto	NR	NR
06-099-0006-42101-1	California	Turlock	500	LOCAL ST OR HY
09-003-1003-42101-1	Connecticut	East Hartford	800	LOCAL ST OR HY
10-003-1008-42101-1	Delaware	Not in a city	NR	NR
10-003-2004-42101-1	Delaware	Wilmington	28,046	MAJ ST OR HY
15-003-0010-42101-1	Hawaii	Ewa Beach	NR	NR
18-063-0002-42101-1	Indiana	Pittsboro	500	LOCAL ST OR HY
25-025-0002-42101-1	Massachusetts	Boston	35,000	MAJ ST OR HY
29-077-0032-42101-1	Missouri	Springfield	1,000	LOCAL ST OR HY
29-189-0004-42101-1	Missouri	Sunset Hills	33,300	MAJ ST OR HY
30-013-0001-42101-1	Montana	Great Falls	26,155	MAJ ST OR HY
31-109-0018-42101-1	Nebraska	Lincoln	NR	NR
34-023-2003-42101-1	New Jersey	Perth Amboy	14,000	LOCAL ST OR HY
34-025-2001-42101-1	New Jersey	Freehold	NR	NR
34-027-0003-42101-1	New Jersey	Morristown	NR	NR
36-001-0012-42101-1	New York	Albany	12,000	MAJ ST OR HY
36-029-0005-42101-1	New York	Buffalo	26,000	ARTERIAL
36-055-1007-42101-1	New York	Rochester	NR	NR
36-067-0017-42101-1	New York	Syracuse	NR	NR
36-081-0124-42101-1	New York	New York	10,000	EXPRESSWAY
36-093-0003-42101-1	New York	Schenectady	37,000	EXPRESSWAY
36-103-0009-42101-2	New York	Holtsville	10,000	THRU ST OR HY
48-479-0016-42101-1	Texas	Laredo	16,180	MAJ ST OR HY
49-057-0006-42101-1	Utah	Ogden	38,000	ARTERIAL
51-013-0020-42101-1	Virginia	Not in a city	6,000	MAJ ST OR HY
51-059-1005-42101-1	Virginia	Annandale	24,000	MAJ ST OR HY
51-059-5001-42101-1	Virginia	McLean	36,845	MAJ ST OR HY
51-510-0009-42101-1	Virginia	Alexandria	3,974	LOCAL ST OR HY
56-039-1012-42101-1	Wyoming	Not in a city	NR	NR

"NR" denotes that the value was not reported.

Table A-8. Numbers of high LOD and trace-level monitors in each state that met completeness criteria for 2005-2007.

State	Number of high LOD monitors	Number of trace-level monitors
Alabama	2	0
Alaska	4	0
Arizona	9	0
Arkansas	0	0
California	65	0
Colorado	9	0
Connecticut	2	0
Delaware	2	0
District of Columbia	2	0
Florida	18	0
Georgia	3	0
Hawaii	1	0
Idaho	0	0
Illinois	8	0
Indiana	6	0
Iowa	0	0
Kansas	2	0
Kentucky	2	0
Louisiana	0	1
Maine	0	1
Maryland	1	0
Massachusetts	4	1
Michigan	0	0
Minnesota	7	0
Mississippi	0	0
Missouri	3	0
Montana	4	0
Nebraska	2	0
Nevada	12	0
New Hampshire	2	0
New Jersey	9	0
New Mexico	7	0
New York	9	0
North Carolina	2	1
North Dakota	0	0
Ohio	14	0
Oklahoma	4	0
Oregon	3	1
Pennsylvania	19	0
Puerto Rico	1	0

State	Number of high LOD monitors	Number of trace-level monitors
Rhode Island	1	0
South Carolina	3	1
South Dakota	0	0
Tennessee	3	0
Texas	19	2
Utah	2	0
Vermont	2	0
Virginia	9	0
Washington	2	0
West Virginia	3	0
Wisconsin	0	0
Wyoming	1	0

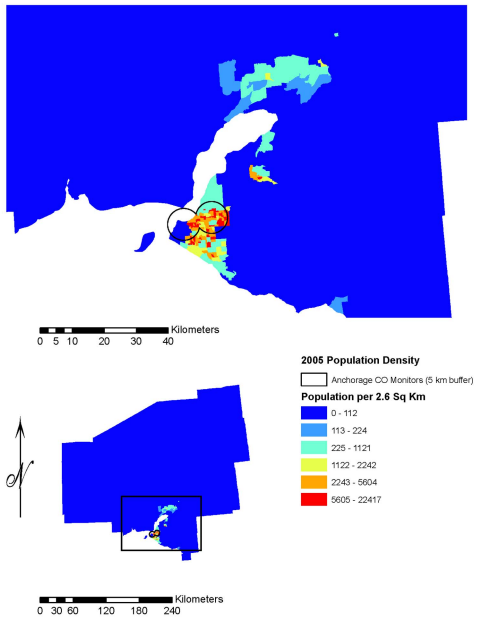


Figure A-8. Map of CO monitor locations with respect to population density in the Anchorage CBSA, total population.

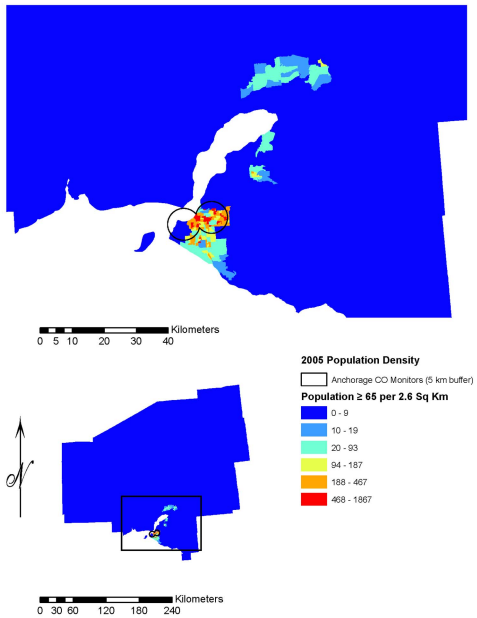


Figure A-9. Map of CO monitor locations with respect to population density in the Anchorage CBSA, ages 65 yr and older.

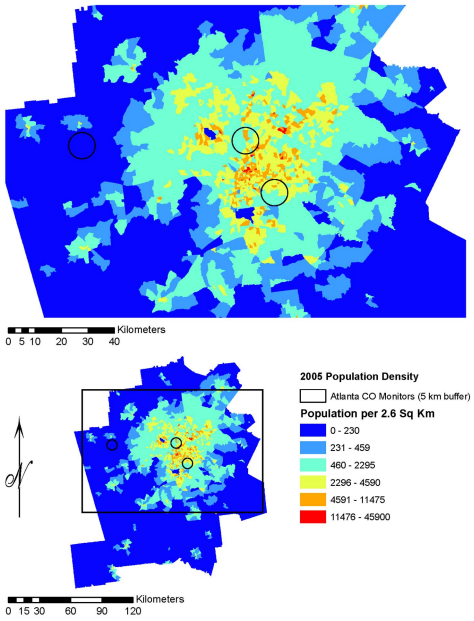


Figure A-10. Map of CO monitor locations with respect to population density in the Atlanta CSA, total population.

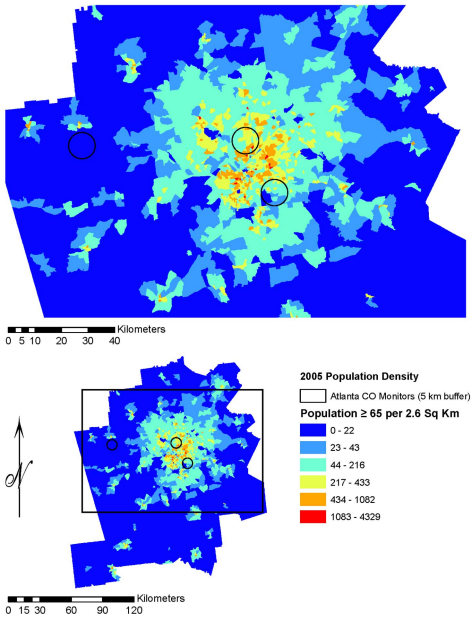


Figure A-11. Map of CO monitor locations with respect to population density in the Atlanta CSA, ages 65 yr and older.

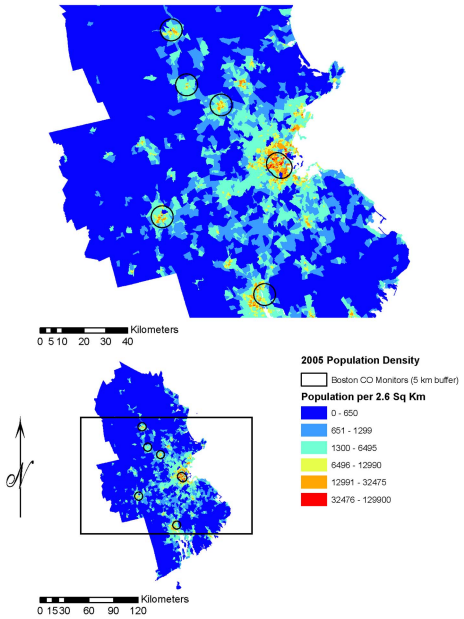


Figure A-12. Map of CO monitor locations with respect to population density in the Boston CSA, total population.

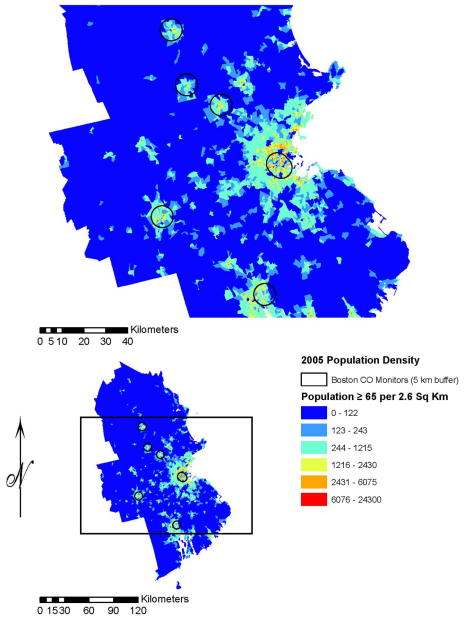


Figure A-13. Map of CO monitor locations with respect to population density in the Boston CSA, ages 65 yr and older.

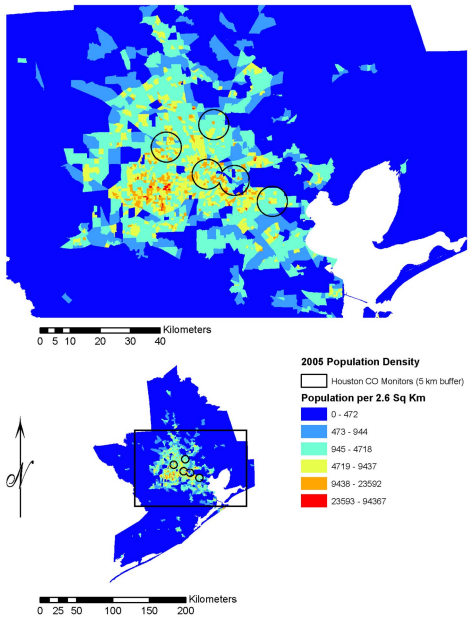


Figure A-14. Map of CO monitor locations with respect to population density in the Houston CSA, total population.

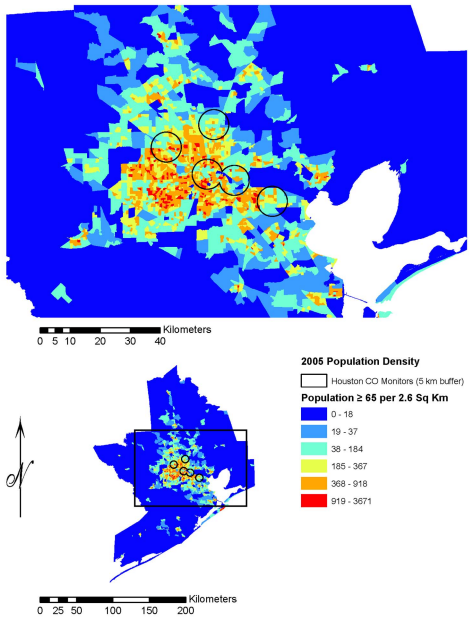


Figure A-15. Map of CO monitor locations with respect to population density in the Houston CSA, ages 65 yr and older.

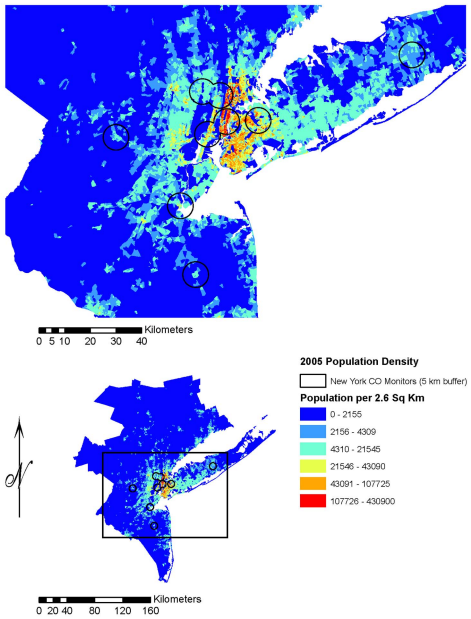


Figure A-16. Map of CO monitor locations with respect to population density in the New York City CSA, total population.

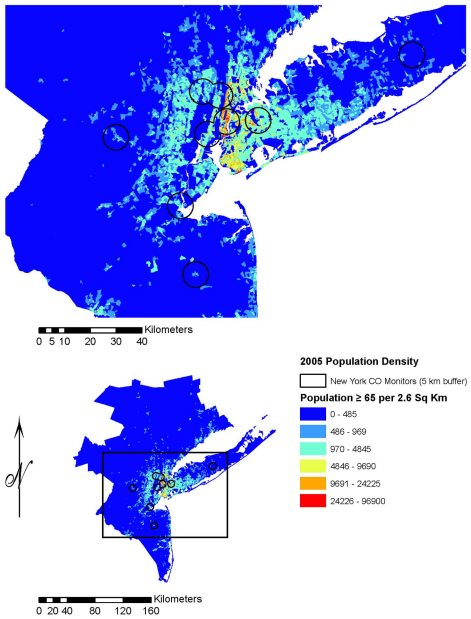


Figure A-17. Map of CO monitor locations with respect to population density in the New York City CSA, ages 65 yr and older.

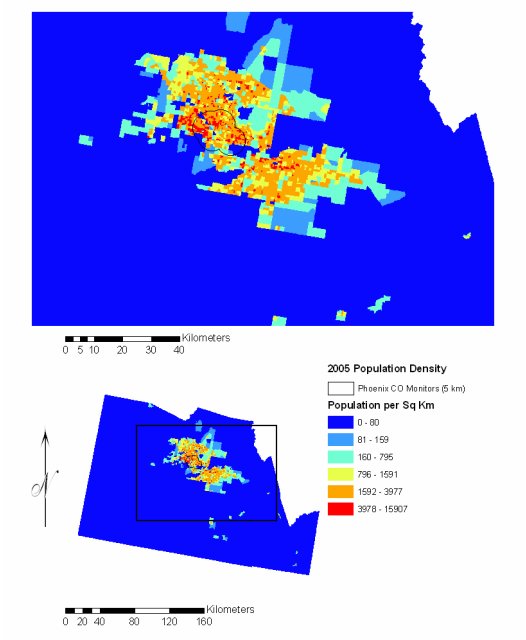


Figure A-18. Map of CO monitor locations with respect to population density in the Phoenix CSA, total population.

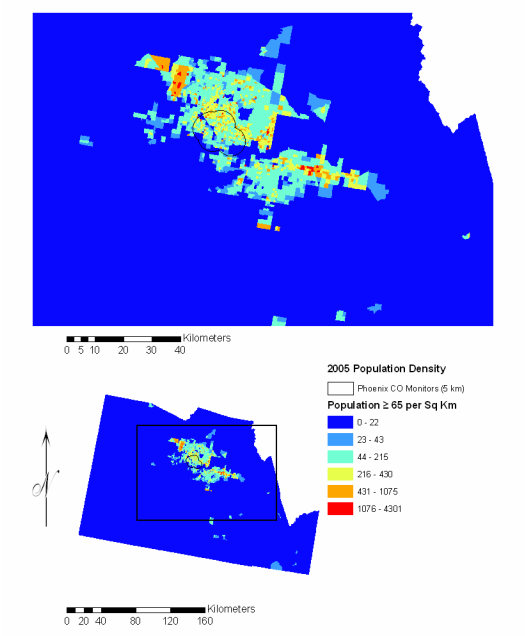


Figure A-19. Map of CO monitor locations with respect to population density in the Phoenix CSA, ages 65 yr and older.

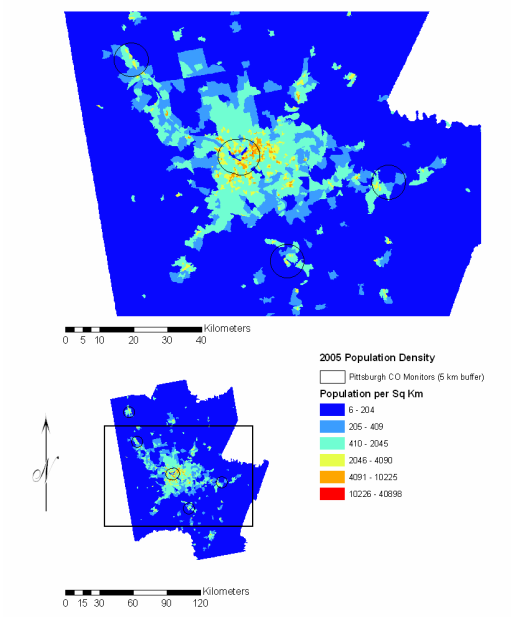


Figure A-20. Map of CO monitor locations with respect to population density in the Pittsburgh CSA, total population.

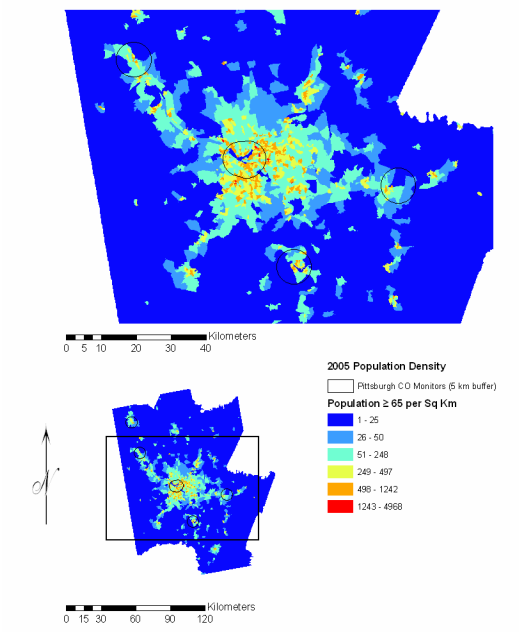


Figure A-21. Map of CO monitor locations with respect to population density in the Pittsburgh CSA, ages 65 yr and older.

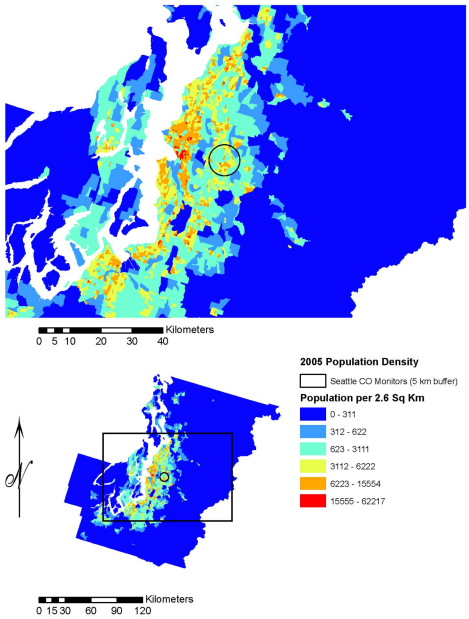


Figure A-22. Map of CO monitor locations with respect to population density in the Seattle CSA, total population.

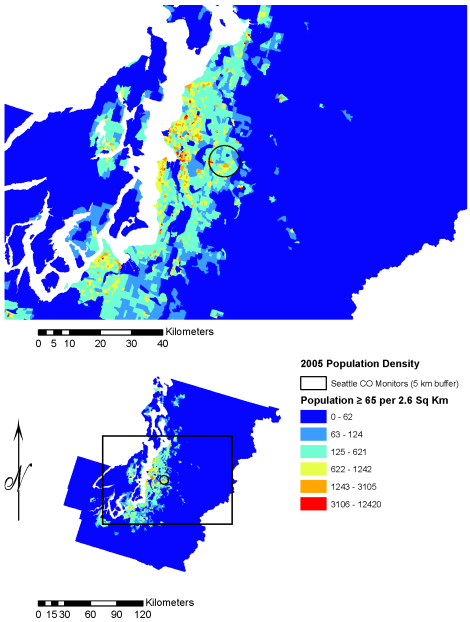


Figure A-23. Map of CO monitor locations with respect to population density in the Seattle CSA, ages 65 yr and older.

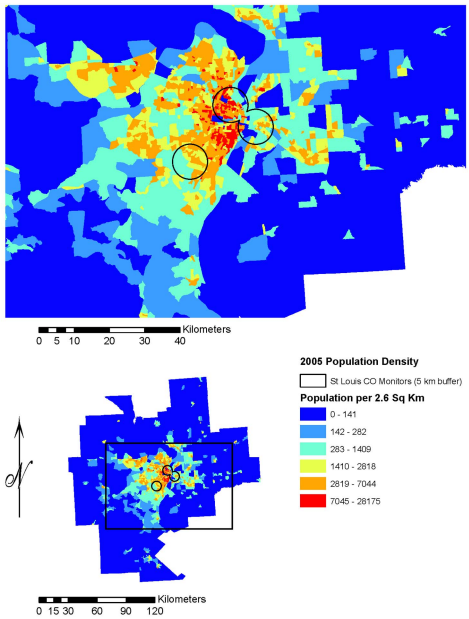


Figure A-24. Map of CO monitor locations with respect to population density in the St. Louis CSA, total population.

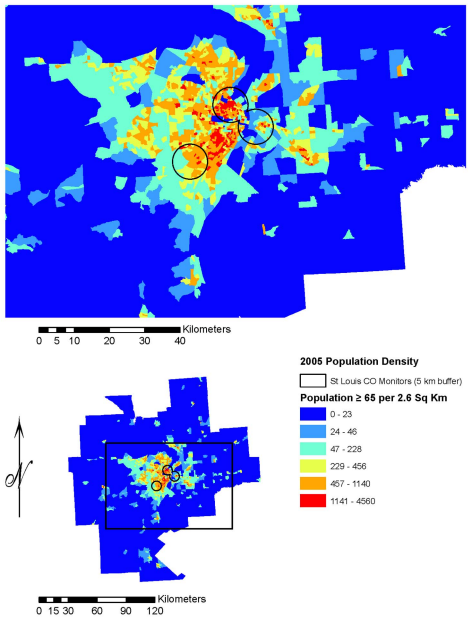


Figure A-25. Map of CO monitor locations with respect to population density in the St. Louis CSA, ages 65 yr and older.

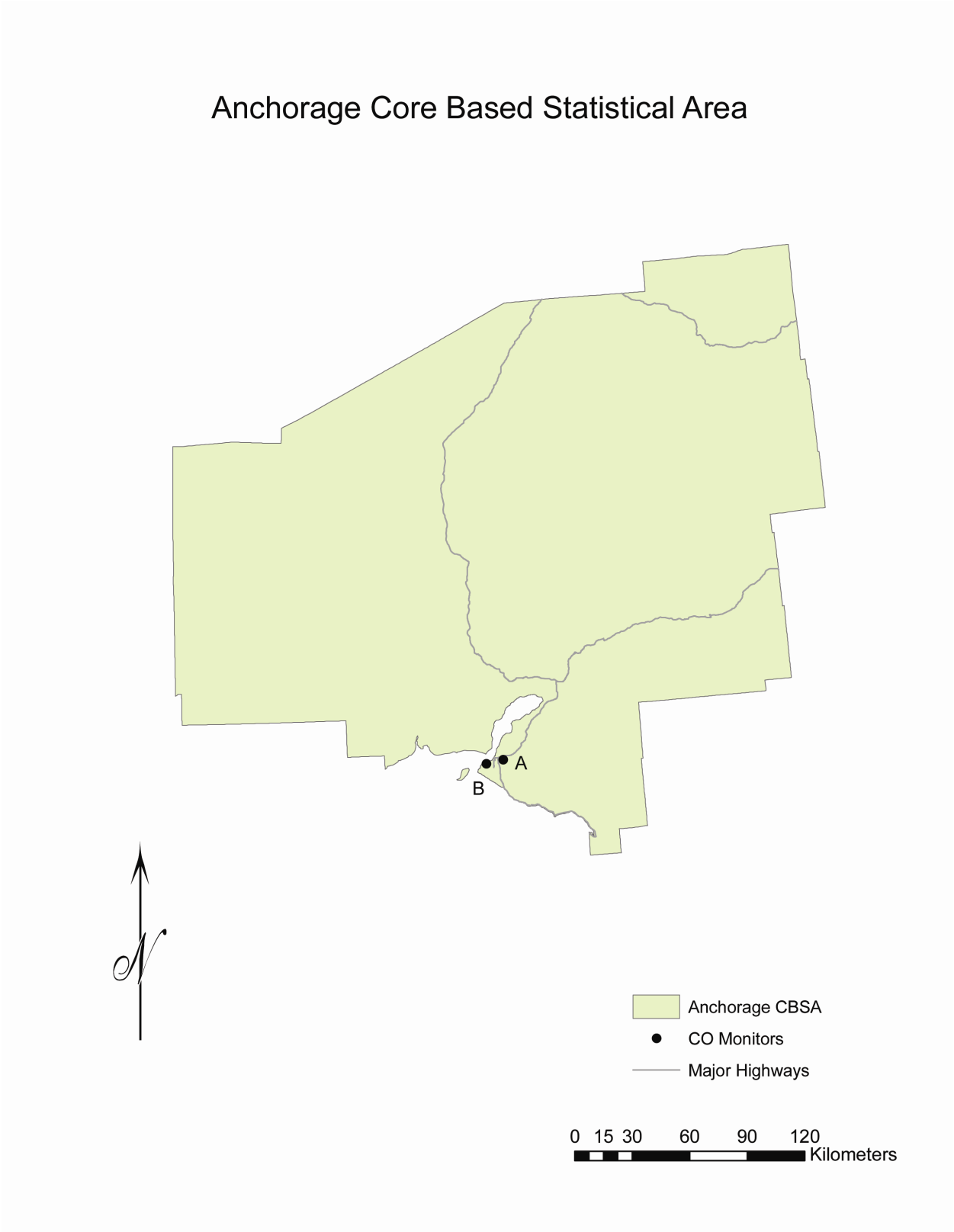


Figure A-26. Map of CO monitor locations with AQS Site IDs for Anchorage, AK.

Table A-9. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Anchorage, AK.

		Neighborhood	
		A	**B**
Neighborhood	**A**	1.00	0.73
		0.0	1.1
		0.00	0.32
		0	9.0
	B	**Legend**	1.00
		r	0.0
		P90	0.00
		COD	0
		d	

	A	B
Site ID	02-020-0018	02-020-0048
Mean	1.04	1.10
SD	0.94	1.04
Obs	12969	12703

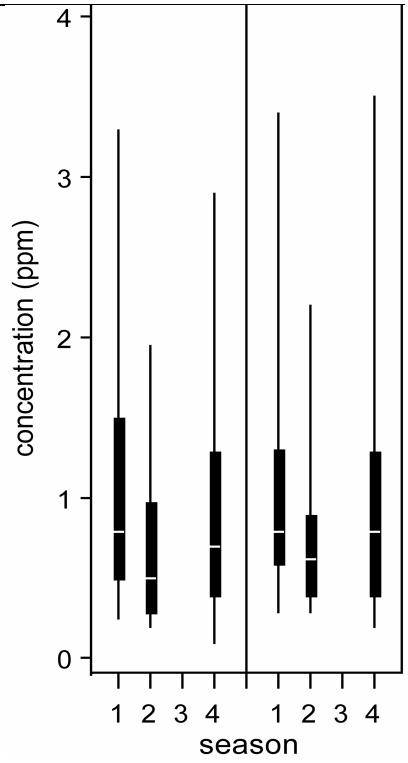


Figure A-27. Box plots illustrating the seasonal distribution of hourly CO concentrations in Anchorage, AK. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

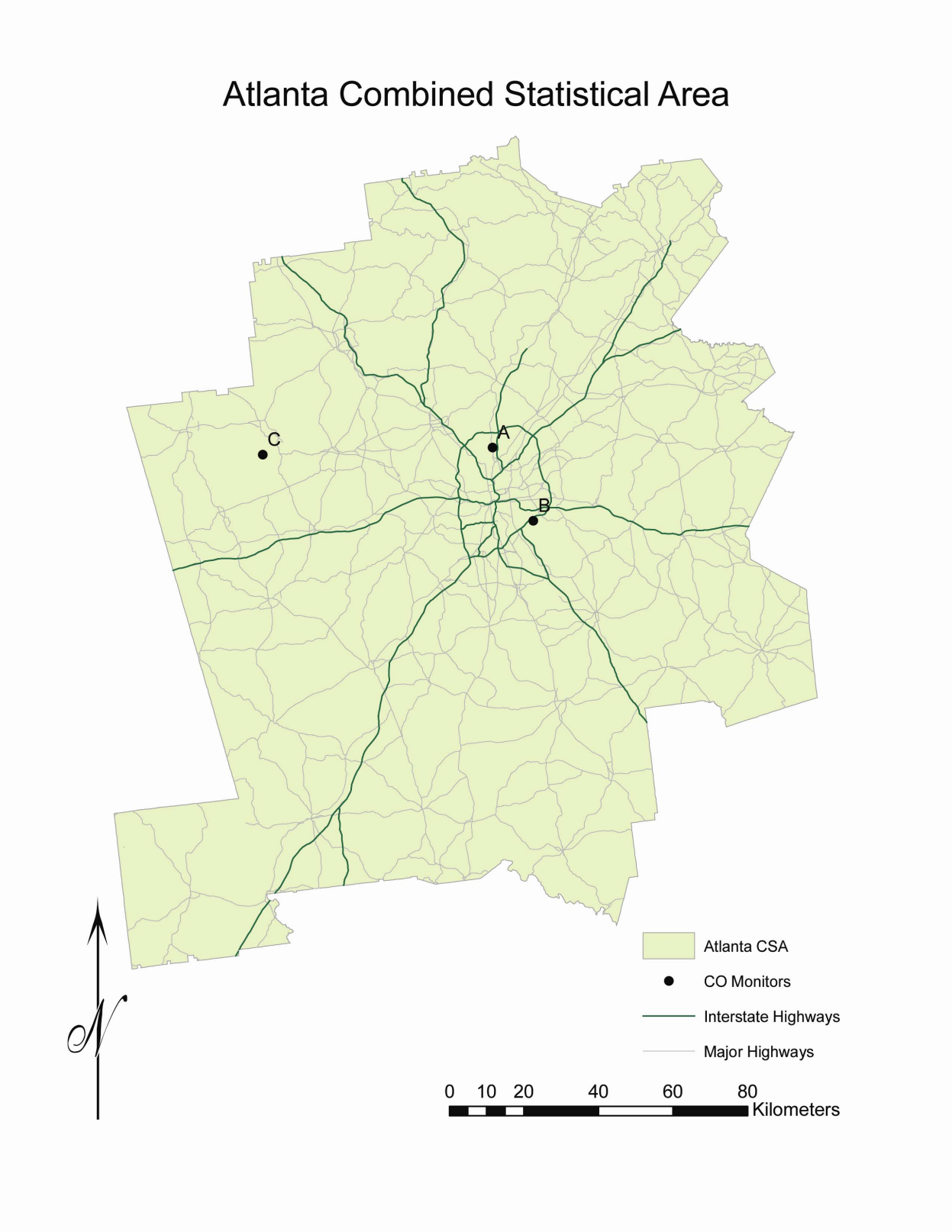


Figure A-28. Map of CO monitor locations with AQS Site IDs for Atlanta, GA.

Table A-10. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Atlanta, GA.

		Micro	Urban	
		A	B	C
Micro	A	1.00	0.60	0.10
		0.0	0.5	0.7
		0.00	0.27	0.38
		0	22.5	61.7
Urban	B		1.00	0.12
			0.0	0.7
			0.00	0.37
			0	74.7
	C	Legend		1.00
		r		0.0
		P90		0.00
		COD		0
		d		

1

	A	B	C
Site ID	13-121-0099	13-089-0002	13-223-0003
Mean	0.58	0.53	0.30
SD	0.30	0.35	0.13
Obs	25440	25531	25712

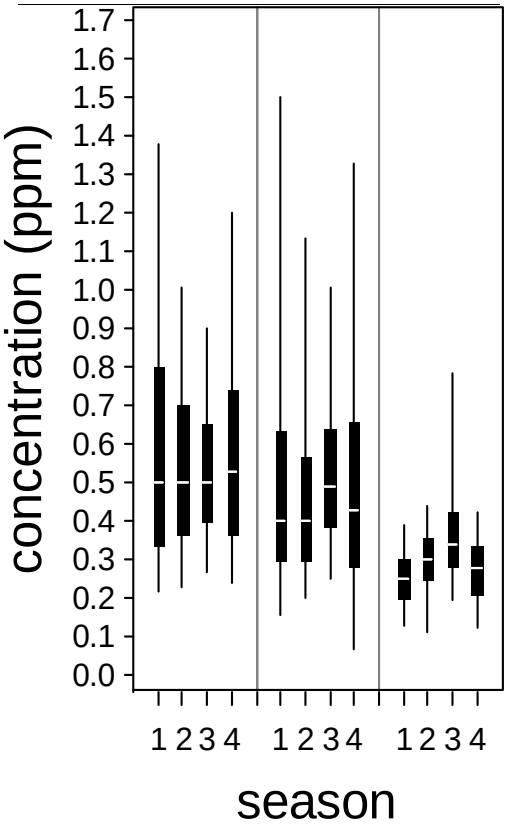


Figure A-29. Box plots illustrating the seasonal distribution of hourly CO concentrations in Atlanta, GA. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

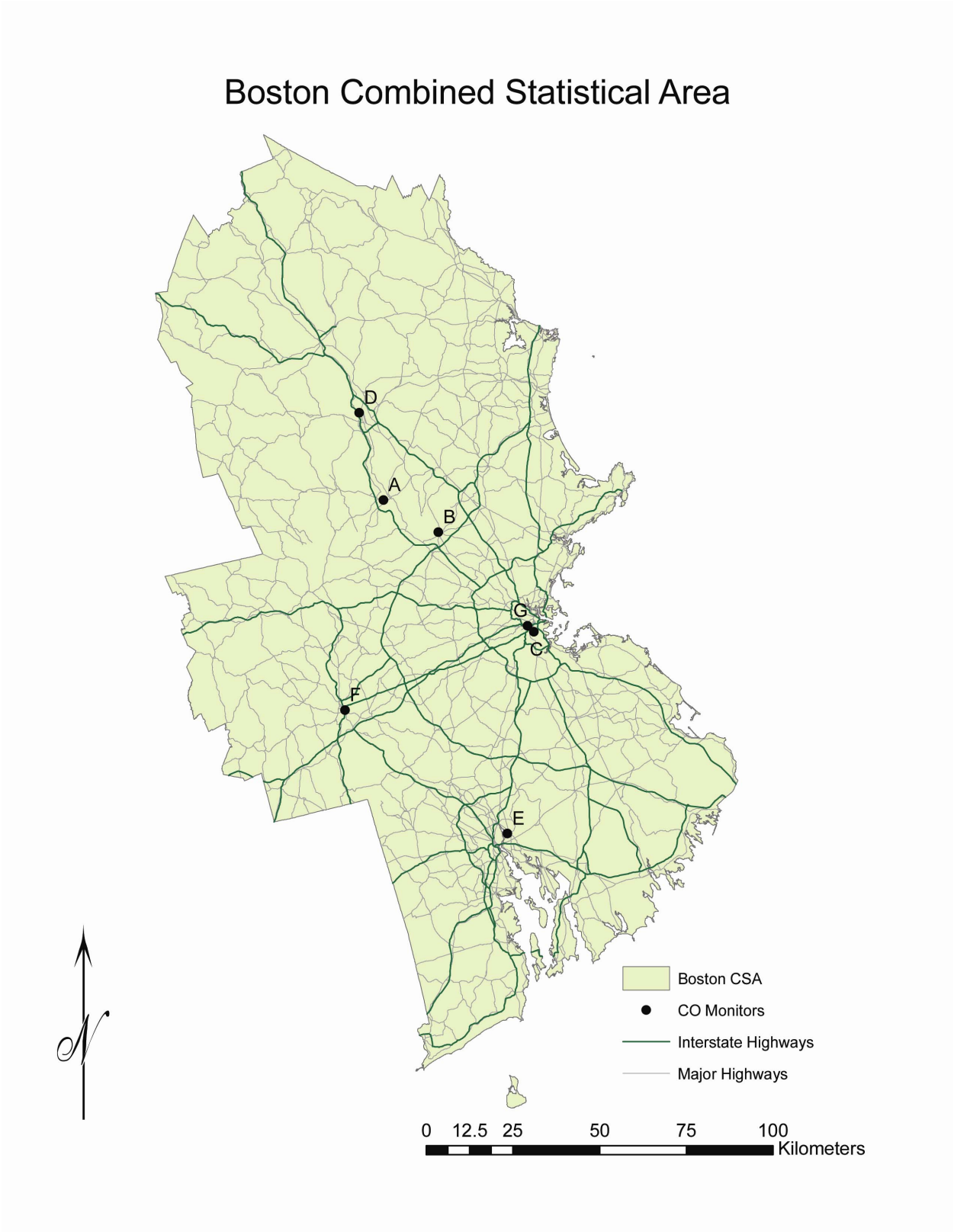


Figure A-30. Map of CO monitor locations with AQS Site IDs for Boston, MA.

Table A-11. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Boston, MA.

		Micro	Neighborhood				Urban	Null
		A	B	C	D	E	F	G
Micro	A	1.00	0.50	0.38	0.49	0.43	0.46	0.35
		0.0	0.6	0.6	0.5	0.6	0.5	0.7
		0.00	0.44	0.46	0.30	0.39	0.25	0.60
		0	18.3	57.5	26.1	102.6	61.5	55.1
Neighborhood	B		1.00	0.50	0.41	0.40	0.49	0.35
			0.0	0.4	0.4	0.4	0.5	0.4
			0.00	0.48	0.41	0.40	0.42	0.58
			0	39.7	41.3	89.1	57.9	37.2
	C			1.00	0.26	0.36	0.37	0.52
				0.0	0.5	0.4	0.5	0.4
				0.00	0.45	0.47	0.45	0.56
				0	80.7	58.7	58.9	2.5
	D				1.00	0.29	0.40	0.27
					0.0	0.4	0.4	0.5
					0.00	0.37	0.28	0.58
			Legend		0	128.6	85.8	78.2
	E		r			1.00	0.34	0.34
			P90			0.0	0.5	0.4
			COD			0.00	0.39	0.55
			d			0	58.9	60.2
Urban	F						1.00	0.34
							0.0	0.6
							0.00	0.59
							0	58.0
Null	G							1.00
								0.0
								0.00
								0

	A	B	C	D	E	F	G
Site ID	33-011-1009	25-017-0007	25-025-0042	33-011-0020	44-007-1010	25-027-0023	25-025-0002
Mean	0.60	0.33	0.36	0.45	0.34	0.53	0.26
SD	0.37	0.22	0.26	0.27	0.22	0.23	0.24
Obs	25869	24362	24260	25197	23707	24446	24134

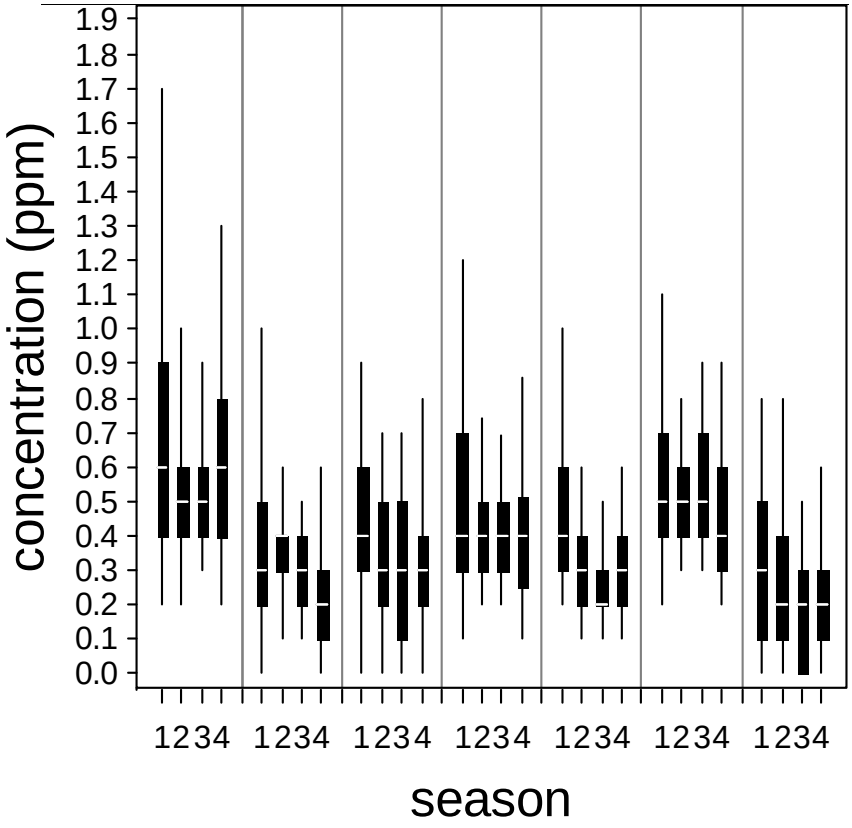


Figure A-31. Box plots illustrating the seasonal distribution of hourly CO concentrations in Boston, MA. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

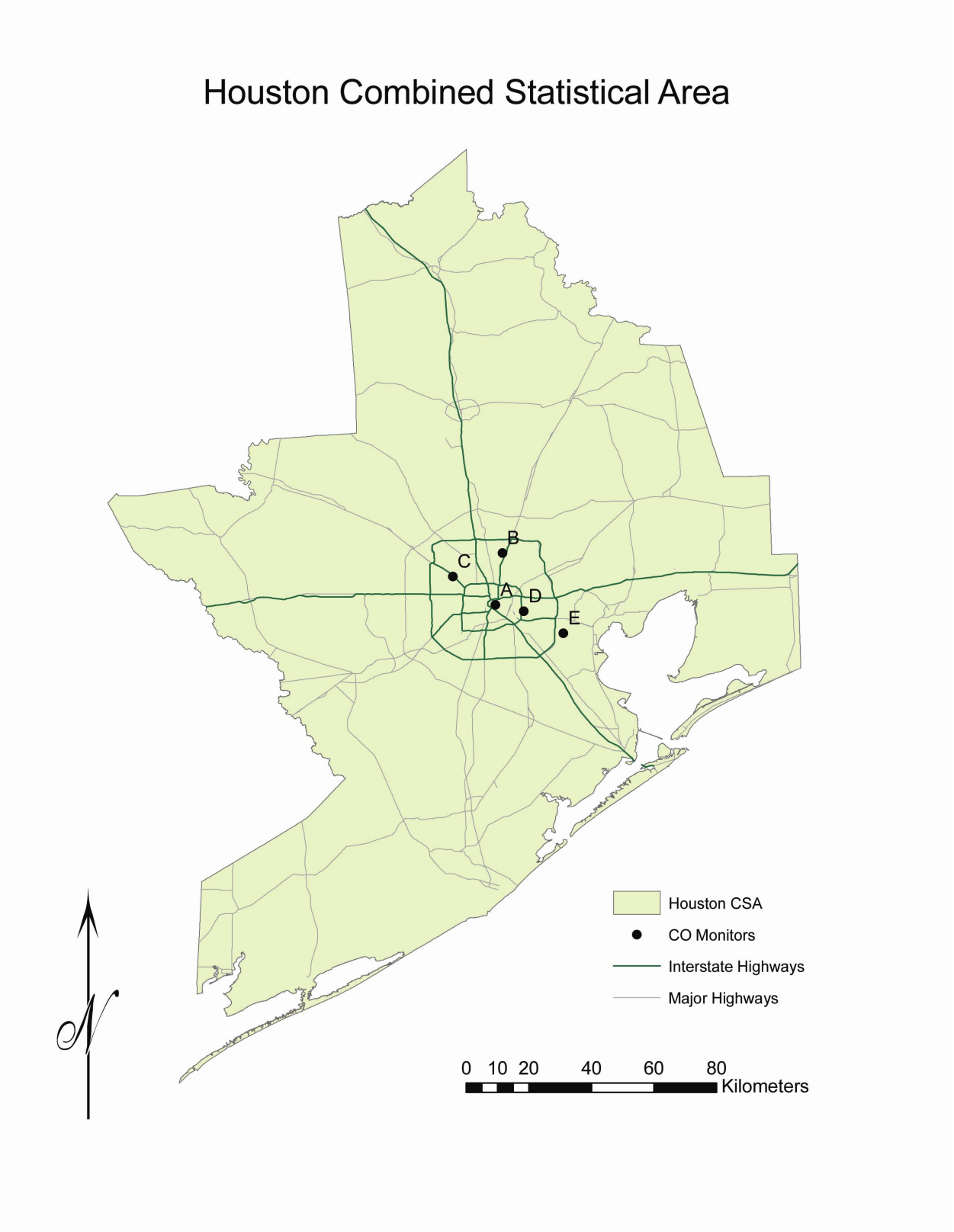


Figure A-32. Map of CO monitor locations with AQS Site IDs for Houston, TX.

Table A-12. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Houston, TX.

		Micro	Neighborhood			
		A	**B**	**C**	**D**	**E**
		1.00	0.45	0.56	0.53	0.43
Micro	**A**	0.0	0.4	0.4	0.5	0.4
		0.00	0.47	0.47	0.74	0.47
		0.0	16.7	16.3	9.3	23.5
			1.00	0.72	0.56	0.68
Neighborhood	**B**		0.0	0.3	0.5	0.3
			0.00	0.29	0.73	0.24
			0.0	17.5	19.8	32.2
				1.00	0.65	0.63
	C			0.0	0.5	0.4
				0.00	0.73	0.29
				0.0	25.2	39.7
					1.00	0.57
	D				0.0	0.4
					0.00	0.72
		Legend			0.0	14.5
		r				1.00
	E	**P90**				0.0
		COD				0.00
		d				0.0

1

	A	B	C	D	E
Site ID	48-201-0075	48-201-0024	48-201-0047	48-201-1035	48-201-1039
Mean	0.35	0.42	0.39	0.14	0.33
SD	0.26	0.27	0.33	0.22	0.16
Obs	24922	23997	25241	25285	24480

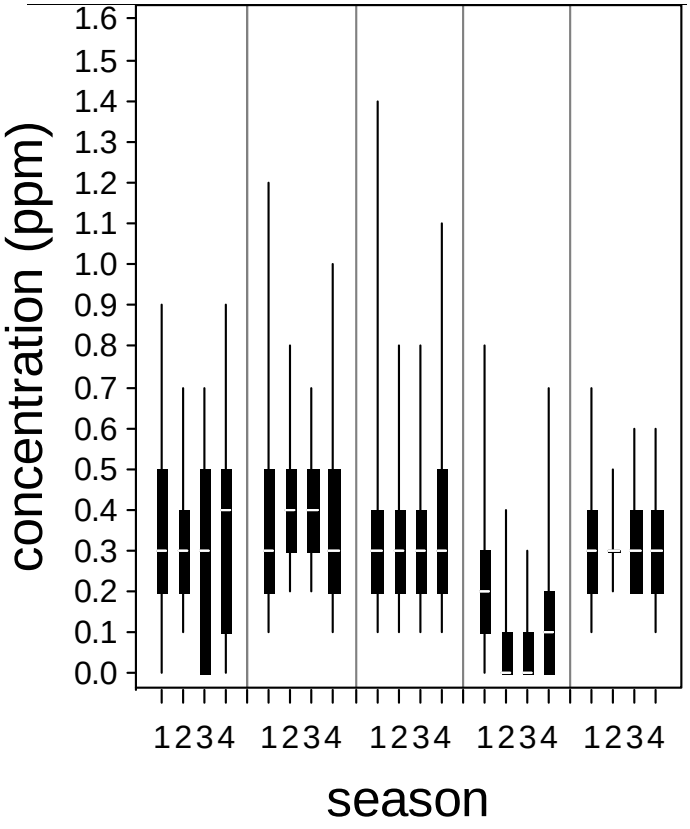


Figure A-33. Box plots illustrating the seasonal distribution of hourly CO concentrations in Houston, TX. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

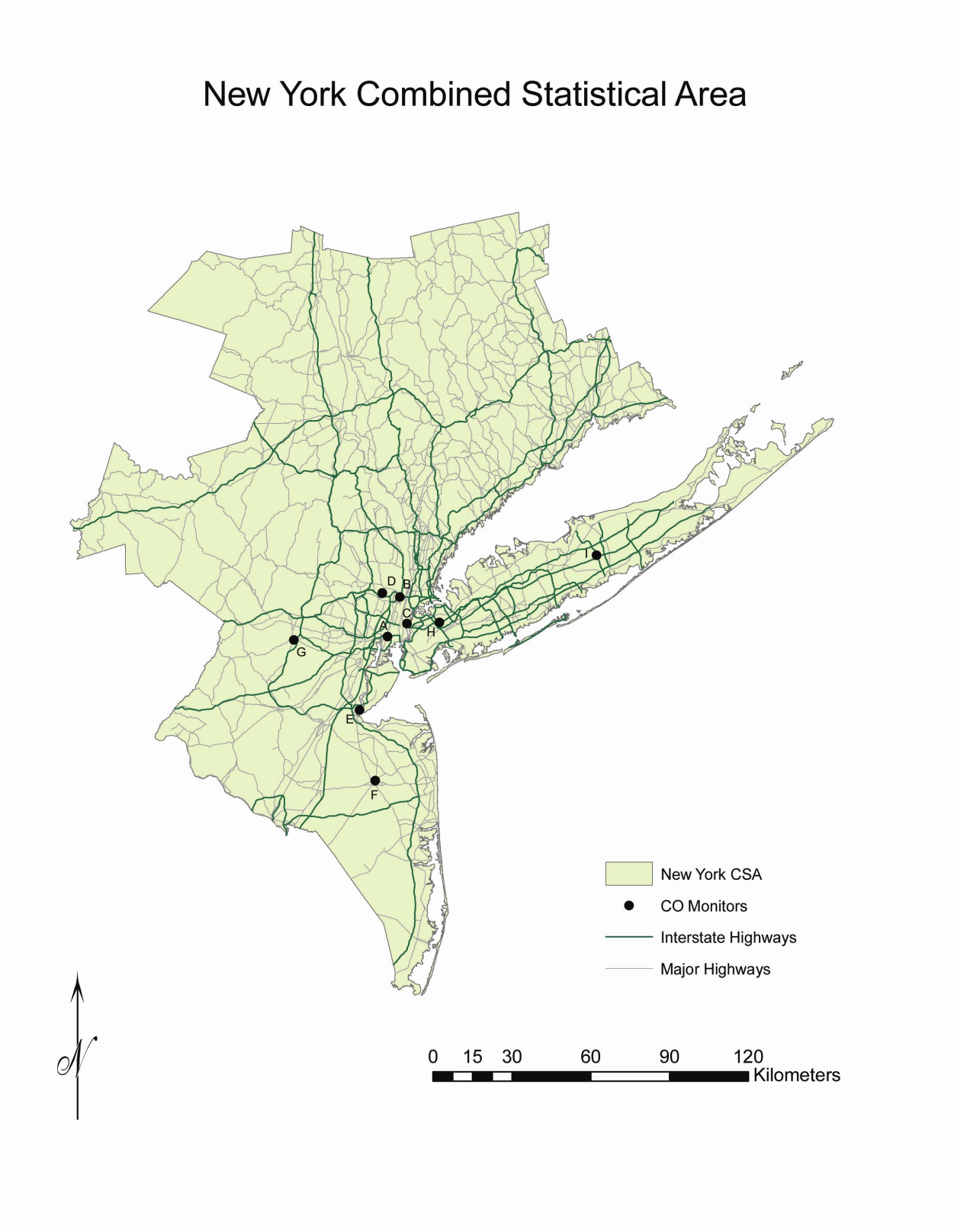


Figure A-34. Map of CO monitor locations with AQS Site IDs for New York City, NY.

Table A-13. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in New York City, NY.

		Micro	Middle		Neighborhood	Null				
		A	B	C	D	E	F	G	H	I
Micro	A	1.00	0.65	0.52	0.64	0.54	0.32	0.48	0.43	0.31
		0.0	0.7	0.7	0.8	0.9	0.9	0.9	0.9	1.3
		0.00	0.28	0.24	0.29	0.35	0.34	0.34	0.35	0.81
		0	15.9	8.9	16.8	29.9	55.0	35.7	20.5	85.5
Middle	B		1.00	0.56	0.58	0.55	0.40	0.56	0.41	0.30
			0.0	0.4	0.4	0.4	0.4	0.4	0.5	0.8
			0.00	0.23	0.22	0.25	0.25	0.24	0.28	0.75
			0	10.5	7.0	45.8	70.6	43.7	17.8	76.5
	C			1.00	0.54	0.41	0.33	0.41	0.46	0.29
				0.0	0.4	0.4	0.4	0.4	0.4	0.7
				0.00	0.23	0.28	0.25	0.26	0.26	0.77
				0	15.0	37.5	61.0	43.6	12.3	76.8
Neighborhood	D				1.00	0.55	0.35	0.54	0.59	0.49
					0.0	0.4	0.5	0.4	0.4	0.7
					0.00	0.23	0.26	0.23	0.23	0.74
					0	45.4	71.5	38.1	24.5	82.9
Null	E					1.00	0.50	0.57	0.46	0.33
						0.0	0.4	0.4	0.4	0.7
						0.00	0.24	0.23	0.27	0.72
						0	27.5	36.7	45.1	107.8
	F						1.00	0.47	0.33	0.32
							0.0	0.4	0.4	0.6
							0.00	0.23	0.27	0.73
							0	61.9	65.0	120.3
	G		Legend					1.00	0.34	0.31
			r					0.0	0.4	0.7
			P90					0.00	0.27	0.72
			COD					0	55.8	119.7
	H		d						1.00	0.43
									0.0	0.6
									0.00	0.73
									0	65.1
	I									1.00
										0.0
										0.00
										0

	A	B	C	D	E	F	G	H	I
Site ID	34-017-1002	34-003-0004	36-061-0056	34-003-5001	34-023-2003	34-025-2001	34-027-0003	36-081-0124	36-103-0009
Mean	0.85	0.55	0.62	0.52	0.48	0.50	0.49	0.47	0.12
SD	0.43	0.27	0.21	0.30	0.27	0.24	0.25	0.23	0.17
Obs	25646	23113	25547	25150	25028	25727	25691	25022	25749

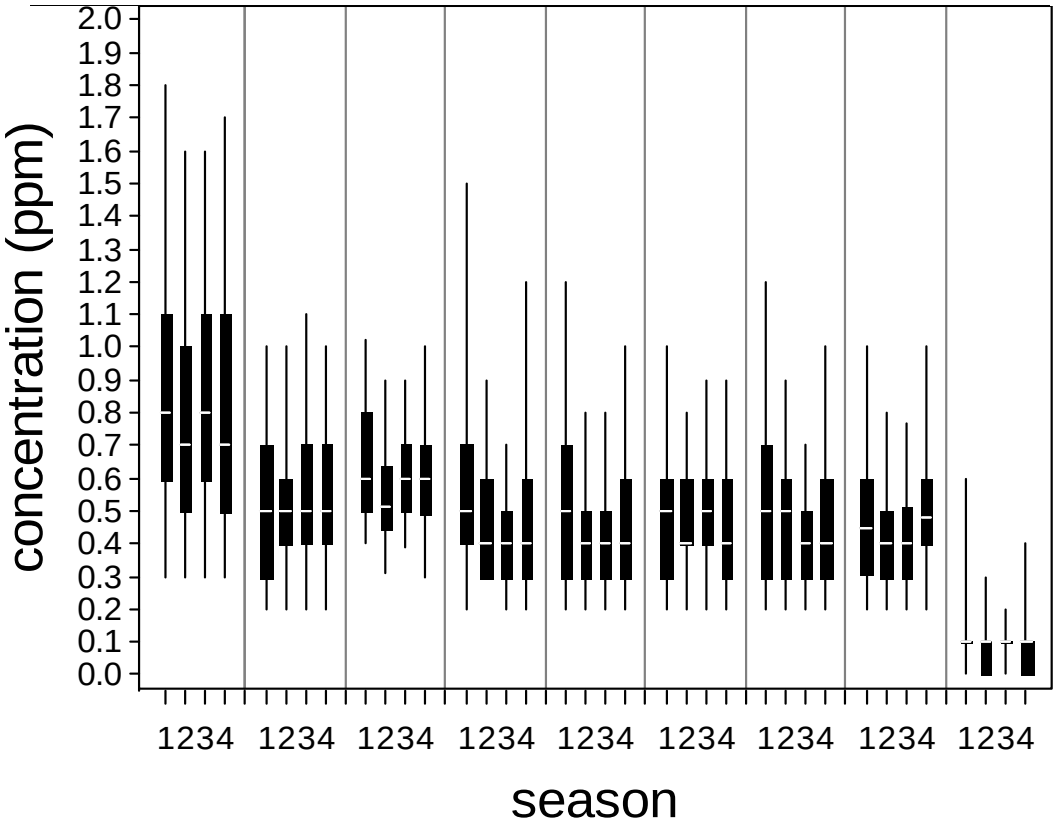


Figure A-35. Box plots illustrating the seasonal distribution of hourly CO concentrations in New York City, NY. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

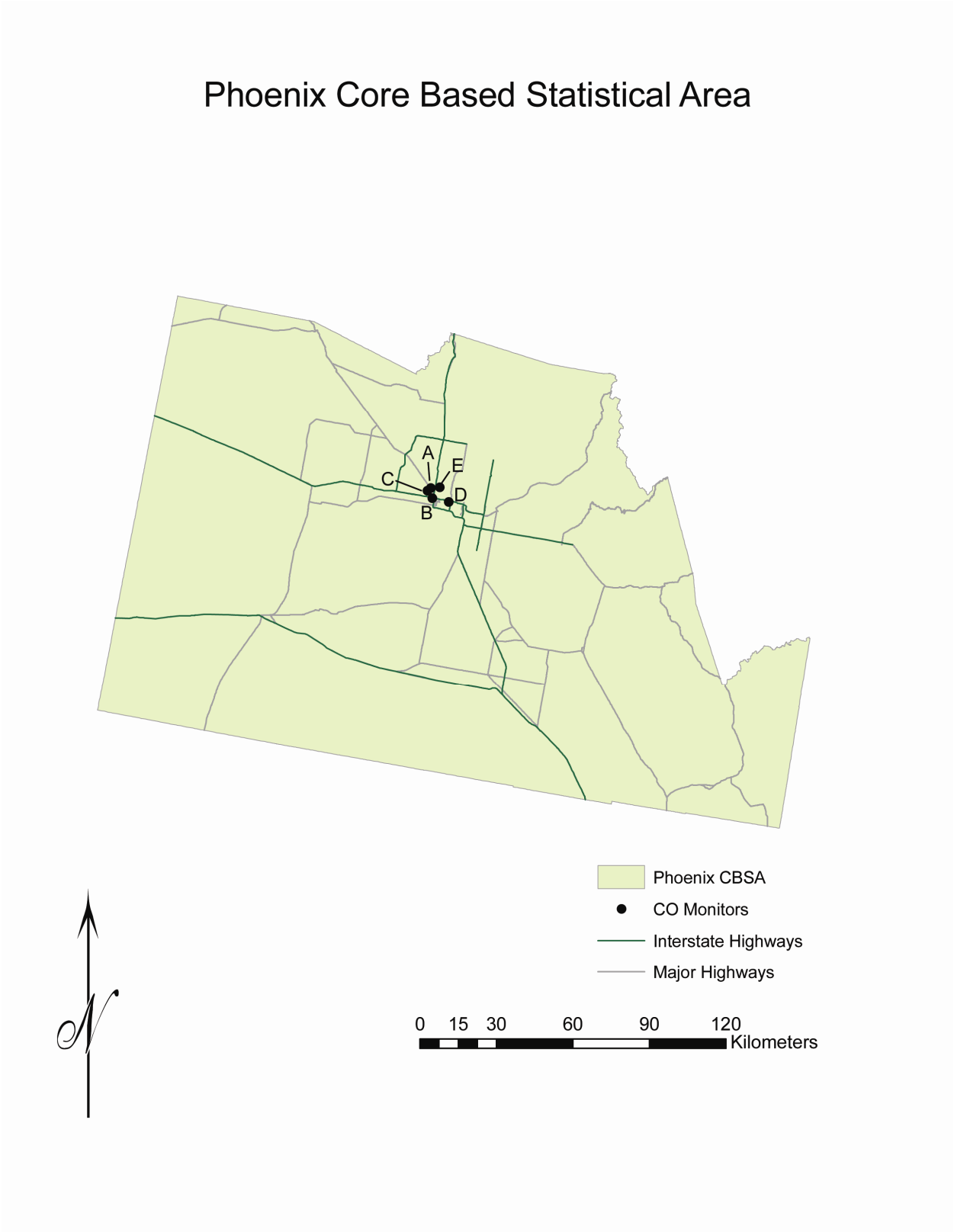


Figure A-36. Map of CO monitor locations with AQS Site IDs for Phoenix, AZ.

Table A-14. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Phoenix, AZ.

		Micro	Middle	Neighborhood		Null
		A	B	C	D	E
Micro	A	1.00	0.86	0.89	0.80	0.84
		0.0	0.8	0.7	1.1	0.9
		0.00	0.39	0.37	0.43	0.37
		0.0	3.9	1.6	8.9	3.5
Middle	B		1.00	0.88	0.81	0.83
			0.0	0.6	0.7	0.6
			0.00	0.34	0.41	0.33
			0.0	3.4	6.6	5.2
Neighborhood	C			1.00	0.81	0.89
				0.0	0.9	0.7
				0.00	0.38	0.24
		Legend		0.0	9.4	4.9
	D	r			1.00	0.85
		P90			0.0	0.6
		COD			0.00	0.36
		d			0.0	6.8
Null	E					1.00
						0.0
						0.00
						0.0

	A	B	C	D	E
Site ID	04-013-0016	04-013-3010	04-013-0019	04-013-3002	04-013-9997
Mean	0.93	0.76	0.84	0.58	0.79
SD	0.95	0.72	0.88	0.64	0.64
Obs	25382	25414	25589	25657	25435

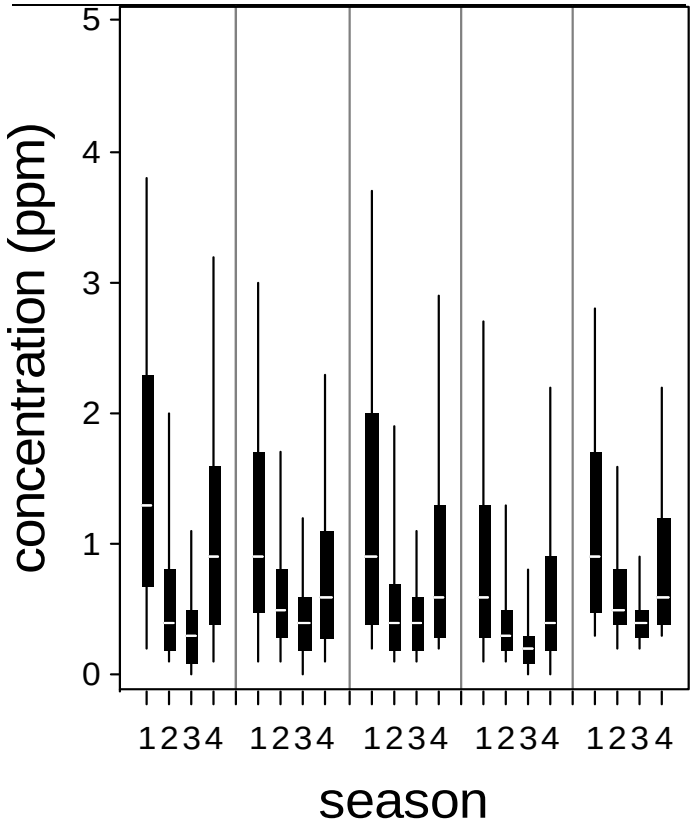


Figure A-37. Box plots illustrating the seasonal distribution of hourly CO concentrations in Phoenix, AZ. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

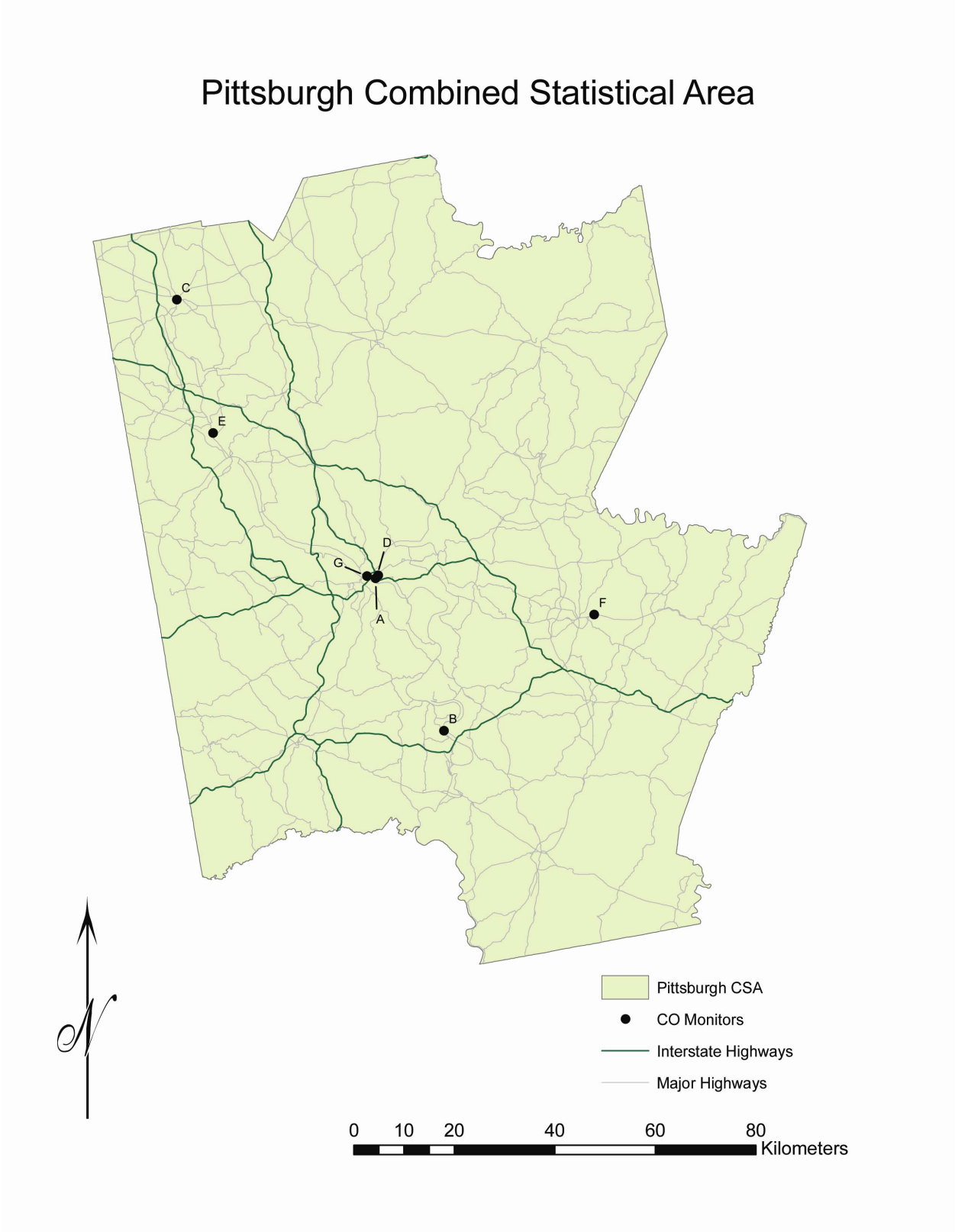


Figure A-38. Map of CO monitor locations with AQS Site IDs for Pittsburgh, PA.

Table A-15. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in Pittsburgh, PA.

		Middle	Neighborhood			Urban		
		A	B	C	D	E	F	G
Middle	A	1.00	0.25	0.39	0.73	0.20	0.30	0.43
		0.0	0.7	0.6	0.4	0.7	0.8	0.6
		0.00	0.65	0.51	0.39	0.56	0.88	0.68
		0	33.3	68.2	0.7	43.4	44.1	1.8
Neighborhood	B		1.00	0.26	0.29	0.09	0.09	0.42
			0.0	0.5	0.5	0.6	0.5	0.5
			0.00	0.68	0.62	0.69	0.90	0.73
			0	101.0	33.6	75.0	37.8	34.4
	C			1.00	0.42	0.16	0.21	0.11
				0.0	0.4	0.6	0.6	0.6
				0.00	0.51	0.57	0.87	0.72
				0	68.0	27.5	104.1	66.8
	D				1.00	0.30	0.35	0.52
					0.0	0.5	0.5	0.5
					0.00	0.54	0.86	0.69
					0	43.4	43.7	2.2
Urban	E					1.00	0.02	0.05
						0.0	0.7	0.7
						0.00	0.87	0.74
						0	84.1	41.9
	F						1.00	0.18
							0.0	0.7
							0.00	0.88
			Legend				0	45.8
	G		r					1.00
			P90					0.0
			COD					0.00
			d					0

	A	B	C	D	E	F	G
SiteID	42-003-0038	42-125-0005	42-073-0015	42-003-0031	42-007-0014	42-129-0008	42-003-0010
Mean	0.47	0.21	0.32	0.32	0.28	0.07	0.28
SD	0.33	0.23	0.26	0.26	0.27	0.15	0.32
Obs	25818	25319	25745	25936	25500	25785	25655

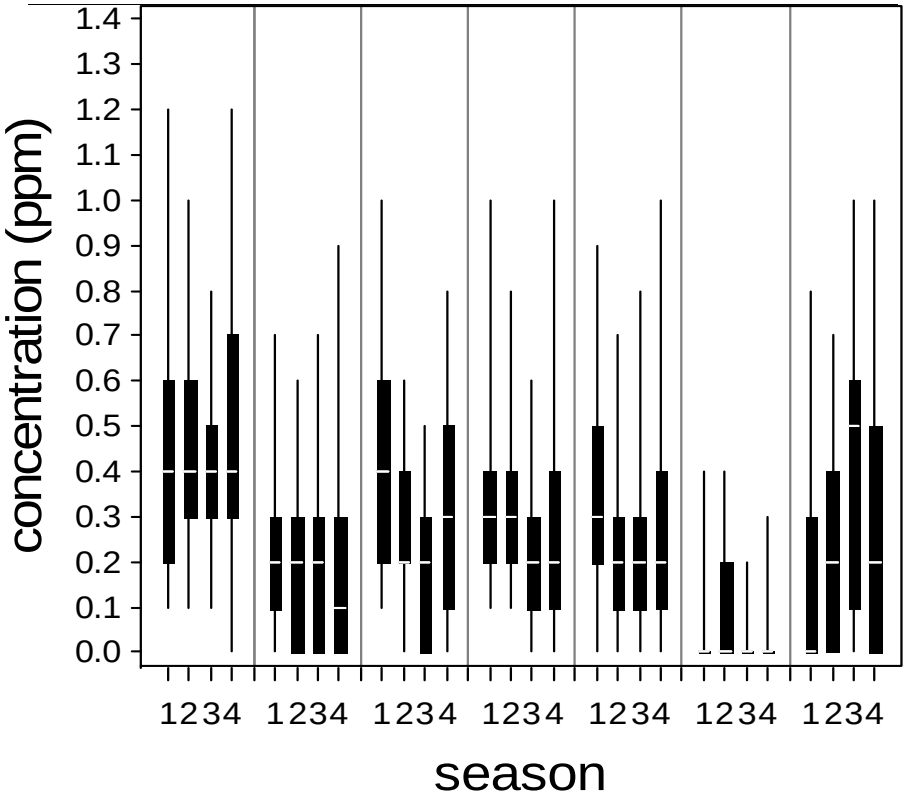


Figure A-39. Box plots illustrating the seasonal distribution of hourly CO concentrations in Pittsburgh, PA. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

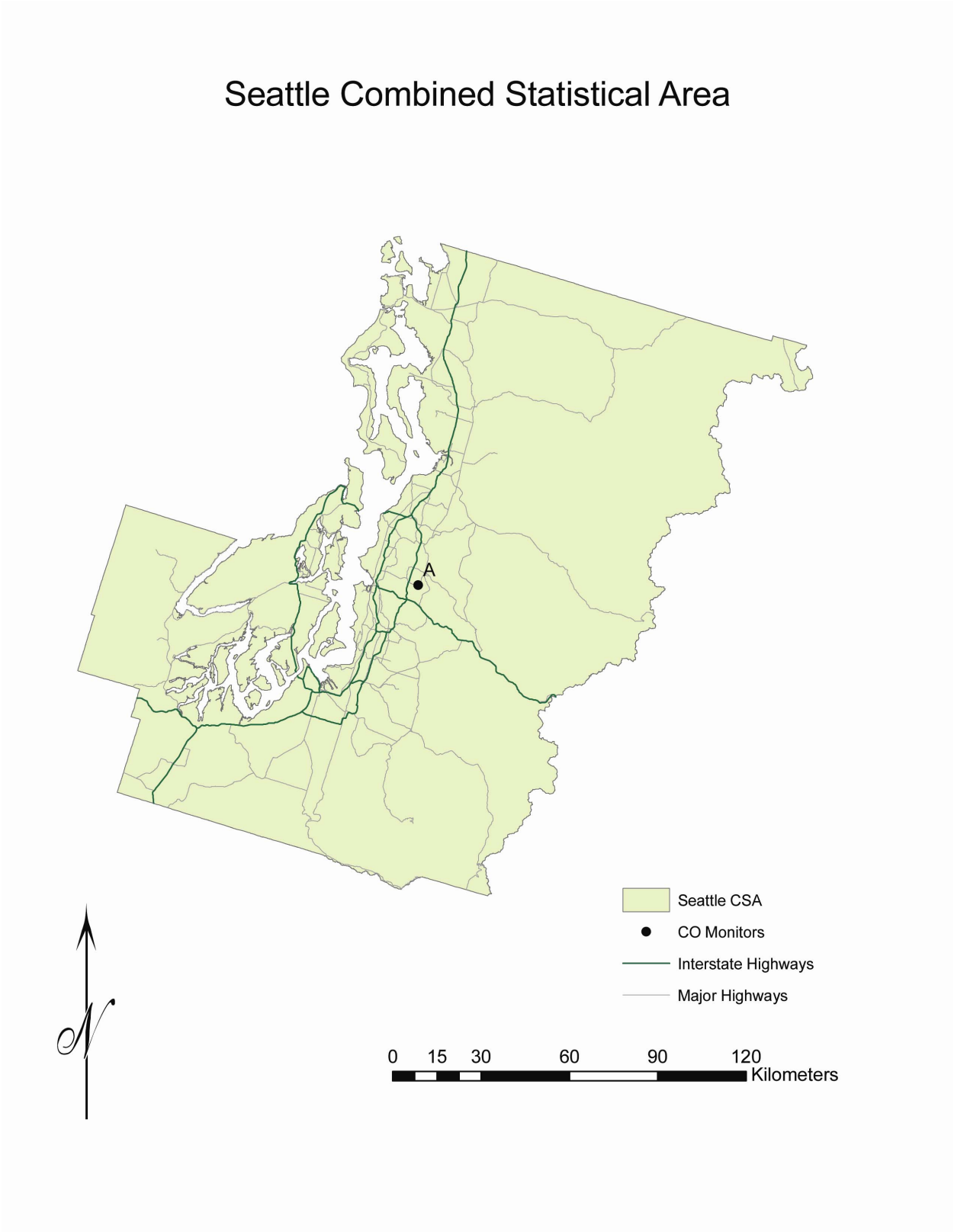


Figure A-40. Map of CO monitor locations with AQS Site IDs for Seattle, WA.

	A
Site ID	53−033−0019
Mean	0.75
SD	0.49
Obs	25818

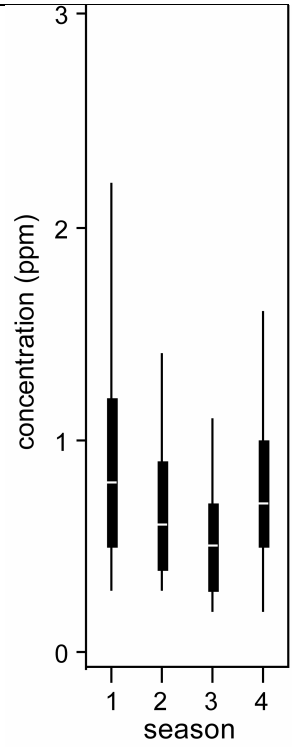


Figure A-41. Box plots illustrating the seasonal distribution of hourly CO concentrations in Seattle, WA. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

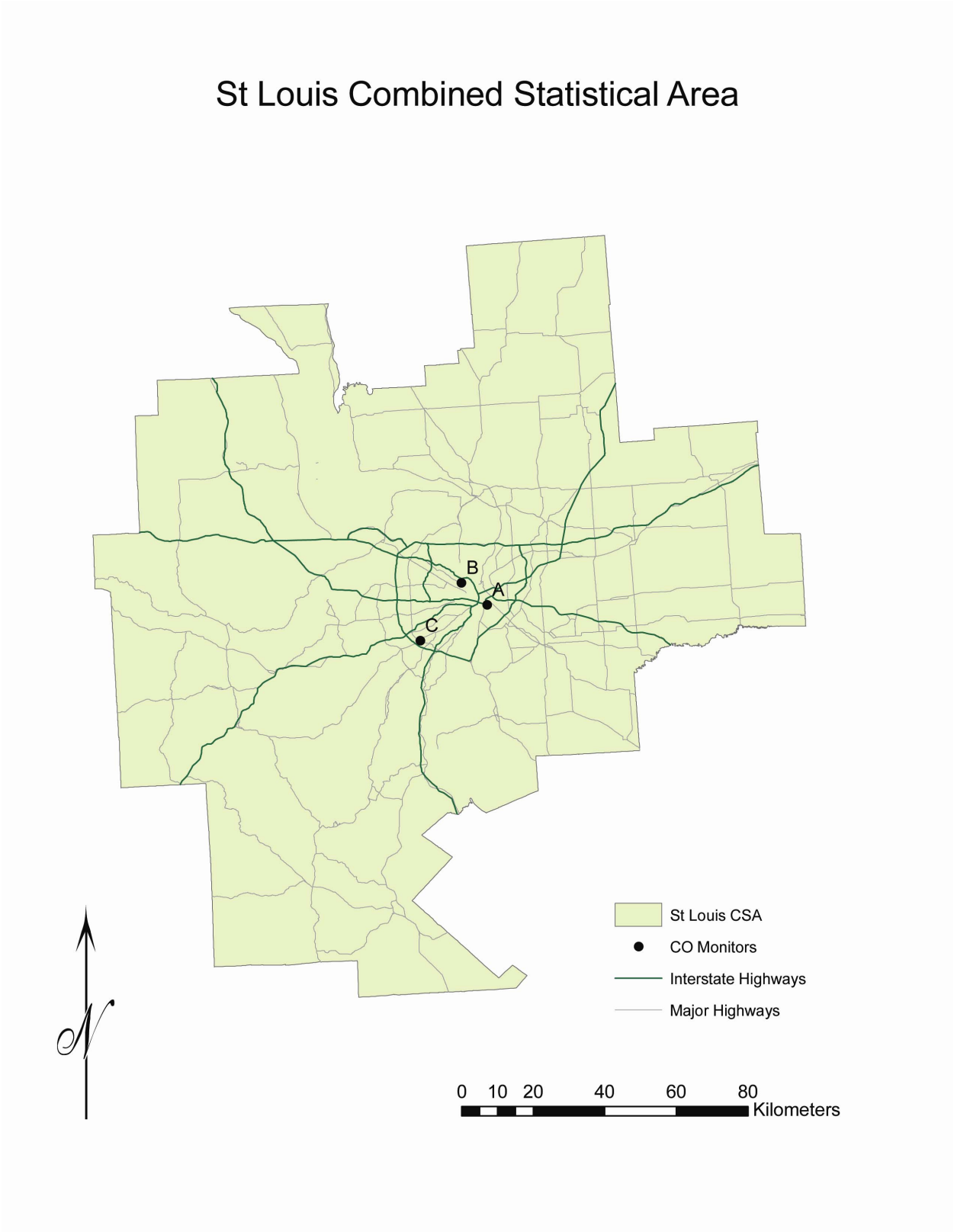


Figure A-42. Map of CO monitor locations with AQS Site IDs for St. Louis, MO.

Table A-16. Table of inter-sampler comparison statistics, including Pearson r, P90 (ppm), COD, and d (km), as defined in the text, for each pair of hourly CO monitors reporting to AQS in St. Louis, MO.

		Neighborhood		Null
		A	B	C
Neighborhood	A	1.00	0.60	0.19
		0.0	0.3	0.5
		0.00	0.24	0.40
		0	9.5	21.2
	B		1.00	0.19
			0.0	0.5
			0.00	0.42
			0	19.8
Null	C	Legend		1.00
		r		0.0
		P90		0.00
		COD		0
		d		

	A	B	C
Site ID	17-163-0010	29-510-0086	29-189-0004
Mean	0.44	0.42	0.43
SD	0.25	0.29	0.25
Obs	25325	25938	25879

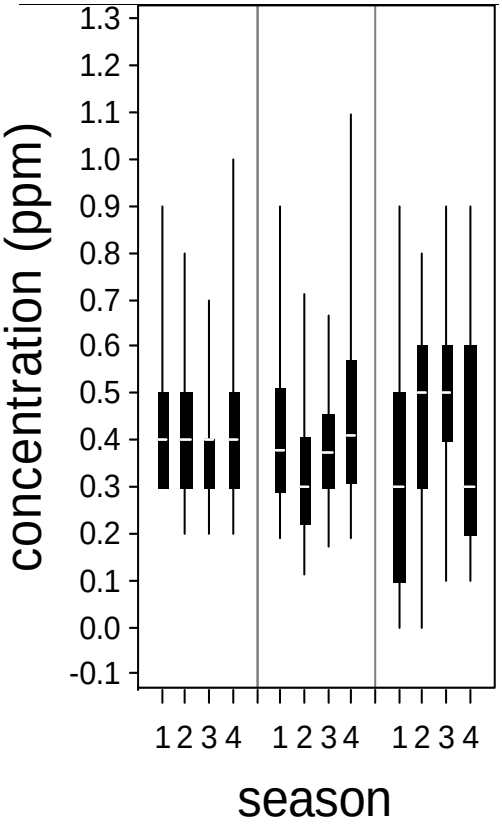


Figure A-43. Box plots illustrating the seasonal distribution of hourly CO concentrations in St. Louis, MO. Note: 1 = winter, 2 = spring, 3 = summer, and 4 = fall on the x-axis.

Table A-17. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Atlanta, GA.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	25,440	0.6	0.0	0.2	0.2	0.3	0.4	0.4	0.5	0.7	0.7	1.0	1.2
Urban Scale	51,243	0.4	0.0	0.0	0.1	0.2	0.3	0.3	0.3	0.4	0.5	0.7	1.0
1-H DAILY MAX													
Microscale	1,075	1.0	0.2	0.3	0.4	0.6	0.7	0.8	1.0	1.2	1.2	1.6	1.9
Urban Scale	2,154	0.7	0.0	0.2	0.2	0.3	0.3	0.4	0.5	0.8	0.9	1.3	1.5
1-H DAILY AVG													
Microscale	1,075	0.6	0.2	0.2	0.3	0.3	0.4	0.5	0.5	0.6	0.7	0.8	1.0
Urban Scale	2,154	0.4	0.0	0.1	0.2	0.2	0.3	0.3	0.4	0.5	0.5	0.7	0.9
8-H DAILY MAX													
Microscale	1,075	0.8	0.3	0.3	0.3	0.4	0.5	0.6	0.7	0.9	0.9	1.2	1.3
Urban Scale	2,154	0.5	0.0	0.1	0.2	0.3	0.3	0.3	0.4	0.6	0.7	1.0	1.3

Table A-18. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Boston, MA.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	25,869	0.6	0.0	0.1	0.2	0.3	0.4	0.4	0.5	0.7	0.7	1.0	1.2
Neighborhood Scale	97,526	0.4	0.0	0.0	0.0	0.1	0.2	0.3	0.3	0.4	0.5	0.6	0.8
Urban Scale	24,446	0.5	0.0	0.1	0.3	0.3	0.4	0.4	0.5	0.6	0.6	0.8	0.9
1-H DAILY MAX													
Microscale	1,080	1.2	0.2	0.4	0.5	0.6	0.7	0.8	0.9	1.2	1.4	2.0	2.5
Neighborhood Scale	4,212	0.6	0.0	0.1	0.2	0.3	0.4	0.4	0.5	0.7	0.7	1.1	1.4
Urban Scale	1,086	0.8	0.0	0.3	0.4	0.5	0.6	0.6	0.8	0.9	1.0	1.2	1.4
1-H DAILY AVG													
Microscale	1,080	0.6	0.1	0.2	0.3	0.3	0.4	0.5	0.6	0.7	0.7	0.9	1.1
Neighborhood Scale	4,212	0.4	0.0	0.0	0.1	0.1	0.2	0.3	0.4	0.4	0.5	0.6	0.7
Urban Scale	1,086	0.5	0.0	0.1	0.3	0.4	0.4	0.5	0.5	0.6	0.6	0.7	0.8
8-H DAILY MAX													
Microscale	1,080	0.8	0.3	0.3	0.3	0.4	0.6	0.6	0.7	0.9	1.0	1.4	1.7
Neighborhood Scale	4,212	0.5	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.6	0.6	0.8	1.0
Urban Scale	1,086	0.7	0.3	0.3	0.3	0.3	0.5	0.5	0.6	0.8	0.8	1.0	1.1

Table A-19. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Denver, CO.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	77,070	0.5	0.0	0.0	0.1	0.1	0.3	0.3	0.4	0.6	0.7	1.0	1.3
Neighborhood Scale	51,968	0.5	0.0	0.0	0.1	0.2	0.3	0.3	0.4	0.6	0.6	1.0	1.3
1-H DAILY MAX													
Microscale	3,190	1.2	0.1	0.3	0.4	0.5	0.7	0.8	1.0	1.4	1.5	2.2	2.7
Neighborhood Scale	2,173	1.1	0.1	0.2	0.3	0.4	0.6	0.6	0.9	1.3	1.5	2.1	2.6
1-H DAILY AVG													
Microscale	3,190	0.5	0.0	0.1	0.2	0.2	0.3	0.4	0.5	0.6	0.6	0.9	1.0
Neighborhood Scale	2,173	0.5	0.0	0.1	0.2	0.3	0.3	0.4	0.5	0.6	0.6	0.9	1.1
8-H DAILY MAX													
Microscale	3,190	0.8	0.3	0.3	0.3	0.4	0.5	0.5	0.7	0.9	1.0	1.4	1.8
Neighborhood Scale	2,173	0.8	0.3	0.3	0.3	0.3	0.4	0.5	0.7	0.9	1.0	1.5	1.8

Table A-20. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Houston, TX.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	24,922	0.3	0.0	0.0	0.0	0.0	0.2	0.2	0.3	0.4	0.5	0.6	0.8
Neighborhood Scale	99,003	0.3	0.0	0.0	0.0	0.0	0.2	0.2	0.3	0.4	0.4	0.6	0.8
1-H DAILY MAX													
Microscale	1,043	0.7	0.0	0.0	0.2	0.3	0.4	0.5	0.6	0.8	0.9	1.2	1.4
Neighborhood Scale	4,145	0.7	0.0	0.0	0.1	0.2	0.4	0.4	0.5	0.8	0.8	1.3	1.7
1-H DAILY AVG													
Microscale	1,043	0.3	0.0	0.0	0.0	0.1	0.2	0.3	0.4	0.5	0.5	0.6	0.6
Neighborhood Scale	4,145	0.3	0.0	0.0	0.0	0.1	0.2	0.2	0.3	0.4	0.4	0.5	0.6
8-H DAILY MAX													
Microscale	1,043	0.5	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.6	0.6	0.8	1.0
Neighborhood Scale	4,145	0.5	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.5	0.6	0.9	1.1

Table A-21. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Los Angeles, CA.

				PERCENTILES								
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	24,885	0.7	0.0	0.2	0.3	0.3	0.4	0.4	0.5	0.7	0.8	1.2	1.6
Middle Scale	98,564	0.5	0.0	0.0	0.0	0.0	0.1	0.2	0.4	0.6	0.7	1.1	1.6
Neighborhood Scale	49,757	0.3	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.3	0.3	0.6	0.8
Urban Scale	24,264	0.4	0.0	0.0	0.1	0.1	0.1	0.2	0.3	0.4	0.5	1.0	1.4
1-H DAILY MAX													
Microscale	1,080	1.3	0.2	0.4	0.5	0.6	0.8	0.8	1.1	1.6	1.7	2.3	2.7
Middle Scale	4,299	1.2	0.0	0.1	0.1	0.2	0.5	0.6	0.9	1.3	1.5	2.5	3.7
Neighborhood Scale	2,164	0.7	0.0	0.0	0.0	0.1	0.3	0.3	0.5	0.8	0.9	1.3	1.7
Urban Scale	1,053	1.0	0.0	0.1	0.2	0.3	0.4	0.4	0.7	1.3	1.5	2.2	2.6
1-H DAILY AVG													
Microscale	1,080	0.7	0.2	0.3	0.3	0.4	0.5	0.5	0.6	0.7	0.8	1.1	1.2
Middle Scale	4,299	0.5	0.0	0.0	0.0	0.1	0.2	0.2	0.4	0.6	0.7	1.1	1.5
Neighborhood Scale	2,164	0.3	0.0	0.0	0.0	0.0	0.1	0.2	0.2	0.3	0.4	0.5	0.6
Urban Scale	1,053	0.4	0.0	0.0	0.1	0.1	0.2	0.2	0.3	0.5	0.6	0.9	1.1
8-H DAILY MAX													
Microscale	1,080	0.9	0.3	0.3	0.4	0.4	0.6	0.6	0.8	1.1	1.2	1.6	1.8
Middle Scale	4,299	0.8	0.3	0.3	0.3	0.3	0.3	0.3	0.6	0.9	1.0	1.8	2.4
Neighborhood Scale	2,164	0.5	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.5	0.6	0.9	1.2
Urban Scale	1,053	0.7	0.3	0.3	0.3	0.3	0.3	0.3	0.5	0.8	0.9	1.5	1.8

Table A-22. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for New York City, NY.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	25,646	0.8	0.0	0.2	0.3	0.4	0.5	0.6	0.8	1.0	1.1	1.4	1.6
Middle Scale	48,660	0.6	0.0	0.1	0.3	0.3	0.4	0.5	0.6	0.7	0.7	0.9	1.0
Neighborhood Scale	25,150	0.5	0.0	0.2	0.2	0.3	0.3	0.4	0.4	0.6	0.6	0.9	1.1
1-H DAILY MAX													
Microscale	1,077	1.4	0.3	0.4	0.6	0.8	1.0	1.1	1.4	1.7	1.8	2.1	2.4
Middle Scale	2,053	0.9	0.2	0.4	0.5	0.6	0.7	0.7	0.8	1.0	1.1	1.3	1.5
Neighborhood Scale	1,053	0.9	0.2	0.3	0.4	0.4	0.6	0.6	0.8	1.0	1.1	1.5	1.9
1-H DAILY AVG													
Microscale	1,077	0.8	0.2	0.3	0.4	0.5	0.6	0.7	0.8	1.0	1.0	1.3	1.4
Middle Scale	2,053	0.6	0.0	0.2	0.3	0.4	0.5	0.5	0.6	0.7	0.7	0.8	0.9
Neighborhood Scale	1,053	0.5	0.1	0.2	0.3	0.3	0.4	0.4	0.5	0.6	0.6	0.8	1.0
8-H DAILY MAX													
Microscale	1,077	1.2	0.3	0.4	0.6	0.7	0.9	0.9	1.1	1.4	1.4	1.7	1.9
Middle Scale	2,053	0.7	0.3	0.3	0.4	0.4	0.6	0.6	0.7	0.8	0.9	1.0	1.2
Neighborhood Scale	1,053	0.7	0.3	0.3	0.3	0.3	0.4	0.5	0.6	0.8	0.8	1.2	1.5

Table A-23. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Phoenix, AZ.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	25,382	0.9	0.0	0.0	0.1	0.1	0.3	0.3	0.6	1.1	1.3	2.3	3.0
Middle Scale	25,414	0.8	0.0	0.0	0.1	0.1	0.3	0.3	0.5	0.9	1.0	1.8	2.3
Neighborhood Scale	51,246	0.7	0.0	0.0	0.1	0.1	0.2	0.3	0.4	0.7	0.8	1.8	2.4
1-H DAILY MAX													
Microscale	1,063	2.2	0.0	0.2	0.5	0.7	1.1	1.2	1.9	2.8	3.1	4.2	4.7
Middle Scale	1,066	1.8	0.1	0.3	0.5	0.7	1.0	1.1	1.6	2.2	2.4	3.2	3.8
Neighborhood Scale	2,156	1.8	0.1	0.2	0.4	0.5	0.8	0.9	1.5	2.3	2.6	3.6	4.2
1-H DAILY AVG													
Microscale	1,063	0.9	0.0	0.0	0.2	0.2	0.4	0.4	0.7	1.2	1.3	2.0	2.3
Middle Scale	1,066	0.8	0.0	0.1	0.2	0.3	0.4	0.5	0.7	0.9	1.0	1.5	1.7
Neighborhood Scale	2,156	0.7	0.0	0.1	0.2	0.2	0.3	0.4	0.5	0.9	0.9	1.5	1.8
8-H DAILY MAX													
Microscale	1,063	1.5	0.3	0.3	0.3	0.4	0.6	0.7	1.2	2.0	2.2	3.1	3.5
Middle Scale	1,066	1.2	0.3	0.3	0.3	0.4	0.7	0.7	1.0	1.5	1.7	2.3	2.7
Neighborhood Scale	2,156	1.2	0.3	0.3	0.3	0.3	0.5	0.6	0.9	1.5	1.7	2.5	3.0

Table A-24. Comparison of distributional data at different monitoring scales for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Pittsburgh, PA.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Middle Scale	25,818	0.5	0.0	0.0	0.1	0.1	0.3	0.3	0.4	0.5	0.6	0.8	1.1
Neighborhood Scale	77,000	0.3	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.3	0.4	0.6	0.8
Urban Scale	76,940	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.3	0.6	0.8
1-H DAILY MAX													
Middle Scale	1,079	0.9	0.0	0.2	0.4	0.4	0.6	0.6	0.8	1.1	1.1	1.6	1.9
Neighborhood Scale	3,210	0.6	0.0	0.0	0.1	0.2	0.3	0.3	0.5	0.7	0.7	1.1	1.3
Urban Scale	3,208	0.4	0.0	0.0	0.0	0.0	0.1	0.2	0.4	0.6	0.7	1.0	1.2
1-H DAILY AVG													
Middle Scale	1,079	0.5	0.0	0.1	0.2	0.2	0.3	0.3	0.4	0.5	0.6	0.8	0.9
Neighborhood Scale	3,210	0.3	0.0	0.0	0.0	0.0	0.1	0.2	0.3	0.3	0.4	0.6	0.7
Urban Scale	3,208	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.3	0.6	0.7
8-H DAILY MAX													
Middle Scale	1,079	0.7	0.3	0.3	0.3	0.3	0.4	0.4	0.6	0.7	0.8	1.1	1.3
Neighborhood Scale	3,210	0.5	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.5	0.5	0.8	1.0
Urban Scale	3,208	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.5	0.8	1.0

Table A-25. Comparison of distributional data for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for Seattle, WA. Microscale was the only scale at which monitoring was performed in Seattle, WA.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Microscale	25,818	0.8	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.9	0.9	1.3	1.6
1-H DAILY MAX													
Microscale	1,079	1.5	0.2	0.4	0.5	0.7	0.9	1.0	1.3	1.7	1.8	2.4	2.9
1-H DAILY AVG													
Microscale	1,079	0.8	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.9	0.9	1.2	1.4
8-H DAILY MAX													
Microscale	1,079	1.1	0.3	0.3	0.4	0.5	0.7	0.8	1.0	1.3	1.4	1.8	2.2

Table A-26. Comparison of distributional data for hourly, 1-h daily max, 24-h avg, and 8-h daily max data for St. Louis, MO. Neighborhood scale was the only scale at which monitoring was performed in St. Louis, MO.

				PERCENTILES									
Time Scale	**N**	**Mean**	**Min**	**1**	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**99**	**max**
ALL HOURLY													
Neighborhood Scale	51,263	0.4	0.0	0.1	0.2	0.2	0.3	0.3	0.4	0.5	0.5	0.6	0.8
1-H DAILY MAX													
Neighborhood Scale	2,138	0.8	0.1	0.2	0.3	0.4	0.5	0.5	0.6	0.9	1.0	1.5	2.0
1-H DAILY AVG													
Neighborhood Scale	2,138	0.4	0.0	0.1	0.2	0.3	0.3	0.3	0.4	0.5	0.5	0.6	0.7
8-H DAILY MAX													
Neighborhood Scale	2,138	0.6	0.3	0.3	0.3	0.3	0.3	0.3	0.5	0.6	0.7	1.0	1.3

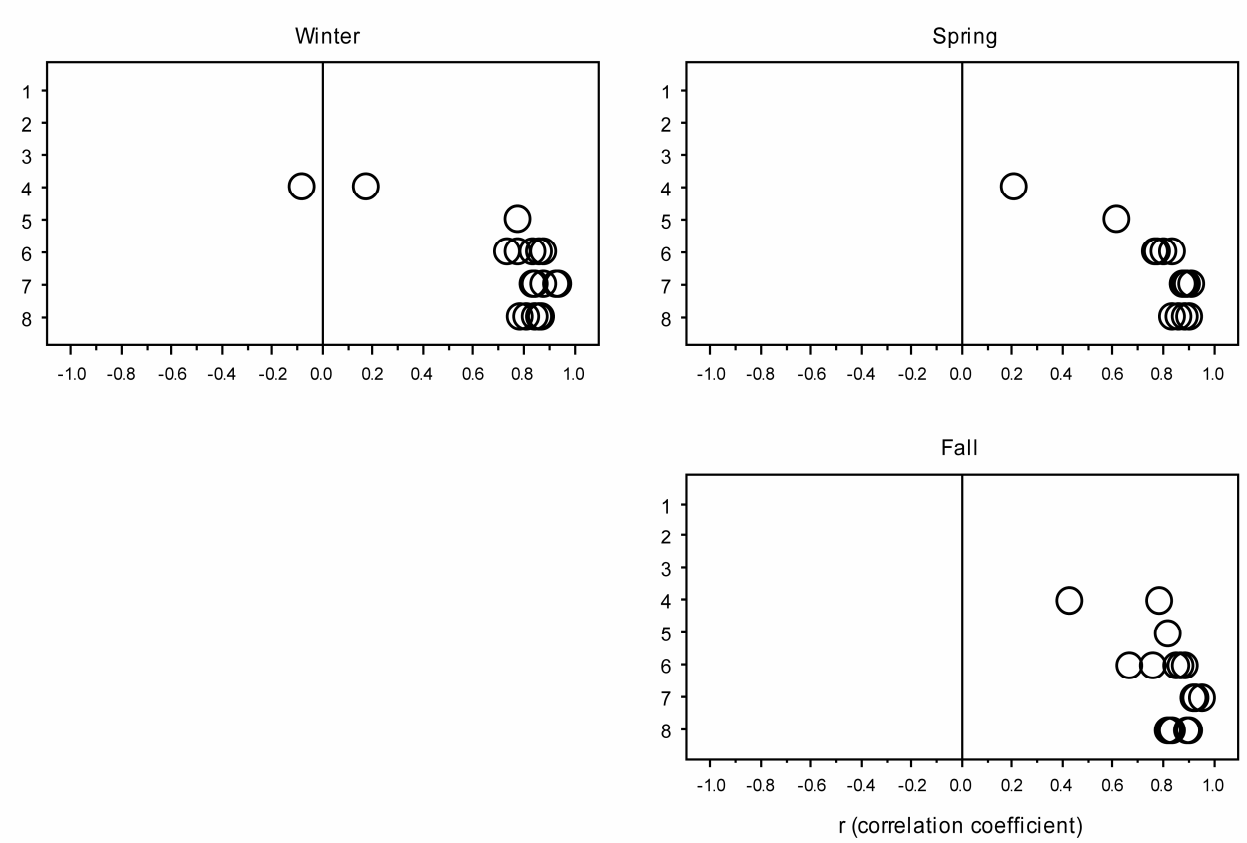


Figure A-44. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for Anchorage, AK. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot. Note that the data are not obtained for Anchorage during the summer, and so are not presented here.

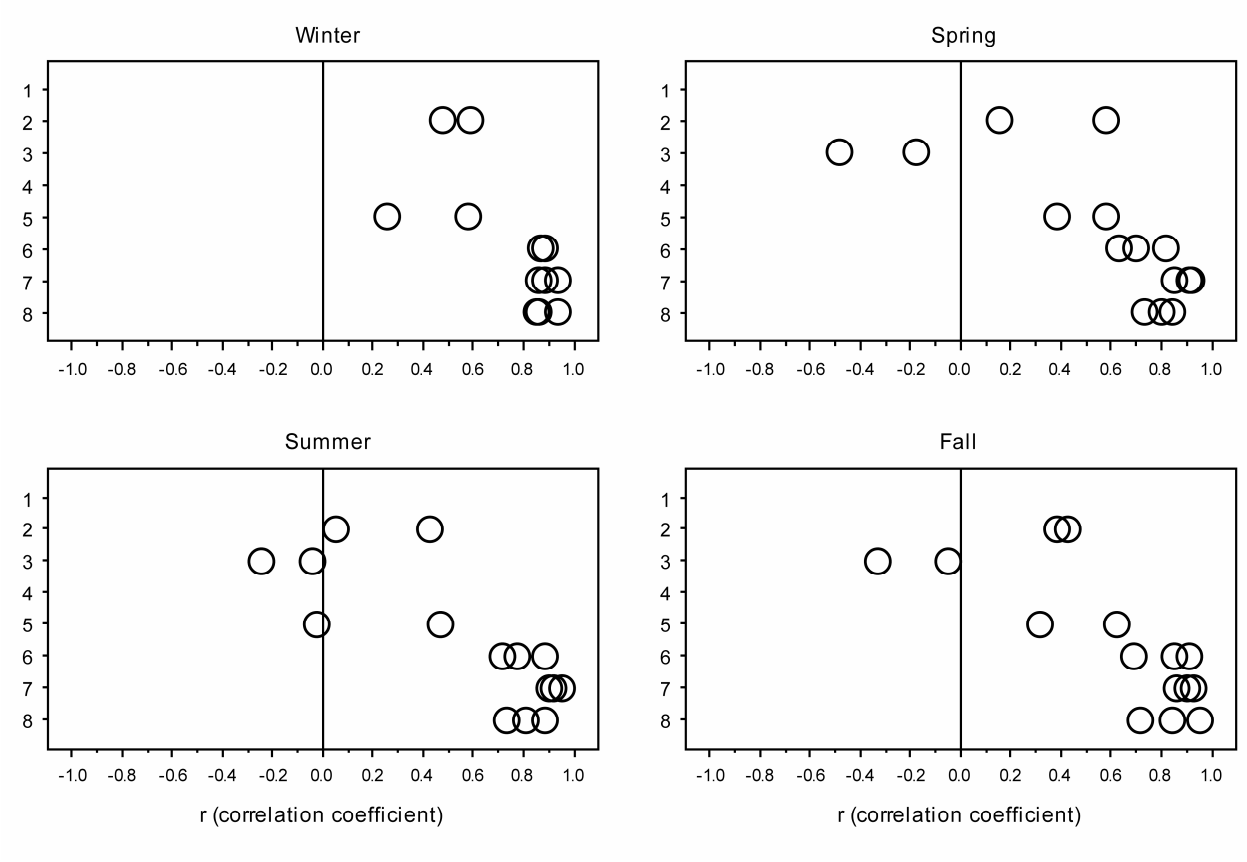


Figure A-45. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for Atlanta, GA. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot.

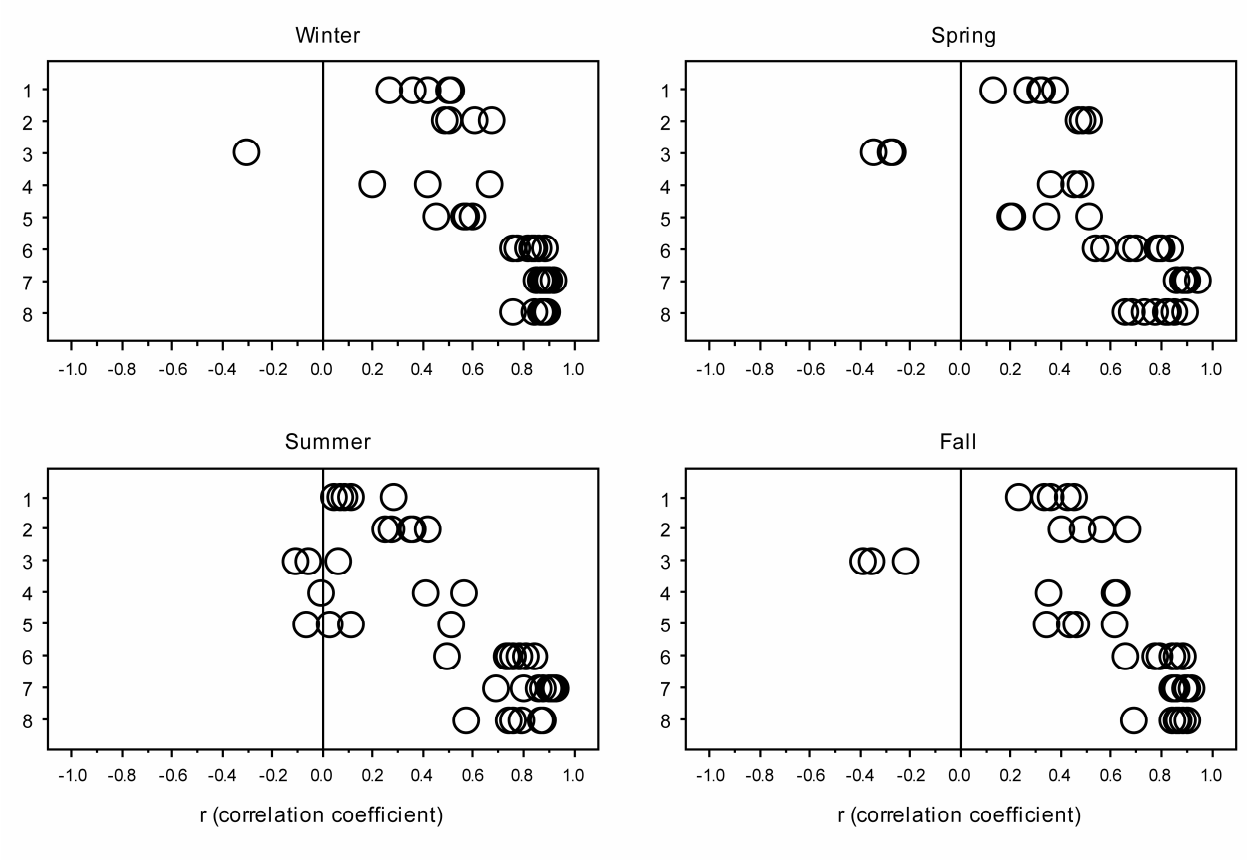


Figure A-46. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for Boston, MA. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot.

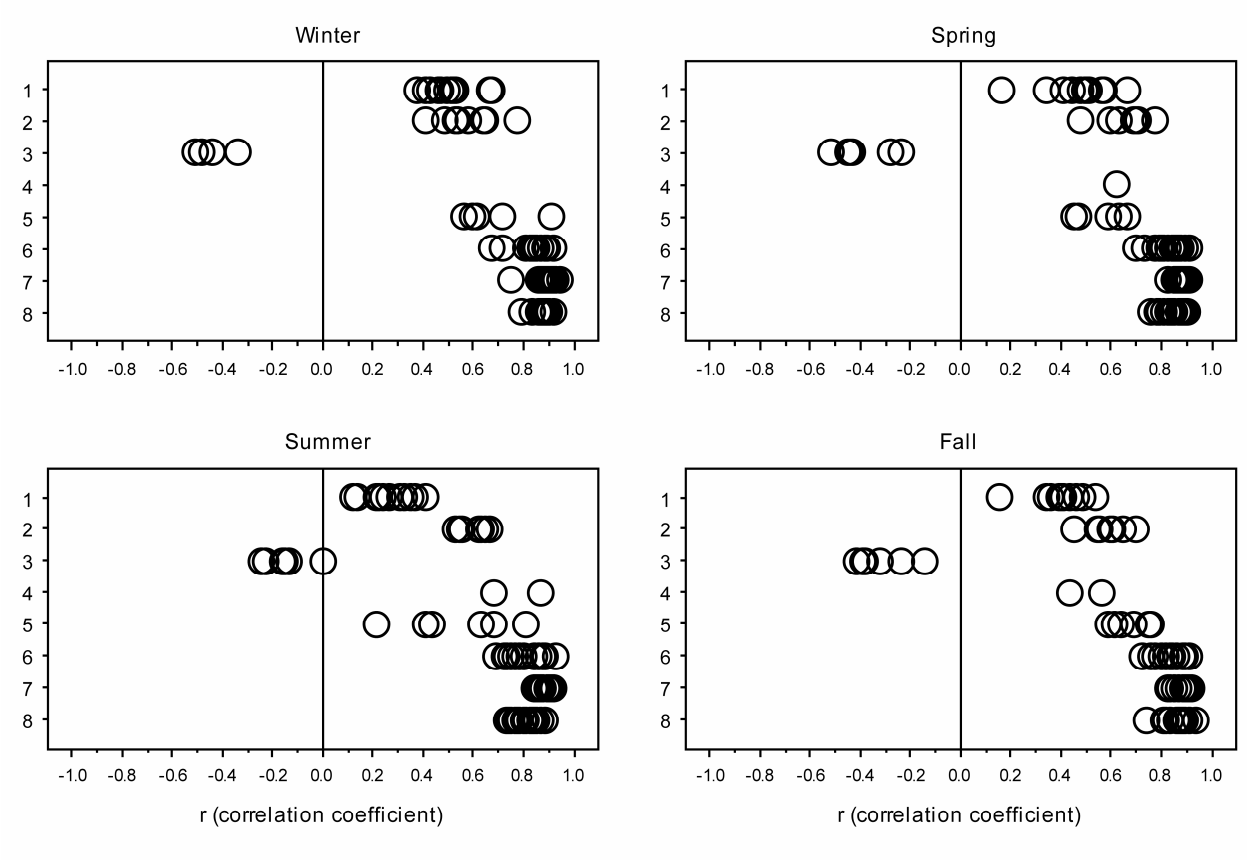


Figure A-47. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for New York City, NY. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot.

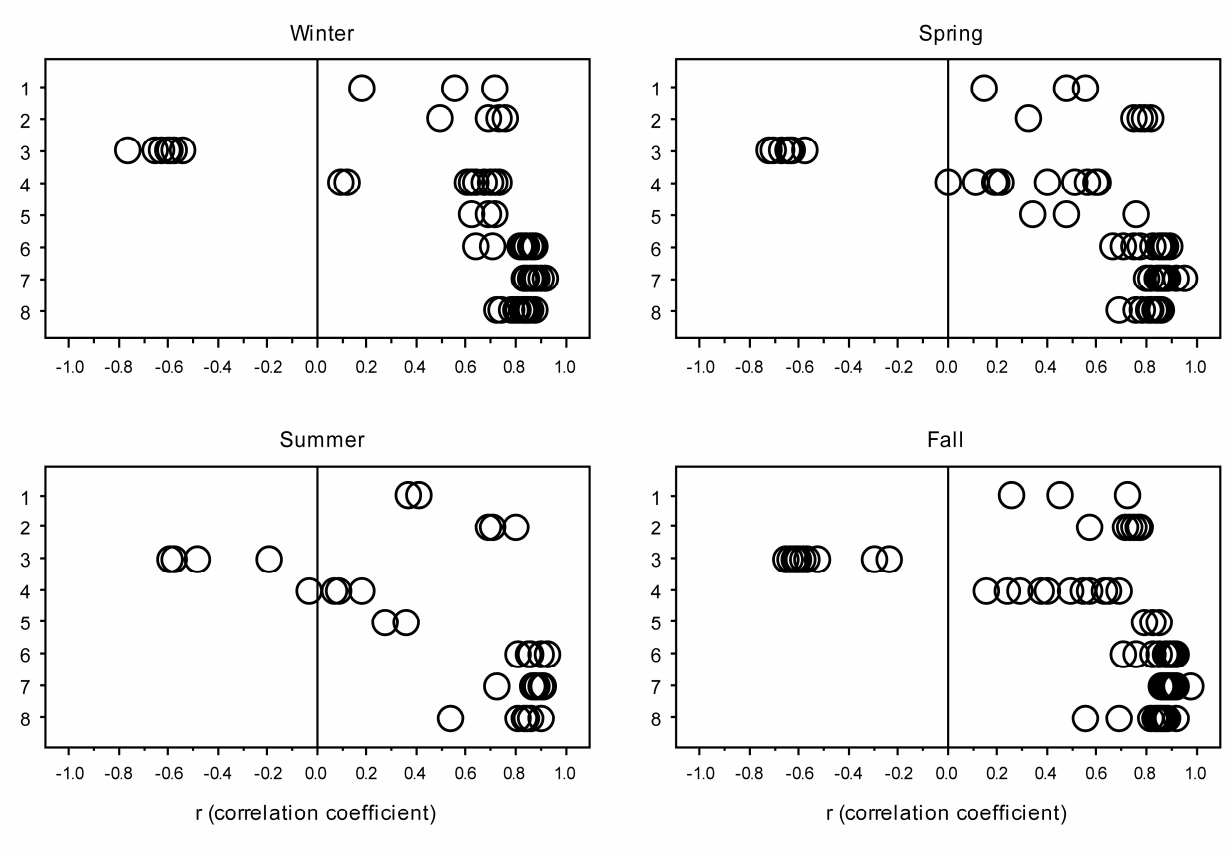


Figure A-48. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for Phoenix, AZ. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot.

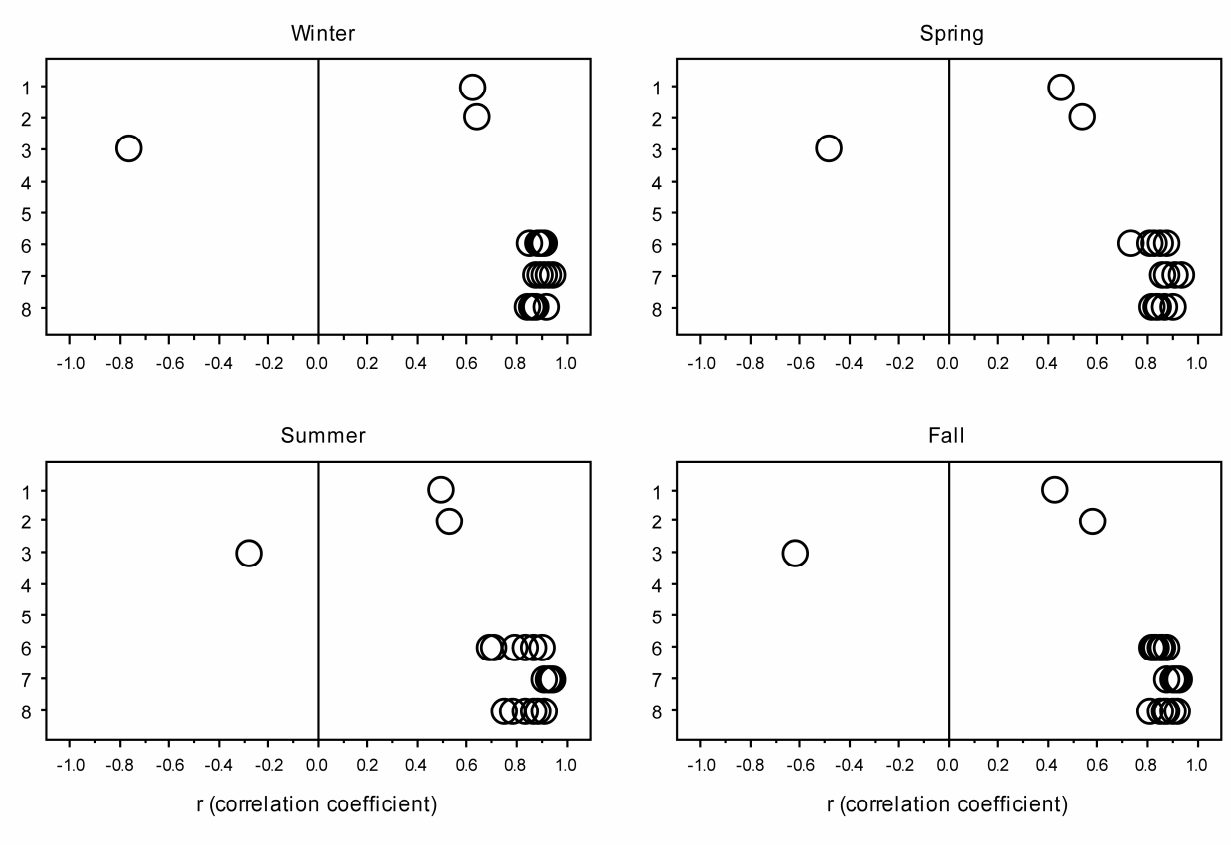


Figure A-49. Seasonal plots of correlations between hourly CO concentration with hourly (1) SO_2, (2) NO_2, (3) O_3, (4) PM_{10}, and (5) $PM_{2.5}$ concentrations for Seattle, WA. Also shown are correlations between 24-h avg CO concentration with (6) daily max 1-h and (7) daily max 8-h CO concentrations and (8) between daily max 1-h and daily max 8-h CO concentrations. Refer the numbers in this caption to those on the y-axis of each seasonal plot.

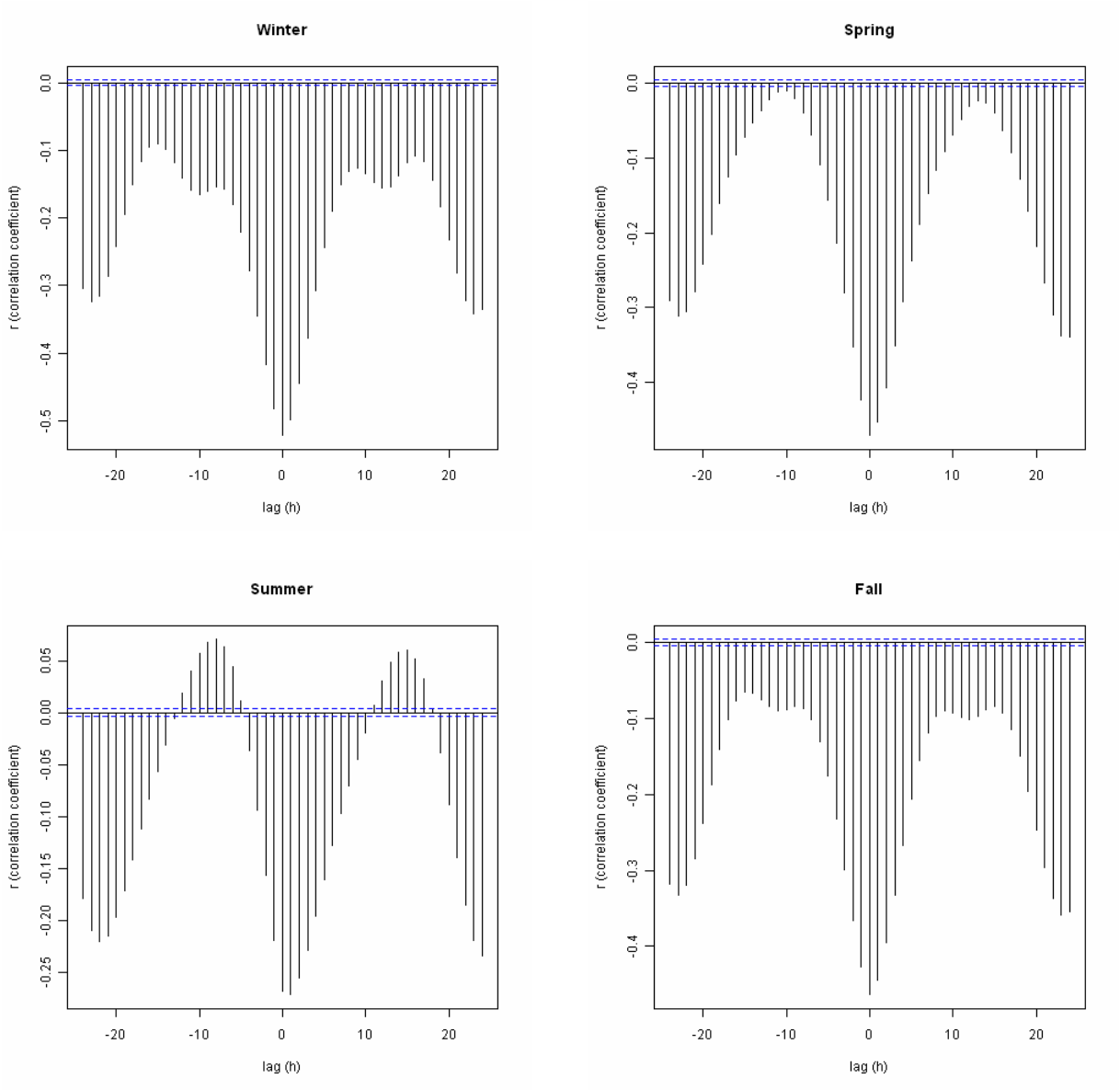


Figure A-50. Cross-correlation functions for each season combined across sites where CO and O_3 monitors were co-located in Atlanta, Boston, Denver, Los Angeles, New York City, and Phoenix.

Annex B. Dosimetry Studies

Table B-1. Recent studies related to CO dosimetry and pharmacokinetics.

Reference	Purpose	Findings
Aberg et al. (2009, 194082)	To investigate CO concentrations in blood donors in Sweden.	The mean CO concentration in blood donors was 84.5 µmol/L. Concentrations over 130 µmol/L were found in 6% of blood, and the highest concentration was 561 µmol/L . By using a calculation, 23% of banked blood bags could exceed 1.5% COHb, with a highest fraction of 7.2% COHb.
Abram et al. (2007, 193859)	To present the Quantitative Circulatory Physiology (QCP) model as a teaching module in the practice of medicine.	QCP is a dynamic mathematical model based on published models and parameters of biological interactions.
Alcantara et al. (2007, 193867)	To use a quantum mechanics/molecular mechanics approach to understand the cooperativity of Hb ligand binding and differences in energy between T and R Hb functional states.	The ligand binding energies between R and T states differ due to strain induced in the heme and its ligands and in protein contacts in the α and β chains.
Adir et al. (1999, 001026)	To determine if low concentrations of CO would affect exercise performance and myocardial perfusion in young healthy men.	Men with COHb levels between 4 and 6% had decreased exercise performance measured by decreased mean duration of exercise (1.52 min) and maximal effort described by metabolic equivalent units (2.04). No changes were seen in lactate/pyruvate ratio, arrhythmias, or myocardial perfusion.
Anderson et al. (2000, 011836)	To investigate if CO could be endogenously produced in the nose and paranasal sinuses.	Both nose and paranasal sinuses contained HO-like immunoreactivity, mostly in the respiratory epithelium, indicating local CO production in the upper respiratory airways.
Arora et al. (2001, 186713)	To evaluate the effect of multiple transfusion recipient thalassemics on pulmonary function.	D_LCO was decreased in all the patients with restrictive lung disease and fall in D_LCO showed a good correlation with the severity of restrictive disease. Thalassemics had a decrease in lung volume and a proportional decrease in flow rate.
Benignus et al. (2006, 151344)	To adapt and use a human model for toluene uptake and elimination including a brain compartment.	The QCP 2004 model was used to construct simulations of scenarios of toxicant exposure and human activities. QCP accurately predicted toluene blood concentrations from inhaled exposure.
Bos et al. (2006, 194084)	To use a PBPK model to set AEGL for methylene chloride.	This model adequately predicted COHb levels formed by various methylene chloride concentrations, specifically in nonconjugators lacking the GSTT-1 enzyme, and proposed AEGL values.
Bruce and Bruce (2003, 193975)	To create a mathematical model to predict uptake and distribution of CO in both vascular and tissue compartments during constant or variable inhalation levels of CO.	This model contains 5 compartments: lung, arterial blood, venous blood, muscle tissue, and nonmuscle tissue. It was constructed to include tissue compartment flux and difference between venous and arterial COHb for short exposures which is not possible with the CFK model.
Bruce and Bruce (2006, 193980)	To use their mathematical multicompartment model along with experimental data to predict the factors that influence the washout rates of CO, along with predicting the rates of CO uptake, distribution in vascular and extravascular (muscle and nonmuscle tissue) compartments, and washout over a range of exposure and conditions.	Rates of CO washout follow a biphasic elimination where washout was faster immediately post exposure. The difference in rates is likely due to slow equilibration between vascular and extravascular compartments. Important factors contributing to washout kinetics include: peak COHb level, exposure duration and concentration, time after exposure samples were obtained, and individual variability.
Bruce and Bruce (2008, 193977)	To develop a mathematical model able to integrate a large body of indirect experimental findings on the uptake and distribution of CO by accounting for arteriole to venule shunting via intratissue pathways and diffusion of blood gases into tissues from pre-capillary vessels like arterioles.	The former model of Bruce and Bruce (2006, 193980) was altered by adding a mass balance equation for O_2 so pO_2 is directly calculated in the compartments, and the muscle compartment is divided into two sub-compartments of muscle and nonmuscle tissue. CO uptake from blood by muscle is much slower than O_2, thus COHb% will fall rapidly while COMb% could remain high.

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Reference	Purpose	Findings
Carraway et al. (2000, 021096)	To test the hypothesis that HO-1 gene expression and protein are upregulated in the lungs of rats during chronic hypoxia.	Rats were exposed to HH (17,000 ft) for 1-21 days. COHb increased after 1 day and progressively after 14 days. HO-1 protein and activity were upregulated during early chronic hypoxia. This HO-1 was localized to inflammatory cells and then to newly muscularized arterioles.
Castillo et al. (2006, 193234)	To describe a new method for measurement of CO D_LCO and V_A in sleeping infants (6-22 mo old), using a single 4-s breath-hold technique.	V_{A30} and D_LCO increased with increasing body length, and the method could be used as a measurement of lung development and growth.
Chakraborty et al. (2004, 193759)	To present an analytical expression for diffusing capacity of CO, NO, CO_2, and O_2 to the red blood cell in terms of optimum size and shape of the RBC, thickness of the unstirred plasma layer surrounding the RBC, diffusivities and solubilities of the gas in RBC and boundary layer, hematocrit, and the slope of the dissociation curve.	Results indicate the discoidal shape of the RBC is optimal for O_2 uptake and reaction velocity is limited by mass transfer resistance in surrounding stagnant plasma layer. The paper overviews rate constants and reaction kinetics for CO binding to Hb. CO diffusing capacity is shown to be reaction-rate limited at low pCO under normoxic and hyperoxic conditions, but diffusion-rate limited under hypoxic and high pCO conditions.
Cronenberger et al. (2008, 194085)	To develop a population-based model to describe and predict the pharmacokinetics of COHb in adult smokers.	This two-compartment model included zero-order input and first-order elimination and required a compartment for extravascular binding of CO to accurately predict COHb formation during multiple short and rapid inhalations, followed by a period of no exposure, as occurs in smoking. Smokers' COHb ranged from 0.8 to 11.1%.
Cronje et al. (2004, 180440)	To analyze CO uptake and elimination in the brain, muscle, heart, and blood of rats, with the intent of testing the Warburg hypothesis that CO partitioning is directly proportional to the CO/O_2 ratio.	Results indicate that tissue and blood CO concentration dissociate during CO inhalation, but CO concentration does not follow blood CO concentration or $1/pO_2$ as in the Warburg theory during intake or elimination. Tissue CO concentration increases later during the resolution period and varies significantly among animals and tissues. The deviation from the predicted values in the brain is likely due to the release of heme and increase in NADPH stimulating endogenous CO production by HO.
De las Heras et al. (2003, 194087)	To assess production of CO (venous COHb measured by CO-oximeter and exhaled CO) in patients with cirrhosis with and without spontaneous bacterial peritonitis.	Patients with SBP had higher CO production than noninfected cirrhotic patients and both groups of patients had higher CO production compared to healthy controls. CO production decreased slowly after resolution of the disease.
Dutton et al. (2001, 021307)	To monitor CO, NO_2, and PAH emissions during the operation of unvented natural gas fireplaces in two residences in Boulder, CO, at various times between 1997 and 2000.	Results showed significant accumulation of CO, NO_2, and PAH indoors when the fireplaces were used. CO concentrations could exceed 100 ppm. NO_2 concentrations averaged 0.36 ppm over 4 h. PAH 4-h time avg reached 35 ng/m^3.
Ehlers et al. (2009, 194089)	To determine the level of COHb found in banked blood in the Albany, NY region.	The avg COHb level was 0.78%. The highest recorded COHb level was 12%, and 10.3% of packed red blood cell units had levels of 1.5% COHb or higher.
Gosselin et al. (2009, 190946)	To develop a variant of the CFK model that links COHb levels in humans to ambient CO levels under various environmental or occupational exposure conditions.	The model adds alveoli-blood and blood-tissue CO exchanges and mass conservation of CO at all times to the CFK equation. The model better predicted COHb formation over a wide range of CO levels and scenarios with linear regression analysis of predicted vs observed values generating a slope of 0.996 (95% CI: 0.986-1.001) compared to 0.917 (95% CI: 0.906-0.927) using the CFK model
Hampson and Weaver (2007, 190272)	To present a case study of a man with drug-induced hemolytic anemia and hepatic failure.	The man had elevated endogenous CO production resulting in levels of COHb as high as 9.7%.
Hart et al. (2006, 194092)	To investigate the relationship between COHb and smoking habit and mortality.	COHb was related to self-reported smoking in a dose-dependent manner. COHb was positively associated with all causes of mortality analyzed including CHD, COPD, stroke, and lung cancer. Mean COHb levels ranged from 1.59% in never-smokers to 6.02% in the most often smoking group.
Hsia (2002, 193857)	To review the current concepts and practical relevance of the diffusing capacity/cardiac output interaction, in hopes of aiding in the interpretation of diffusing capacity, membrane diffusing capacity, and capillary blood volume.	This review helped to understand the determinants of changes in diffusing capacity, including hematocrit, erythrocyte distribution, blood volume, lung volume, and cardiac output.
Johnson et al. (2006, 193874)	To test that heme-derived CO formation is increased and contributes to hypertension and arteriolar endothelial dysfunction in obese Zucker rats.	Obese Zucker rats showed increased respiratory CO excretion that was lowered by HO inhibition. Skeletal muscle arterioles of obese rats had attenuated ACh and flow responses that were abolished by HO inhibition (HO inhibition enhanced dilation).
Lamberto et al. (2004, 193845)	To evaluate which component, alveolar membrane diffusing capacity (Dm) and pulmonary capillary blood volume (Vc), is responsible for decreased resting D_LCO in sarcoidosis patients and which component is the best predictor of gas exchange abnormalities.	Patients with pulmonary sarcoidosis had decreased lung volumes, a loss in D_LCO, and gas exchange abnormalities during exercise, including decreased P_aO_2 and increased alveolar-arterial oxygen pressure difference. Dm accounted for the majority of the decrease in D_LCO and was predictive for gas exchange abnormalities.

Reference	Purpose	Findings
Levesque et al. (2000, 011886)	To describe the results of air quality monitoring in an indoor ice skating rink during Monster Truck and car demolition exhibitions.	Maximum time-weighted avg levels of CO were 100 ppm, with several peaks exceeding 200 ppm (max: 1,600 ppm).
Lim et al. (2000, 126969)	To investigate the expression of HO-1 and HO-2 in bronchial biopsies obtained from patients with mild asthma compared with that of subjects without asthma.	HO-1 and HO-2 expression is widely distributed equally in healthy subjects and subjects with asthma and is not modulated by inhaled corticosteroid therapy.
Mahoney et al. (1993, 013859)	To compare CO-oximeter measurements of COHb against a gas chromatography reference method.	In general, the 5 CO-oximeters that were tested underestimated COHb concentrations for COHb >2.5% and overestimated COHb concentration for COHb ≤ 2.5%, when compared to reference gas chromatography method.
Marks et al. (2002, 030616)	To review the analytical methods for measurement of endogenous formation of CO in a variety of tissues.	A variety of methods have been used to measure endogenous CO. The rate of formation varies over a narrow range, from 0.029 nmol/mg protein/h to 0.28 nmol/mg protein/h depending on tissue. Brain and liver regions tend to have the highest rates of CO formation, likely due to high levels of HO activity in these tissues.
Marvisi et al. (2007, 186702)	To evaluate D_LCO impairment and microalbuminuria in patients with active ulcerative colitis (UC) and to assess whether these tests correlate with intestinal inflammation.	Reduced D_LCO was present in 67% of patients. Microalbuminuria was present in 63% of patients with ulcerative colitis.
Merx et al. (2001, 002006)	To investigate the effect of CO inactivation of Mb in wild-type and myo-/- mice on hemodynamics and oxygen dynamics.	Fully oxygenated Mb treated with 20% CO had no change in left ventricular developed pressure or coronary venous pO_2. Partially O_2-saturated Mb (87% O_2Mb) exposed to 20% CO had significantly decreased LVDP (12%) and PvO_2 (30%) in wild-type but not myo-/- hearts.
Monma et al. (1999, 180426).	To study whether exhaled CO levels were increased in seasonal allergic rhinitis.	Exhaled CO concentrations were higher in allergic rhinitis patients during cedar pollen season (3.6 ppm; SD 0.3 ppm) that out (1.2 ppm; SD 0.1 ppm).
Morimatsu et al. (2006, 194097)	To examine exhaled CO, arterial COHb, and bilirubin IXα levels in critically ill patients.	Exhaled CO concentrations were significantly higher in critically ill patients compared to controls. There was a significant correlation between exhaled CO and COHb or bilirubin. There was no correlation between exhaled CO and disease severity or degree of inflammation. There was higher exhaled CO in survivors compared to nonsurvivors.
Muchova et al. (2007, 194098)	To determine if long-term use of statins affects HO activity and blood and organ CO and bilirubin in FvB mice (6-8 wk).	Rosuvastatin and atorvastatin treatment increased COHb, plasma bilirubin, and heart tissue CO content. Both statins caused an increase in HO activity in heart tissue, whereas no changes were seen in brain or lung. Liver HO activity was inconsistent over time and between statins. Both statins decreased the heart antioxidant capacity, and changes in HO activity and antioxidant capacity can be reversed by HO inhibitor treatment.
Neto et al. (2008, 194672)	To develop a model of the respiratory system to analyze CO transport in the human body submitted to several physical activity levels.	The model contains 6 compartments including: alveolar, pulmonary capillaries, arterial, venous, tissue capillary, and tissues (muscular and nonmuscular). The highest and lowest COHb levels were simulated in the walking individual, suggesting that greater variability in COHb occurs in higher physical activity levels.
Pelham et al. (2002, 025716)	To review the literature on exposure and effects of mainly CO and NO_2 in enclosed ice rinks.	CO levels as high as 300 ppm were recorded after episodes of malfunctioning ice resurfacing equipment or inadequate ventilation.
Paredi et al. (1999, 194102)	To investigate the level of exhaled CO produced by diabetic patients.	Diabetic patients (types 1 and 2) had higher levels of exhaled CO than healthy subjects. Exhaled CO levels correlated with the incidence of glycemia and the duration of diabetes.
Paredi et al. (1999, 118798)	To investigate whether cystic fibrosis patients have higher exhaled levels of CO and if this is reduced by corticosteroid therapy.	Cystic fibrosis patients had higher exhaled CO concentrations compared to healthy controls. Patients receiving corticosteroid therapy had lower exhaled CO concentrations.
Pesola et al. (2004, 193842)	To determine if healthy African Americans may be misdiagnosed as having respiratory deficient due to comparison using Caucasian-derived prediction equation estimates of D_LCO.	The lung volume of African-American individuals is 10-15% lower than Caucasians. The measured D_LCO was consistently significantly lower in African-Americans than what would be predicted. Thus, the authors suggest a race correction reduction of the Miller PEE for diffusion of 12%.
Pesola et al. (2006, 193855)	To determine if healthy Asians may be misdiagnosed as having respiratory deficient due to comparison using Caucasian-derived prediction equation estimates of D_LCO.	The lung volume of Asian individuals is 10-15% lower than Caucasians. Thus a Chinese-derived prediction for D_LCO should be used.

Reference	Purpose	Findings
Prommer and Schmidt (2007, 180421)	To determine the error in total Hb mass measurements using the optimized CO-rebreathing method due to loss of CO to Mb	Optimal blood mixing (when venous and arterial blood COHb% are equivalent) was determined to be after 6 min. A small volume of administered CO leaves the vascular space (0.32% per min). A 2.3% increase in total Hb mass would be found if CO diffusion was not included.
Proudman et al. (2007, 186705)	To review the signs of pulmonary arterial hypertension, including a drop in D_LCO in patients with systemic sclerosis.	
Richardson et al. (2002, 037513)	To combine invasive vascular measures of arterial and venous blood and muscle blood flow with noninvasive magnetic spectroscopy of deoxy-myoglobin and high energy phosphates to determine the effects of mild CO poisoning (20% COHb) in humans during muscular work.	Five humans were analyzed under normoxia, hypoxia, normoxia + CO (20% COHb), and 100% O_2 + CO. Maximum works rates and maximal oxygen uptake were reduced in H, COnorm, and COhyper. CO and H caused elevated blood flow. Net muscle CO uptake from blood was less during 20% COHb trials than during normoxia and hypoxia (1-2%) trials.
Sakamaki et al. (2002, 186706)	To evaluate the association of patients with aortic aneurysm to the prevalence obstructive airway disease.	Patients with AA had lower FEV_1 and D_LCO than controls. Presence of AA and male gender were associated with a higher risk of airway obstruction.
Scharte et al. (2000, 194112)	To investigate whether exhaled CO concentrations are increased in critically ill patients.	Critically ill patients had higher exhaled CO concentrations and higher total CO production rates compared to healthy controls. No correlation was found between exhaled CO concentration and venous or arterial COHb.
Scharte et al. (2006, 194115)	To investigate the relationship between the severity of illness and endogenous CO production in critically ill patients.	CO production rates weakly correlated with the multiple organ dysfunction score (R=0.27). Cardiac disease patients and patients undergoing dialysis produced higher amounts of CO compared to critically ill control patients.
Schachter et al. (2003, 186707)	To evaluate the association between severe gastroesophageal reflux and lung function.	Patients with severe gastroesophageal reflux had reduced D_LCO, remaining significant after adjusting for age, gender, BMI, and smoking.
Shimazu et al. (2000, 016420)	To study the effects of short-term (min) or long-term (several h) CO exposure on COHb elimination and developing a mathematical model to simulate this event.	COHb exhibited an initial rapid decrease followed by a slower phase which is compatible with a 2-compartment model and biphasic elimination. Both exposures fit the 2-compartment, single-central-outlet mathematical model.
Shimazu (2001, 016331)	To discuss the findings of Weaver et al. (2000, 016421) on COHb t1/2.	The authors discuss that CO elimination is biphasic and is heavily affected by duration of exposure which was not taken into account in the Weaver et al. (2000, 016421) paper.
Sylvester et al. (2005, 191954)	To assess the usage of end tidal CO levels in children with sickle cell disease for measurement of hemolysis.	Children with sickle cell disease had higher exhaled CO levels (4.9 ppm; SD 1.7 ppm) compared to healthy controls (1.3 ppm; SD 0.4 ppm). A positive correlation existed between end-tidal CO levels and COHb and bilirubin.
Takeuchi et al. (2000, 005675)	To examine the relationship between min ventilation and rate of COHb reduction during breathing 100% O_2 and during normocapnic hyperoxic hyperpnea.	Patients were exposed to 400-1,000 ppm CO, resulting in 10-12% COHb. The half-time of COHb reduction was 78 ± 24 min during 100% O_2 treatment and 31 ± 6 min during normocapnic hyperpnea with O_2 treatment.
Tarquini et al. (2009, 194117)	To measure plasma CO levels in patients with liver cirrhosis and portal hypertension.	Plasma CO was higher in ascetic patients than nonascitic patients and both were higher than healthy controls. HO activity was higher in cirrhotic patients than healthy subjects and highest in patients with ascites.
Terzano et al. (2009, 108046)	To investigate the effect of postural changes on gas exchange in patients with COPD and healthy subjects.	D_LCO increased in healthy individuals from upright to supine position and upright to prone position. D_LCO did not significantly change in COPD patients from upright to prone position. This is explained by homogeneous perfusion in healthy individuals and increased rigidity of lung capillaries due to COPD.
Tran et al. (2007, 194120)	To assess the correlation of COHb to severity of liver disease.	No correlation was found with the Model for End Stage Liver Disease score, Child Turcotte Pugh score, or other biochemical or clinical measures of disease severity, such as spleen size, bilirubin, disease duration, or AST/ALT. The mean COHb was 2.1%.
Vreman et al. (2005, 193786)	To develop a sensitive and reproducible method of CO quantification in rodent (mouse and rat) tissue pre- and postexposure in hopes of understanding endogenous CO production.	Tissues were sonicated mixed with sulfosalicylic acid for 30 min at 0°C and then liberated CO was analyzed by gas chromatograph. Blood contained the highest CO concentration. Lowest concentrations were found in brain, testes, intestine, and lung (endogenously).
Vreman et al. (2006, 098272)	To test a method of CO quantification in frozen postmortem human tissues from 3 determined categories of fatalities: trauma with no suspected CO exposure (controls), fire-related, and CO asphyxiation.	CO levels were analyzed in adipose, brain, muscle, heart, kidney, lung, spleen, and blood (ordered from approximate low to high tissue concentration). It was suggested that blood, muscle, brain, lung, and kidney are suitable for diagnosing death due to lethal CO exposure due to regression analysis against COHb values.

Reference	Purpose	Findings
Weaver et al. (2000, 016421)	To determine in COHb half-life is influenced by CO poisoning vs experimental CO exposure, loss of consciousness, concurrent tobacco smoking, or P_aO_2.	COHb t1/2 determined was 74 ± 25 min with a range from 26 to 148 min by a single exponential decrease function. This is shorter than most clinical studies and was inversely proportionate to P_aO_2, however, not influenced by age, gender, smoke inhalation, loss of consciousness, tobacco smoking, or method of O_2 treatment.
Whincup et al. (2006, 195129)	To report COHb levels from a population-based study in men aged 60-79 yr during the 20-yr follow-up of the British Regional Heart Study cohort.	Mean COHb: 0.46%; Median COHb: 0.5% 9.2% of men had COHb levels of 2.5% or greater (93% were smokers) 0.1% of men had COHb levels of 7.5% or greater Smoking is the highest influence on COHb levels; however, other factors independently related were season, region, gas cooking and central heating, and active smoking
Widdop (2002, 030493)	To review carbon monoxide analysis methods, including CO-oximeters and gas chromatography.	
Wu and Wang (2005, 180411)	To review the endogenous production of CO through HO, as well as discuss physiological roles for CO both toxic and therapeutic.	CO is produced endogenously by HO-1 and -2 and acts as a gasotransmitter, inducing cell signaling cascades. The review discusses possible roles for CO in the various organ systems and the potential pharmacological and therapeutic applications for CO.
Yamaya et al. (1998, 047525)	To determine whether upper respiratory tract infections increase exhaled CO concentrations.	Exhaled CO increased in patients at the time of upper respiratory tract infection symptoms but decreased to nonsmoking healthy control levels during recovery.
Yamaya et al. (2001, 180130)	To determine whether the level of CO is related to the severity of asthma.	Severe asthmatics exhaled more CO than nonsmoking controls. Exhaled CO concentrations in unstable severe asthmatics were higher than in stable severe asthmatics. Mild and moderate asthmatics did not differ from controls. Exhaled CO was correlated with FEV_1 in all asthmatics.
Yasuda et al. (2002, 035206)	To determine whether arterial COHb is increased in patients with inflammatory pulmonary diseases.	Arterial COHb concentrations are increased in patients with inflammatory pulmonary diseases, including exacerbated bronchial asthma (1.05%), pneumonia (1.08%), and idiopathic pulmonary fibrosis (1.03%) over controls (0.6%).
Yasuda et al. (2004, 191955)	To determine if COHb levels in the venous blood and arteriovenous COHb (a-vCOHb) differences are increased in patients with inflammatory pulmonary diseases compared to patients with extrapulmonary inflammation and control subjects.	Patients with inflammatory pulmonary diseases, including bronchial asthma and pneumonia, had a large a-vCOHb difference. Both arterial and venous blood COHb increased in patients with inflammatory pulmonary disease, such as bronchial asthma, pneumonia, pyelonephritis and active rheumatoid arthritis.
Yasuda et al. (2005, 102183)	To study the relationship between COHb and disease severity in patients with COPD.	COHb concentrations increased in patients with COPD at a stable condition over controls and patients with COPD with exacerbations were further increased.
Yerushalmi et al. (2009, 186711)	To evaluate the association of dose-dense chemotherapy in breast cancer patients with pulmonary dysfunction.	Patients receiving dose-dense chemotherapy for breast cancer had a significant reduction in D_LCO.
Zegdi et al. (2002, 037461)	To compare endogenous CO production in mechanically ventilated critically ill adult patients with and without severe sepsis.	CO production was higher in septic patients during the first 3 days of treatment compared to controls. Survivors of sepsis had a significantly higher CO production compared to nonsurvivors.

References

Aberg AM; Sojka BN; Winsö O; Abrahamsson P; Johansson G; Larsson JE (2009). Carbon monoxide concentration in donated blood: Relation to cigarette smoking and other sources. Transfusion, 49: 347-353. 194082

Abram SR; Hodnett BL; Summers RL; Coleman TG; Hester RL (2007). Quantitative circulatory physiology: An integrative mathematical model of human physiology for medical education. Adv Physiol Educ, 31: 202-210. 193859

Adir Y; Merdler A; Haim SB; Front A; Harduf R; Bitterman H (1999). Effects of exposure to low concentrations of carbon monoxide on exercise performance and myocardial perfusion in young healthy men. Occup Environ Med, 56: 535-538. 001026

Alcantara RE; Xu C; Spiro TG; Guallar V (2007). A quantum-chemical picture of hemoglobin affinity. PNAS, 104: 18451-18455. 193867

Andersson JA; Uddman R; Cardell L-O (2000). Carbon monoxide is endogenously produced in the human nose and paranasal sinuses. J Allergy Clin Immunol, 105: 269-273. 011836

Arora M; Chandra J; Suri JC; Narayan S; Dutta AK (2001). Pulmonary function tests in beta thalassemia. Indian J Pediatr, 68: 239-242. 186713

Benignus VA; Coleman T; Eklund CR; Kenyon EM (2006). A general physiological and toxicokinetic (GPAT) model for simulating complex toluene exposure scenarios in humans. Toxicol Mech Meth, 16: 27-36. 151344

Bos PM; Zeilmaker MJ; van Eijkeren JC (2006). Application of physiologically based pharmacokinetic modeling in setting acute exposure guideline levels for methylene chloride. Toxicol Sci, 91: 576-585. 194084

Bruce EN; Bruce MC (2003). A multicompartment model of carboxyhemoglobin and carboxymyoglobin responses to inhalation of carbon monoxide. J Appl Physiol, 95: 1235-1247. 193975

Bruce EN; Bruce MC; Erupaka K (2008). Prediction of the rate of uptake of carbon monoxide from blood by extravascular tissues. Respir Physiol Neurobiol, 161: 142-159. 193977

Bruce MC; Bruce EN (2006). Analysis of factors that influence rates of carbon monoxide uptake, distribution, and washout from blood and extravascular tissues using a multicompartment model. J Appl Physiol, 100: 1171-1180. 193980

Carraway MS; Ghio AJ; Carter JD; Piantadosi CA (2000). Expression of heme oxygenase-1 in the lung in chronic hypoxia. Am J Physiol, 278: L806-L812. 021096

Castillo A; Llapur CJ; Martinez T; Kisling J; Williams-Nkomo T; Coates C; Tepper RS (2006). Measurement of single breath-hold carbon monoxide diffusing capacity in healthy infants and toddlers. Pediatr Pulmonol, 41: 544-550 . 193234

Chakraborty S; Balakotaiah V; Bidani A (2004). Diffusing capacity reexamined: relative roles of diffusion and chemical reaction in red cell uptake of O2, CO, CO2, and NO. J Appl Physiol, 97: 2284-2302. 193759

Cronenberger C; Mould DR; Roethig HJ; Sarkar M (2008). Population pharmacokinetic analysis of carboxyhaemoglobin concentrations in adult cigarette smokers. Br J Clin Pharmacol, 65: 30-39. 194085

Cronje FJ; Carraway MS; Freiberger JJ; Suliman HB; Piantadosi CA (2004). Carbon monoxide actuates O2-limited heme degradation in the rat brain. Free Radic Biol Med, 37: 1802-1812. 180440

De las Heras D; Fernández J; Ginès P; Cárdenas A; Ortega R; Navasa M; Barberá JA; Calahorra B; Guevara M; Bataller R; Jiménez W; Arroyo V; Rodés J (2003). Increased carbon monoxide production in patients with cirrhosis with and without spontaneous bacterial peritonitis. Hepatology, 38: 452-459. 194087

Dutton SJ; Hannigan MP; Miller SL (2001). Indoor pollutant levels from the use of unvented natural gas fireplaces in Boulder, Colorado. J Air Waste Manag Assoc, 51: 1654-1661. 021307

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Ehlers M; Labaze G; Hanakova M; McCloskey D; Wilner G (2009). Alarming levels of carboxyhemoglobin in banked blood. J Cardiothorac Vasc Anesth, 23: 336-338 . 194089

Gosselin NH; Brunet RC; Carrier G (2009). Determination of carboxyhaemoglobin in humans following low-level exposures to carbon monoxide. Inhal Toxicol, 21: 1077-1091. 190946

Hampson NB; Weaver LK (2007). Carbon monoxide poisoning: a new incidence for an old disease. Undersea Hyperb Med, 34: 163-168. 190272

Hart CL; Smith GD; Hole DJ; Hawthorne VM (2006). Carboxyhaemoglobin concentration, smoking habit, and mortality in 25 years in the Renfrew/Paisley prospective cohort study. Heart, 92: 321-324. 194092

Hsia CC (2002). Recruitment of lung diffusing capacity: Update of concept and application. Chest, 122: 1774-1783. 193857

Johnson FK; Johnson RA; Durante W; Jackson KE; Stevenson BK; Peyton KJ (2006). Metabolic syndrome increases endogenous carbon monoxide production to promote hypertension and endothelial dysfunction in obese Zucker rats. Am J Physiol Regul Integr Comp Physiol, 290: 601-608. 193874

Lamberto C; Nunes H; Le Toumelin P; Duperron F; Valeyre D; Clerici C (2004). Membrane and capillary blood components of diffusion capacity of the lung for carbon monoxide in pulmonary sarcoidosis: relation to exercise gas exchange. Chest, 125: 2061-2068. 193845

Levesque B; Allaire S; Prud'homme H; Dupuis K; Bellemare D (2000). Air quality monitoring during indoor monster truck and car demolition shows. J Expo Sci Environ Epidemiol, 10: 58-65. 011886

Lim S; Groneberg D; Fischer A; Oates T; Caramori G; Mattos W; Adcock I; Barnes PJ; Chung KF (2000). Expression of heme oxygenase isoenzymes 1 and 2 in normal and asthmatic airways: Effect of inhaled corticosteroids. Am J Respir Crit Care Med, 162: 1912-1918. 126969

Mahoney JJ; Vreman HJ; Stevenson DK; Van Kessel AL (1993). Measurement of carboxyhemoglobin and total hemoglobin by five specialized spectrophotometers (CO-oximeters) in comparison with reference methods. Clin Chem, 39: 1693-1700. 013859

Marks GS; Vreman HJ; McLaughlin BE; Brien JF; Nakatsu K (2002). Measurement of endogenous carbon monoxide formation in biological systems. Antioxid Redox Signal, 4: 271-277. 030616

Marvisi M; Bassi E; Bonassi R; Civardi G; Delsignore R (2007). DLCO correlates with intestinal inflammation in ulcerative colitis, but albuminuria does not. Minerva Gastroenterol Dietol, 53: 321-7. 186702

Merx MW; Flogel U; Stumpe T; Godecke A; Decking UK; Schrader J (2001). Myoglobin facilitates oxygen diffusion. FASEB J, 15: 1077-1079. 002006

Monma M; Yamaya M; Sekizawa K; Ikeda K; Suzuki N; Kikuchi T; Takasaka T; Sasaki H (1999). Increased carbon monoxide in exhaled air of patients with seasonal allergic rhinitis. Clin Exp Allergy, 29: 1537-1541. 180426

Morimatsu H; Takahashi T; Maeshima K; Inoue K; Kawakami T; Shimizu H; Takeuchi M; Yokoyama M; Katayama H; Morita K (2006). Increased heme catabolism in critically ill patients: Correlation among exhaled carbon monoxide, arterial carboxyhemoglobin, and serum bilirubin IXalpha concentrations. Am J Physiol Lung Cell Mol Physiol, 290: L114-L119. 194097

Muchova L; Wong RJ; Hsu M; Morioka I; Vitek L; Zelenka J; Schröder H; Stevenson DK (2007). Statin treatment increases formation of carbon monoxide and bilirubin in mice: A novel mechanism of in vivo antioxidant protection. Can J Physiol Pharmacol, 85: 800-810. 194098

Neto CA; Yanagihara JI; Turri F (2008). A carbon monoxide transport model of the human respiratory system applied to urban atmosphere exposure analysis. J Braz Soc Mech Sci & Eng, 30: 253-260. 194672

Paredi P; Biernacki W; Invernizzi G; Kharitonov SA; Barnes PJ (1999). Exhaled carbon monoxide levels elevated in diabetes and correlated with glucose concentration in blood: A new test for monitoring the disease? Chest, 116: 1007-1011. 194102

Paredi P; Shah PL; Montuschi P; Sullivan P; Hodson ME; Kharitonov SA; Barnes PJ (1999). Increased carbon monoxide in exhaled air of patients with cystic fibrosis. Thorax, 54: 917-20. 118798

Pelham TW; Holt LE; Moss MA (2002). Exposure to carbon monoxide and nitrogen dioxide in enclosed ice arenas. Occup Environ Med, 59: 224-233. 025716

Pesola GR; Huggins G; Sherpa TY (2006). Abnormal predicted diffusion capacities in healthy Asians: an inequality with a solution. Respiration, 73: 799-807. 193855

Pesola GR; Sunmonu Y; Huggins G; Ford JG (2004). Measured diffusion capacity versus prediction equation estimates in blacks without lung disease. Respiration, 71: 484-492. 193842

Prommer N; Schmidt (2007). Loss of CO from the intravascular bed and its impact on the optimised CO-rebreathing method. Eur J Appl Physiol, 100: 383-391. 180421

Proudman SM; Stevens WM; Sahhar J; Celermajer D (2007). Pulmonary arterial hypertension in systemic sclerosis: the need for early detection and treatment. J Intern Med, 37: 485-94. 186705

Richardson RS; Noyszewski EA; Saltin B; Gonzalez-Alonso J (2002). Effect of mild carboxy-hemoglobin on exercising skeletal muscle: Intravascular and intracellular evidence. Am J Physiol, 283: R1131-R1139. 037513

Sakamaki F; Oya H; Nagaya N; Kyotani S; Satoh T; Nakanishi N (2002). Higher prevalence of obstructive airway disease in patients with thoracic or abdominal aortic aneurysm. J Vasc Surg, 36: 35-40. 186706

Schachter LM; Dixon J; Pierce RJ; O'Brien P (2003). Severe gastroesophageal reflux is associated with reduced carbon monoxide diffusing capacity. Chest, 123: 1932-8. 186707

Scharte M; Bone HG; Van Aken H; Meyer J (2000). Increased carbon monoxide in exhaled air of critically ill patients. Biochem Biophys Res Commun, 267: 423-426. 194112

Scharte M; von Ostrowski TA; Daudel F; Freise H; Van Aken H; Bone HG (2006). Endogenous carbon monoxide production correlates weakly with severity of acute illness. Eur J Anaesthesiol, 23: 117-122. 194115

Shimazu T (2001). Half-life of blood carboxyhemoglobin. Chest, 119: 661-663. 016331

Shimazu T; Ikeuchi H; Sugimoto H; Goodwin CW; Mason AD Jr; Pruitt BA Jr (2000). Half-life of blood carboxyhemoglobin after short-term and long-term exposure to carbon monoxide. J Trauma, 49: 126-131. 016420

Sylvester KP; Patey RA; Rafferty GF; Rees D; Thein SL; Greenough A (2005). Exhaled carbon monoxide levels in children with sickle cell disease. Eur J Pediatr, 164: 162-165. 191954

Takeuchi A; Vesely A; Rucker J; Sommer LZ; Tesler J; Lavine E; Slutsky AS; Maleck WA; Volgyesi G; Fedorko L; Iscoe S; Fisher JA (2000). A simple "new" method to accelerate clearance of carbon monoxide. Am J Respir Crit Care Med, 161: 1816-1819. 005675

Tarquini R; Masini E; La Villa G; Barletta G; Novelli M; Mastroianni R; Romanelli RG; Vizzutti F; Santosuosso U; Laffi G (2009). Increased plasma carbon monoxide in patients with viral cirrhosis and hyperdynamic circulation. Am J Gastroenterol, 104: 891-897. 194117

Terzano C; Conti V; Petroianni A; Ceccarelli D; De Vito C; Villari P (2009). Effect of Postural Variations on Carbon Monoxide Diffusing Capacity in Healthy Subjects and Patients with Chronic Obstructive Pulmonary Disease. Respiration, 77: 51-57. 108046

Tran TT; Martin P; Ly H; Balfe D; Mosenifar Z (2007). Carboxyhemoglobin and its correlation to disease severity in cirrhotics. J Clin Gastroenterol, 41: 211-215. 194120

Vreman HJ; Wong RJ; Kadotani T; Stevenson DK (2005). Determination of carbon monoxide (CO) in rodent tissue: effect of heme administration and environmental CO exposure. Anal Biochem, 341: 280-289. 193786

Vreman HJ; Wong RJ; Stevenson DK; Smialek JE; Fowler DR; Li L; Vigorito RD; Zielke HR (2006). Concentration of Carbon Monoxide (CO) in Postmortem Human Tissues: Effect of Environmental CO Exposure. J Forensic Sci, 51: 1182-1190. 098272

Weaver LK; Howe S; Hopkins R; Chan K (2000). Carboxyhemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. Chest, 117: 801-808. 016421

Whincup P; Papacosta O; Lennon L; Haines A (2006). Carboxyhaemoglobin levels and their determinants in older British men. BMC Public Health, 6: 189-197. 195129

Widdop B (2002). Analysis of carbon monoxide. Ann Clin Biochem, 39: 378-391. 030493

Wu L; Wang R (2005). Carbon monoxide: endogenous production, physiological functions, and pharmacological applications. Pharmacol Rev, 57: 585-630. 180411

Yamaya M; Hosoda M; Ishizuka S; Monma M; Matsui T; Suzuki T; Sekizawa K; Sasaki H (2001). Relation between exhaled carbon monoxide levels and clinical severity of asthma. Clin Exp Allergy, 31: 417-422. 180130

Yamaya M; Sekizawa K; Ishizuka S; Monma M; Mizuta K; Sasaki H (1998). Increased carbon monoxide in exhaled air of subjects with upper respiratory tract infections. Am J Respir Crit Care Med, 158: 311-314. 047525

Yasuda H; Sasaki T; Yamaya M; Ebihara S; Maruyama M; Kanda A; Sasaki H (2004). Increased arteriovenous carboxyhemoglobin differences in patients with inflammatory pulmonary diseases. Chest, 125: 2160-2168. 191955

Yasuda H; Yamaya M; Nakayama K; Sasaki H (2005). Blood carbon monoxide will increase from a decline in pulmonary function alone 7. Am J Respir Crit Care Med, 172: 1231-1232. 102183

Yasuda H; Yamaya M; Yanai M; Ohrui T; Sasaki H (2002). Increased blood carboxyhaemoglobin concentrations in inflammatory pulmonary diseases. Thorax, 57: 779-783. 035206

Yerushalmi R; Kramer MR; Rizel S; Sulkes A; Gelmon K; Granot T; Neiman V; Stemmer SM (2009). Decline in pulmonary function in patients with breast cancer receiving dose-dense chemotherapy: a prospective study. Ann Oncol, 20: 437-440. 186711

Zegdi R; Perrin D; Burdin M; Boiteau R; Tenaillon A (2002). Increased endogenous carbon monoxide production in severe sepsis. Intensive Care Med, 28: 793-796. 037461

Annex C. Epidemiology Studies

Table C-1. Studies of CO exposure and cardiovascular morbidity.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
CHANGES IN HEART RATE AND HEART RATE VARIABILITY			
Author: Chan et al. (2005, 088988) **Period of Study:** December 2001-February 2002 **Location:** Taipei, Taiwan	**Health Outcome:** Various measures of HRV via ambulatory ECG (Holter system) **Study Design:** Panel **Statistical Analyses:** Linear regression (mixed effects) **Age Groups Analyzed:** 40-75 yr **Sample Description:** 83 patients from the National Taiwan University Hospital	**Averaging Time:** 1−h ma **Mean (SD) unit:** 1.1 ppm **Range (Min, Max):** 0.1, 7.7 **Copollutant**: NR	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] **Lags examined (-h ma):** 1, 2, 3, 4, 5, 6, 7, 8 CO had no statistically significant effect on SDNN, rMSSD, LF, HF.
Author: Chuang (2008, 155731) **Period of Study:** NR **Location: Boston, MA**	**Health Outcome:** HRV (changes in ST-segment) **Study Design:** Panel **Statistical Analyses:** Linear additive models; Additive mixed logistic regression models **Age Groups Analyzed:** 43-75 **Sample Description:** 48 patients with documented CAD who had undergone percutaneous coronary intervention for acute coronary syndrome (acute MI or unstable angina pectoris) or who had worsened CAD	**Averaging Time:** 12 h, 24 h **Mean (SD) unit:** 12 h: 0.48ppm, 24 h: 0.46ppm **Range (Min, Max):** 12-h: 25th percentile- 0.35, 75th percentile- 0.62, Max- 1.88; 24 h: 25th percentile- 0.37, 75th percentile- 0.62, Max- 1.56 **Copollutant**: NR	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] **Lags examined:** NR **Estimated RR for ST-segment depression ≥0.1 mm (ppm): 12-h:** 0.70 (0.58-0.84) **24 h:** 0.84 (0.68-1.03) **Estimated ST-segment change, mm (ppm):** 12-h mean: 0.013 (0.003-0.024) **24 h mean:** 0.007 (-0.004-0.019) CO not significantly associated with ST-segment depression.
Author: Dales et al. (2004, 099036) **Period of Study:** NR **Location:** Toronto, Canada.	**Health Outcome:** Various measures of HRV via Holter system **Study Design:** Panel **Statistical Analyses:** Linear regression (mixed effects) **Age Groups Analyzed:** 51-88 yr (mean 65 yr) **Sample Description:** 36 subjects with pre-existing CAD	**Averaging Time:** 24 h **Mean (SD) unit:** 2.40 ppm (95th percentile) Personal monitoring **Range (Min, Max):**0.4, 16.5 **Copollutant: correlation** $PM_{2.5}$: r = 0.17	**Increment:** NR **Regression co-efficient** [Lower CI, Upper CI] **Lags examined:** NR CO had no statistically significant effect on LF, HF, HFLFR, SDNN among those taking beta-blockers, whereas CO had a positive effect on SDNN among those not taking beta-blockers. Slope = 0.0111 (0.002-0.020, p = 0.02)

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Gold et al. (2000, 011432) **Period of Study:** June-September 1997 **Location:** Boston, MA	**Health Outcome (ICD9 or ICD10):** Heart rate and various measures of HRV via Holter system **Study Design:** Panel/Cohort **Statistical Analyses:** Linear regression (fixed effects/random effects) **Age Groups Analyzed:** 53-87 yr **Sample Description:** 21 active Boston residents observed up to 12 times.	**Averaging Time:** 24 h **Mean (SD) unit:** 0.47 ppm **Range (Min, Max):** 0.12, 0.82 **Copollutant:** NR	**Increment:** 0.6 ppm **% Change [Lower CI, Upper CI]** **Lags examined:** 24 h No significant effect with CO (no results recorded)
Author: Gold et al. (2005, 087558) **Period of Study:** June-September 1999 **Location:** Boston, MA	**Health Outcome:** ST- segment. **Study Design:** Panel **Statistical Analyses:** Linear regression (mixed models) **Age Groups Analyzed:** 61-88 yr **Sample Description:** 24 active Boston residents each observed up to 12 times.	**Averaging Time:** 1 h, 24 h **Mean (SD) unit:** NR **Range (Min, Max):** (ppm) (personal monitoring) 10th = 0.20 90th = 1.08 **Copollutant:** NR	**Increment:** NR **RR Estimate [Lower CI, Upper CI]** **Lags examined:** 1 24 h Although CO was associated with ST-segment depression in single pollutant models, this result did not persist in multiple pollutant models.
Author: Goldberg et al. (2008, 180380) **Period of Study:** July 2002-October 2003 **Location:** Montreal, Quebec	**Health Outcome:** Oxygen saturation and heart rate **Study Design:** Panel **Statistical Analyses:** Mixed regression models **Age Groups Analyzed:** 50-85 yr **Sample Description:** 31 subjects with CHF and limits in physical functioning in the Heart Failure and Heart Transplant Center at the McGill University Health Center	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** $PM_{2.5}$: r = 0.72 NO_2: r = 0.84 SO_2 and NO_2: r = 0.43	**Increment:** NR **Adjusted Mean Difference [Lower CI, Upper CI]** **Lags examined:** 0, 1, 2 **Oxygen Saturation:** Lag 0: 0.004 ppm (-0.060, 0.067) Lag 1: -0.001 ppm (-0.066, 0.065) 3-day: -0.005 ppm (-0.098. 0.088) **Pulse Rate:** Lag 0: 0.011 ppm (-0.290, 0.312) Lag 1: 0.227 ppm (-0.080,0.535) 3-day: 0.245 ppm (-0.209, 0.700)
Author: Holguin et al. (2003, 057326) **Period of Study:** February-April 2000 **Location:** Mexico City, Mexico	**Health Outcome:** Various measures of HRV via ECG **Study Design:** Panel **Statistical Analyses:** GEE **Age Groups Analyzed:** 60-96 yr (mean age 79 yr) **Sample Description:** 34 patients who were permanent residents of a nursing home in the Northeast metropolitan area.	**Averaging Time:** 24 h **Mean (SD) unit:** 3.3 ppm **Range (Min, Max):** 1.8, 4.8 **Copollutant:** NR	**Increment:** 10 ppm **Regression Coefficients [Lower CI, Upper CI]** **Lags examined:** 0 **Lag 0:** HF: 0.003 (-0.004 to 0.001) LF: 0.001 (-0.006 to 0.008) LF/HF: 0.001 (-0.005 to 0.002)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Ibald-Mulli et al. (2004, 087415) **Period of Study:** 1998-1999 **Location:** Helsinki, Finland Erfurt, Germany Amsterdam, Netherlands	**Health Outcome:** BP and HR via ECG **Study Design:** Panel **Statistical Analyses:** Linear regression **Age Groups Analyzed:** ≥ 50 yr **Sample Description:** 131 nonsmokers with coronary heart disease	**Averaging Time:** 24 h **Mean (SD) unit:** Amsterdam: 0.6 mg/m^3 Erfurt: 0.4 mg/m^3 Helsinki: 0.4 mg/m^3 **Range (Min, Max):** Amsterdam: 0.4, 1.6 Erfurt: 0.1, 2.5 Helsinki: 0.1, 1.0 **Copollutant:** Amsterdam $PM_{2.5}$: r = 0.58 µg/m^3 NO_2: r = 0.76 µg/m^3 SO_2: r = 0.50 mg/m^3 UFP: r = 0.22 n/cm^3 ACP: r = 0.60 n/cm^3 Erfurt $PM_{2.5}$: r = 0.77 µg/m^3 NO_2: r = 0.86 µg/m^3 SO_2: r = 0.68 mg/m^3 UFP: r = 0.72 n/cm^3 ACP: r = 0.78 n/cm^3 Helsinki $PM_{2.5}$: r = 0.40 µg/m^3 NO_2: r = 0.32 µg/m^3 SO_2: r = 0.19 mg/m^3 UFP: r = 0.35 n/cm^3 ACP: r = 0.51 n/cm^3	**Increment:** NR **RR Estimate [Lower CI, Upper CI]** **Lags examined:** 0, 1, 2, 3 Results presented graphically
Author: Liao et al. (2004, 056590) **Period of Study:** 1996-1998 **Location:** Forsyth County, NC; Selected suburbs of Minneapolis, MN; Jackson, MI	**Health Outcome:** Heart rate & various rates of HRV. **Study Design:** Cohort **Statistical Analyses:** Linear regression **Age Groups Analyzed:** 45-64 yr (mean 62 yr) **Sample Description:** 6,784 study subjects from the atherosclerosis risk in communities study	**Averaging Time:** 24 h **Mean (SD) unit:** 0.65 ppm (0.44) **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** 0.44 ppm **Regression coefficients Lags examined:** 1 **Lag 1:** HF (log transformed): -0.033 LF (log transformed): 0.006 SDNN: -0.274 Heart rate (bpm): 0.404* Confidence intervals: not recorded *p < 0.05

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Min (2009, 199514) **Period of Study:** December 2003 – January 2004 **Location: Tae-in island community in South Korea**	**Health Outcome:** HRV **Study Design:** Panel **Statistical Analyses:** Time-lag model **Age Groups Analyzed:** 20-87 **Sample Description:** 986 subjects, 367 with metabolic syndrome (MetS), 619 without MetS	**Averaging Time:** 8 h **Mean (SD) unit:** 0.454 ppm (0.560) **Range (Min, Max):** 0.100, 7.200 ppm **Copollutant:** PM_{10}	**Increment:** NR **Estimated % Increase in subjects with MetS** [Lower CI, Upper CI] **Lags examined:** 0-1, 1-2, 2-3, 3-4, 4-5, 5-6 Single pollutant: Lag 0-1: Log(SDNN): -0.29 (-0.59, 0.00), p < 0.1 Log(LF): -0.34 (-1.02, 0.33) Log(HF): -0.67 (-1.41, 0.08), p < 0.1 Lag 1-2: Log(SDNN): -0.45 (-0.81, -0.10), p < 0.05 Log(LF): -0.65 (-1.46, 0.17) Log(HF): -1.04 (-1.94, -0.14), p < 0.05 Lag 2-3: Log(SDNN): -0.28 (-0.57, 0.02), p < 0.1 Log(LF): -0.19 (-0.87, 0.48) Log(HF): -0.82 (-1.57, -0.07), p < 0.05 Lag 3-4: Log(SDNN): -0.18 (-0.47, 0.10) Log(LF): -0.14 (-0.80, 0.51) Log(HF): -0.46 (-1.19, 0.27) Lag 4-5: Log(SDNN): -0.20 (-0.49, 0.09) Log(LF): -0.36 (-1.04, 0.31) Log(HF): -0.42 (-1.17, 0.33) Lag 5-6: Log(SDNN): 0.13 (-0.18, 0.44) Log(LF): 0.50 (-0.21, 1.20) Log(HF): -0.03 (-0.81, 0.76) Co-pollutant (with PM_{10}): Lag 0-1: Log(SDNN): -0.25 (-0.56, 0.05) Log(LF): -0.35 (-1.04, 0.31) Log(HF): -0.67 (-1.44, 0.10), p<0.1 Lag 1-2: Log(SDNN): -0.48 (-0.88, -0.09), p<0.05; Log(LF): -0.72 (-1.63, 0.18); Log(HF): -1.09 (-2.09, -0.09), p<0.05 Lag 2-3: Log(SDNN): -0.35 (-0.67, -0.03), p < 0.05 Log(LF): -0.17 (-0.90, 0.56) Log(HF): -0.78 (-1.59, 0.03), p < 0.1 Lag 3-4: Log(SDNN): -0.22 (-0.55, 0.11) Log(LF): -0.11 (-0.86, 0.63) Log(HF): -0.34 (-1.17, 0.49) Lag 4-5: Log(SDNN): -0.18 (-0.48, 0.12); Log(LF): -0.21 (-0.89, 0.48); Log(HF): -0.37 (-1.14, 0.40) Lag 5-6: Log(SDNN): 0.17 (-0.14, 0.49) Log(LF): 0.54 (-0.18, 1.25) Log(HF): 0.00 (-0.80, 0.80) No significant results for subjects without MetS.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Park et al. (2005, 057331) **Period of Study:** 2000-2003 **Location:** Boston, MA	**Health Outcome:** Various measures of HRV via ECG **Study Design:** Panel/Cohort **Statistical Analyses:** Linear regression **Age Groups Analyzed:** 21-81 yr **Sample Description:** 497 men from the normative aging study in Greater Boston area	**Averaging Time:** 24 h **Mean (SD) unit:** 0.50 ppm **Range (Min, Max):** 0.13, 1.8 **Copollutant:** NR	**Increment:** 0.24 ppm **% Change in HRV [Lower CI, Upper CI]** **Lags examined:** 4-h ma, 24-h ma, 48-h ma Lag 4-h ma: SDNN (Log10): 2.0 (-2.9 to 7.3) HF (Log10): 8.8 (-4.6 to 24.1) LF(Log10): 3.2 (-7.0 to 14.6) LF:HF(Log10): -5.1 (-13.5 to 4.1) Lag 24-h ma: SDNN (Log10): -2.2 (-7.7 to 3.6) HF (Log10): -13.2 (-25.4 to 1.0) LF(Log10): -0.6 (-11.9 to 12.1) LF:HF(Log10): 14.5 (2.9-27.5) Lag 48-h ma: SDNN(Log10): -3.4 (-10.2 to 3.9) HF (Log10): -13.8 (-.28.9 to 4.4) LF (Log10): -2.4 (-16.2 to 13.6) LF:HF (Log10): 13.2 (-1.1 to 29.6)
Author: Peters et al. (1999, 011554) **Period of Study:** 1984-1985 **Location:** Augsburg, Germany	**Health Outcome:** Heart rate **Study Design:** Cohort **Statistical Analyses:** Linear regression (GEE) **Age Groups Analyzed:** 25-64 yr **Sample Description:** 2681 men and women who participated in the MONICA study	**Averaging Time:** 24 h **Mean (SD) unit:** During air pollution episode: 4.54 mg/m^3 Outside air pollution episode: 4.51 mg/m^3 **Range (Min, Max):** During air pollution episode: 2.39, 6.85 Outside air pollution episode: 0.91, 11.51 **Copollutant:** NR	**Increment:** 6.6 mg/m^3 **Mean Change in Heart Rate (beats/min) [Lower CI, Upper CI]** **Lags examined:** 0, 5-day avg All Lag 0: 0.97 (0.02-1.91) Lag 5-day avg: 0.70 (-0.09 to 1.48) Men Lag 0: 0.95 (-0.37 to 2.27) Lag 5-day avg: 0.91 (-0.25 to 2.07) Women Lag 0: 0.98 (-0.37 to 2.34) Lag 5-day avg: 0.52 (-0.55 to 1.59)
Author: Riojas-Rodriguez et al. (2006, 156913) **Period of Study:** December 2001-April 2002 **Location:** Mexico City, Mexico	**Health Outcome:** Various measures of HRV via Holter system **Study Design:** Panel **Statistical Analyses:** Linear regression (mixed effects models) **Age Groups Analyzed:** 25-76 yr (mean 55 yr) **Sample Description:** 30 patients from the Outpatient Clinic of the National Institute of Cardiology of Mexico	**Averaging Time:** 24 h **Mean (SD) unit:** 2.9 ppm (personal monitor) **Range (Min, Max):** 0.1, 18.0 **Copollutant:** NR	**Increment:** 1 ppm **Regression Coefficients [Lower CI, Upper CI]** **Lags examined (per min):** 5, 10 Lag 5 min: HF: -0.006 (-0.023 to 0.010) LF: -0.024 (-0.041 to -0.007) VLF: -0.034 (-0.061 to -0.007) Notes: VLF = Very low frequency
Author: Schwartz et al. (2005, 074317) **Period of Study:** 1999 **Location:** Boston, MA	**Health Outcome:** Measures of HRV via Holter system **Study Design:** Panel **Statistical Analyses:** Linear regression (hierarchical model) **Age Groups Analyzed:** 61-89 yr **Sample Description:** 28 subjects living at or near an apartment complex located on the same street as the Harvard School of Public Health	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** ppm 25th = 0.38; 75th = 0.54 **Copollutant:** correlation $PM_{2.5}$: r = 0.61 NO_2: r = 0.55 SO_2: r = -0.18 O_3: r = 0.21	**Increment:** 0.16 ppm **% Change in HRV [Lower CI, Upper CI]** **Lags examined:** 24 h, 1 h Lag 1 h: SDNN: -2.6 (-5.6 to 0.5); rMSSD: -3.9 (-10.6 to 3.3); PNN50: -3.5 (-13.7 to 8.0); LF:HF: 4.5 (-1.2 to10.5) Lag 24 h: SDNN: -4.2 (-0.6 to -7.7); rMSSD: -10.2 (-2.4 to -17.4); PNN50: -14.8 (-3.0 to -25.2); LF:HF: 6.2 (-0.6 to 13.4)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Tarkiainen et al. (2003, 053625) **Period of Study:** October 1997-May 1998 **Location:** Kuopio, Finland	**Health Outcome:** Various measures of HRV via Ambulatory ECG (Holter system) **Study Design:** Panel **Statistical Analyses**: ANOVA for repeated errors (GLM) **Age Groups Analyzed:** 55-68 yr **Sample Description:** 6 male patients with angiographically- verified CAD	**Averaging Time:** 24 h **Mean (SD) unit:** 4.6 ppm (max of CO episode) (personal monitoring) **Range (Min, Max):** 0.5, 27.4 (max of CO episode) **Copollutant:** NR	**Increment:** NR **RR Estimate [Lower CI, Upper CI]** **Lags examined:** 5 min prior to CO episode, 5 min during CO episode CO had no statically significant effect on NN, SDNN or rMSSD. However, during high CO exposure (>2.7 ppm), CO was associated with an increase in rMSSD of 2.4ms (p=0.034).
Author: Timonen et al. (2006, 088747) **Period of Study:** 1998-1999 **Location:** 3 Cities in Europe: Amsterdam, Netherlands; Erfert, Germany; Helsinki, Finland	**Health Outcome:** Stable CAD: Various measures of HRV via ambulatory ECG (Holter system) **Study Design: Panel** **Statistical Analyses:** Linear regression (mixed model) **Age Groups Analyzed:** Mean age across 3 cities; 64-71 yr. **Sample Description:** 131 subjects with stable CAD followed for 6 mo with biweekly clinical visits.	**Averaging Time:** 24 h **Mean (SD) unit:** Amsterdam: 0.6 mg/m^3 Erfert: 0.4 mg/m^3 Helsinki: 0.4 mg/m^3 **Range (Min, Max):** Amsterdam: 0.4, 1.6 Erfert: 0.1, 2.5 Helsinki: 0.1, 1.0 **Copollutant:** correlation Amsterdam: $PM_{2.5}$: r = 0.58 NO_2: r = 0.76 Erfert: PM_{10}: r = 0.77 NO_2: r = 0.86 Helsinki: PM_{10}: r = 0.40 NO_2: r = 0.32	**Increment:** 1 mg/m^3 **Regression co-efficient [Lower CI, Upper CI]** **Lags examined (days):** 0, 1, 2, 3, 5-day avg SDNN: Lag 0: -1.21 (-4.44 to 2.03); Lag 1: -1.71 (-6.05 to 2.63); Lag 2: -5.69 (-10.7 to -0.72); Lag 3: 0.66 (-3.83 to 5.15); 5-day avg: -3.60 (-9.88 to 2.68) HF: Lag 0: 5.0 (-15.1 to 25.1); Lag 1: -2.0 (-37.1 to 33.1); Lag 2: -30.7 (-59.8 to -1.5); Lag 3: -9.3 (-35.8 to -17.3); 5-day avg: -15.2 (-53.0 to 22.6) LF/HF: Lag 0: -3.6 (-21.8 to 14.5); Lag 1: -28.6 (-52.0 to -5.3); Lag 2: -10.1 (-36.9 to 16.7); Lag 3: 7.7 (-16.5 to 31.9); 5-day avg: -16.9 (-51.2 to 17.3)
Author: Wheeler et al. (2006, 088453) **Period of Study:** 1999-2000 **Location:** Atlanta, GA	**Health Outcome:** Various measures of HRV via Holter system **Study Design:** Panel **Statistical Analyses:** Linear regression (mixed effects models) **Age Groups Analyzed:** Mean 65 yr;IQR 55-73 yr **Sample Description:** 18 subjects with COPD and 12 subjects with recent MI.	**Averaging Time:** 1 h **Mean (SD) unit:** 362.0 ppb **Range (Min, Max):** 25th = 221.5; 75th = 398.1 **Copollutant:** correlation $PM_{2.5}$: r = 0.43	**Increment:** NR **RR Estimate [Lower CI, Upper CI] ; lag:** **Lags examined (h ma):** 1, 4, 24 No CO results reported.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
ONSET OF CARDIAC ARRHYTHMIA			
Author: Berger et al. (2006, 098702) **Period of Study:** October 2000-April 2001 **Location:** Erfurt, Germany	**Health Outcome:** Runs of supraventricular and ventricular tachycardia recorded via 24-h ECG. **Study Design:** Panel **Statistical Analyses:** Poisson regression (GAM) linear regression **Age Groups Analyzed:** 52-76 yr (mean 76 yr) **Sample Description:** 57 men with CHD	**Averaging Time:** 24 h **Mean (SD) unit:** 0.52 mg/m^3 **Range (Min, Max):** 0.11, 1.93 **Copollutant: correlation** NR	**Increment:** All: 0.27 mg/m^3 5-day avg: 0.22 mg/m^3 **RR Estimate [Lower CI, Upper CI]** **Lags examined (h):** 0, 0-23, 24-47, 48-71, 72-95, 5-day avg Supraventricular extrasystoles: Lag 0: 1.18 (1.00-1.38) Lag 0-23: 1.16 (1.02-1.31); Lag 24-47: 1.13 (1.00-1.28); Lag 48-71: 1.18 (1.03-1.36); Lag 72-95: 1.08 (0.98-1.20); 5-day avg: 1.18 (1.04-1.35) Mean % Change [Lower CI, Upper CI] Hourly Lags examined: 0, 0-23, 24-47, 48-71, 72-95, 5-day avg Ventricular extrasystoles: Lag 0: 0.0 (-4.1 to 4.4); Lag 0-23: 1.1 (-3.3 to 5.7); Lag 24-47: 1.9 (-2.6 to 6.6); Lag 48-71: 4.2 (-0.3 to 8.9); Lag 72-95: 2.7 (-1.3 to 6.9); 5-day avg: 3.0 (-1.8 to 8.0)
Author: Dockery et al. (2005, 078995) **Period of Study:** 1995-2002 **Location:** Boston, MA	**Health Outcome:** Tachyarrhythmias: **Study Design:** Panel **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** 19-90 yr; mean 64 yr **Sample Description:** 203 cardiac patients with ICDs within 40km of air monitoring site at Harvard School of Public Health, Boston	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** 25th = 0.53; 75th = 1.02 **Copollutant:** NR	**Increment:** 0.48 ppm **OR for Ventricular Arrhythmia [Lower CI, Upper CI]** **Lags examined (days):** 0, 1, 2, 3 Lag 2-day ma: 1.14 (0.95-1.29) Among those who had an arrhythmia: within 3 days: 1.65 (1.17-2.33) later than 3 days: 1.04 (0.83-1.29)
Author: Metzger et al. (2007, 092856) **Period of Study:** 1993-2002 **Location:** Atlanta, GA	**Health Outcome:** Cardiac arrhythmia, ICD, ventricular tachyarrhythmia **Study Design:** Panel **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** 15-88 yr **Sample Description:** 518 patients with ICDs with at least one ventricular tachyarrhythmic event	**Averaging Time:** 1 h **Mean (SD) unit:** 1.7 ppm **Range (Min, Max):** 0.1, 7.7 **Copollutant:** NR	**Increment**: 1 ppm O**R for Tachyarrhythmic event [Lower CI, Upper CI]** **Lags examined (days):** 0 Results for all events Lag 0: 0.999 (0.970-1.028) Events resulting in cardiac pacing or defibrillation Lag 0: 1.008 (0.964-1.054) Events resulting defibrillation Lag 0: 1.012 (0.925-1.10.7)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Peters et al. (2000, 011347) **Period of Study:** 1995-1997 **Location:** Eastern Massachusetts	**Health Outcome:** Defibrillated discharges for ventricular tachycardia or fibrillation **Study Design:** Panel **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** Mean 62 yr **Sample Description:** 100 patients with ICDs	**Averaging Time:** 24 h **Mean (SD) unit:** 0.58 ppm **Range (Min, Max):** 25th = 0.43; 75th = 0.66 **Copollutant: correlation** PM_{10}: r = 0.51 $PM_{2.5}$: r = 0.56 NO_2: r = 0.71 SO_2: r = 0.41 O_3: r = -0.40	**Increment:** 0.65 ppm (Lags 0, 1, 2, 3); 0.42 ppm (Lag 5-day mean) **OR for Defibrillated Discharge [Lower CI, Upper CI]** Lags examined (days): 0, 1, 2 ,3, 5-day mean At least one discharge: Lag 0: 1.07 (0.62-1.86); Lag 1: 1.06 (0.61-1.85); Lag 2: 1.05 (0.62-1.77); Lag 3: 0.09 (0.65-1.83); Lag 5-day mean: 1.23 (0.71- 2.12) At least 10 discharges: Lag 0: 1.12 (0.54-2.32); Lag 1: 1.13 (0.54-2.33); Lag 2: 1.62 (0.85-3.09); Lag 3: 1.98 (1.05-3.72); Lag 5-day mean: 1.94 (1.01-.75)
Author: Rich et al. (2004, 055631) **Period of Study:** February-December 2000 **Location:** Vancouver, Canada	**Health Outcome:** Cardiac arrhythmia via patients ICD **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 15-85 yr **Sample Description:** 34 patients who experienced at least 1 ICD discharge (8,201 person days)	**Averaging Time:** 24 h **Mean (SD) unit:** 553.8 ppb **Range (Min, Max):** IQR: 162.7 **Copollutant: correlation** PM_{10}: r = 0.40 SO_2: r =0.75 NO_2: r =0.68 O_3: r = -0.56	**Increment: NR** **RR Estimate [Lower CI, Upper CI]** **Lags examined (days):** 0, 1, 2, 3 No significant effect (results not reported in table).
Author: Rich et al. (2005, 079620) **Period of Study:** 1995-1999 **Location:** Boston, MA	**Health Outcome:** Ventricular arrhythmias via ICD **Study Design:** Panel/Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 203 patients with implanted ICD at the New England Medical Center	**Averaging Time:** 1 h and 24 h **Mean (SD) unit:** NR **Range (percentiles):** 1 h: 25th = 0.46 75th = 1.04 24 h: 25th = 0.52 75th = 1.03 **Copollutant:** NR	**Increment:** 0.56 ppm; 0.54; 0.51; 0.49 respectively for results shown below **OR Estimate [Lower CI, Upper CI]** Ventricular arrythmia Hours prior to event: 0-2: 1.01 (0.87-1.18) 0-6: 1.00 (0.85-1.17) 0-23: 1.03 (0.84-1.25) 0-47: 1.11 (0.88-1.40)
Author: Rich et al. (2006, 089814) **Period of Study:** 2001 & 2002 **Location:** St. Louis, MO	**Health Outcome:** Ventricular arrhythmia **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 60 subjects with at least 1 ICD recorded arrhythmia who lived within 40 km of St. Louis – Midwest supersite.	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** 25th = 0.4; 75th = 0.6 **Copollutant:** NR	**Increment:** 0.2 ppm **OR for Ventricular Arrhythmia [Lower CI, Upper CI]** **Lags examined:** 0 to 23-h ma: 0- to 23-h ma: 0.99 (0.80-1.21)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Rich et al. (2006, 088427) **Period of Study:** 1995-1999 **Location:** Boston, MA	**Health Outcome:** ICD episode of atrial fibrillation **Study Design:** Panel/case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 203 patients with ICDs at the New England Medical Center	**Averaging Time:** 1 h and 24 h **Mean (SD) unit:** NR **Range (Min, Max):** 1 h: 25th = 0.46; 75th = 1.04 24 h: 25th = 0.52; 75th = 1.03 **Copollutant:** NR	**Increment:** Lag (hrs) 0: 0.58 ppm Lag (hrs) 0-23: 0.51 ppm **OR for episode of atrial fibrillation [Lower CI, Upper CI]** Lags (h): 0, 0-23 Lag 0: 0.87 (0.56-1.37) Lag 0-23: 0.71 (0.39-1.28)
Author: Sari et al. (2008, 190315) **Period of Study:** June 2007 **Location:** Gaziantep, Turkey	**Health Outcome:** P-wave dispersion (predictors of atrial fibrillation, ventricular arrhythmias and sudden death) via ECG **Study Design:** Case control **Statistical Analyses:** Pearson correlation analysis **Age Groups Analyzed:** Barbecue workers mean age: 33.66 ± 9.43 yr Control group mean age: 35.15 ± 6.78 yr **Sample Description:** 48 healthy males working at various indoor barbecue restaurants for at least 3 yr (avg:15.6 ± 7.1 yr), 51 age-matched healthy men for control group	**Averaging Time:** NR **Mean (SD) unit:** COHb% Indoor barbecue workers: 6.48% ± 1.43 **Control Group:** 2.19% ± 1.30 **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR Correlation coefficient for COHb [p-value] **Lags examined:** NR Pmin: -0.132 (0.245) Pmax: 0.215 (0.057) Pd: 0.315 (0.005) QTmin: 0.080 (0.454) QTmax: 0.402 (<0.001) QTd: 0.573 (<0.001) cQTd: 0.615 (<0.001)
Author: Sarnat et al. (2006, 090489) **Period of Study:** 24 wk during the summer and fall of 2000 **Location:** Steubenville, OH	**Health Outcome:** Arrhythmia via ECG measurements **Study Design:** Panel **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** 53-90 yr (mean age 71) **Sample Description:** 32 nonsmoking older adults	**Averaging Time:** 24 h **Mean (SD) unit:** 0.02 ppm **Range (Min, Max):** -0.1, 1.5 **Copollutant:** correlation $PM_{2.5}$: r = 0.45 SO_2: r = 0.62 NO_2: r = 0.66 O_3: r = -0.37	**Increment:** 0.2 ppm **RR Estimate** [Lower CI, Upper CI] ; **lag:** **Lags examined (days):** 1, 2, 3, 4, 5, 5-day ma Lag 5-day ma: Supraventricular ectopy SVE: 0.99 (0.76-1.29) Ventricular ectopy VE: 1.05 (0.75-1.46)
Author: Vedal et al. (2004, 055630) **Period of Study:** 1997-2000 **Location:** Vancouver, Canada	**Health Outcome:** Cardiac arrythmia via patients with ICD **Study Design:** Panel **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** Range from 12-77 yr (mean age 53 yr) **Sample Description:** 50 patients who experienced 1 or more arrhythmia event during the 4yr	**Averaging Time:** 24 h **Mean (SD) unit:** 0.6 ppm **Range (Min, Max):** 0.3, 1.6 **Copollutant:** correlation PM_{10}: r = 0.43 SO_2: r = 0.62 NO_2: r = 0.74 O_3: r = -0.52	**Increment:** 0.2 ppm **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3 No significant effect for CO (results shown in plots)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
CARDIAC ARREST			
Author: Levy et al. (2001, 017171) **Period of Study:** 1988-1994 **Location:** Seattle, WA	**Health Outcome:** Out-of-hospital primary cardiac arrest **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 25-75 yr Sample Description: 362 cases	**Averaging Time:** 24 h **Mean (SD) unit:** 1.79 ppm **Range (Min, Max):** 0.52, 5.92 **Copollutant:** correlation PM_{10}: r = 0.81 SO_2: r = 0.29	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1 Lag 1: 0.99 (0.83-1.18)
Author: Sullivan et al. (2003, 043156) **Period of Study:** 1985-1994 **Location:** Washington State	**Health Outcome:** Out-of-Hospital cardiac arrest **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 1,542 members of a large health maintenance organization	**Averaging Time:** 24 h **Mean (SD) unit:** 1.92 ppm **Range (Min, Max):** 0.52, 7.21 **Copollutant:** NR	**Increment:** 1.02 ppm **OR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2 Lag 0: 0.95 (0.85-1.05) Lag 1: 0.97 (0.87-1.08) Lag 2: 0.99 (0.89-1.11)
MYOCARDIAL INFARCTION			
Author: Peters et al. (2001, 016546) **Period of Study:** 1995-1996 **Location:** Boston, MA	**Health Outcome:** Onset of MI **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 772 participants	**Averaging Time:** 24 h **Mean (SD) unit:** 1.09 **Range (percentiles):** ppm 5th = 0.49 95th = 1.78 **Copollutant:** NR	**Increment:** 2 H-1 ppm; 24 h – 0.6 ppm **OR Estimate** [Lower CI, Upper CI] **Onset of MI:** 2-h prior: 1.22 (0.89-1.67) 24 h prior: 0.98 (0.70-1.36)
Author: Rosenlund et al. (2006, 089796) **Period of Study:** 1992-1994 **Location:** Stockholm, Sweden	**Health Outcome:** MI **Study Design:** Case control **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** 45-70 yr **Sample Description:** 1,397 cases;1,870 controls	**Averaging Time:** **Mean (SD) unit:** 66.8 µg/m^3 (Estimated 30-yr residential exposure) **Range (percentiles):** 5th = 13.9; 95th = 295.7 **Copollutant:** NR	**Increment:** 300 µg/m^3 **OR Estimate** [Lower CI, Upper CI] ; lag: Estimated 30-yr avg exposure All cases: 1.04 (0.89-1.21) Nonfatal cases: 0.98 (0.82-1.16) Fatal cases: 1.22 (0.98-1.52) In-hospital death: 1.16 (0.89-1.51) Out-of-hospital death: 1.36 (1.01-1.84)
Author: Rosenlund et al. (2009, 190309) **Period of Study:** NR **Location:** Stockholm County, Sweden	**Health Outcome:** Fatal and nonfatal MI **Study Design:** Case control **Statistical Analyses:** Various multiple regression models **Age Groups Analyzed:** 15-79 yr **Sample Description:** 43,275 MI cases during 1985-1996; 511,065 controls	**Averaging Time:** 1 yr **Mean (SD) unit:** **Cases:** 64.2 µg/m^3 **Controls:** 55.8 µg/m^3 **Range (percentiles):** Cases: 5th = 7.3; 95th =267.4 Controls: 5th =6.1;95th=261.8 **Copollutant:** PM_{10}, NO_2	**Increment:** NR **OR Estimate** [Lower CI, Upper CI] 5-yr avg exposure All subjects (n = 301,273) All cases: 1.01 (0.97-1.05) Nonfatal cases: 0.94 (0.89-1.00) Fatal cases: 1.14 (1.07-1.21) In-hospital death: 1.00 (0.91-1.10) Out-of-hospital death: 1.23 (1.14-1.32) Restriction to subjects who did not move between population census (n = 80,155) All cases: 1.04 (0.94-1.14) Nonfatal cases: 0.96 (0.87-1.06) Fatal cases: 2.03 (1.59-2.60) In-hospital death: 2.04 (1.35-3.08) Out-of-hospital death: 2.03 (1.50-2.74)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
CHANGES IN BLOOD PRESSURE			
Author: Ibalde-Mulli et al. (2001, 016030) **Period of Study:** 1984-1985 **Location:** Augsburg, Germany	**Health Outcome:** BP–SPB **Study Design:** Cohort **Statistical Analyses:** Gaussian regression for repeated measures **Age Groups Analyzed:** 25-64 yr **Sample Description:** 2,607 men and women 25-64 yr	**Averaging Time:** 24 h **Mean (SD) unit:** 4.1 mg/m^3 **Range (Min, Max):** 1.7, 8.2 **Copollutant:** NR	**Increment:** Lag 0: 5.6 mg/m^3 5-day prior avg **Mean Change** [Lower CI, Upper CI] SPB mmHg Lag 0 (days): All: 0.53 (-0.66 to 1.72); Men: 0.68 (-0.94 to 2.31); Women: 0.51 (-1.31 to 2.19) 5-day prior avg: All: 1.06 (-0.17 to 2.29); Men: 0.92 (-0.87 to 2.70); Women: 0.91 (-0.87 to 2.70)
Author: Zanobetti et al. (2004, 087489) **Period of Study:** 1999-2001 **Location:** Boston, MA	**Health Outcome:** BP **Study Design:** Cohort/Panel **Statistical Analyses:** Random effects **Age Groups Analyzed:** 39-90 yr **Sample Description:** 62 subjects with 631 total visits	**Averaging Time:** 1 h and 120 h avg **Mean (SD) unit:** Same h: 0.81 ppm 120-h avg: 0.66 ppm **Range (Min, Max):** Same h: 10th = 0.48; 90th = 1.22 120-h avg: 10th = 0.48; 90th = 0.86 **Copollutant:** NR	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] CO had no significant effect on BP
CHANGES IN BLOOD MARKERS OF COAGULATION AND INFLAMMATION			
Author: Baccarelli et al. (2007, 090733) **Period of Study:** 1995-2005 **Location:** Milan, Italy	**Health Outcome:** Prothrombin time (PT) and activated partial thromboplastin time (APTT) **Study Design:** Panel **Statistical Analyses:** GAMS **Age Groups Analyzed:** 11-84 yr (mean 43 yr) **Sample Description:** 1,218 healthy individuals who were partners or friends of patients with thrombosis who attended the thrombosis center of the University of Milan.	**Averaging Time:** 1 h **Mean (SD) unit:** NR **Range (percentiles):** Sept-Nov: 25th = 1.36; 75th = 3.52 Dec-Feb: 25th = 2.00; 75th = 4.31 Mar-May: 25th = 1.03; 75th = 2.14 Jun-Aug: 25th = 0.73; 75th = 1.58 **Copollutant:** NR	**Increment:** NR **Regression co-efficient** [Lower CI, Upper CI] **Lags examined (time of blood sampling – avg):** 0, 7, 30 PT: Lag 0: -0.11 (-0.18 to -0.05); Lag 7: -0.07 (-0.14 to 0.01); Lag 30: -0.05 (-0.13 to 0.02) APTT: Lag 0: 0.03 (-0.04 to 0.10); Lag 7: 0.04 (-0.04 to 0.11); Lag 30: 0.06 (-0.01 to 0.14) Notes: CO had no effect on fibrinogen, functional antithrombin, functional protein C, protein C antigen, functional protein S, or free protein S for all lag periods.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Delfino et al. (2008, 156390) **Period of Study:** 2005-2006 **Location:** Los Angeles, CA	**Health Outcome:** Biomarkers of systemic inflammation **Study Design:** Panel **Statistical Analyses:** Linear mixed-effects models **Age Groups Analyzed:** ≥ 65 yr (mean 85.7 yr) **Sample Description:** 29 nonsmoking subjects with history of CAD living in retirement communities	**Averaging Time:** 24 h **Mean (SD) unit:** 0.78 ± 0.30 ppb **Range (Min, Max):** 0.22, 1.97 **Copollutant (Outdoor):** EC: r = 0.84 OC: r = 0.69 OCprimary: r = 0.73 NO_2: r = 0.78 O_3: r = -0.35 $PM_{0.25}$: r = 0.84 $PM_{0.25-2.5}$: r = 0.14 $PM_{2.5-10}$: r = 0.51	**Increment:** NR Estimated coefficient **Relationship to outdoor air pollutants:** CRP (ng/mL): Lag 0: 847.52; 3-day avg: 728.79; 9-day avg: 236.51 IL-6 (pg/mL): Lag 0: 0.52; 3-day avg: 0.51; 9-day avg: 0.50 sTNF-RII (pg/mL): Lag 0: 154.05; 3-day avg: 139.45; 9-day avg: 225.60 **Relationship to indoor air pollutants:** CRP (ng/mL): Lag 0: 695.39; 3-day avg: 527.37; 9-day avg: 760.15 IL-6 (pg/mL): Lag 0: 0.54; 3-day avg: 0.47; 9-day avg: 0.77 sTNF-RII (pg/mL): Lag 0: 114.22; 3-day avg: 107.95; 9-day avg: 273.38 **Relationship of sP-selction (ng/mL) to:** Indoor air pollutants: Lag 0: 0.77; 5-day avg: 1.40; 9-day avg: 2.19 Outdoor air pollutants: Lag 0: 0.84; 5-day avg: 1.23; 9-day avg: 4.29 **Relationship of Cu, Zn-SOD (U/g Hb) to:** Indoor air pollutants: Lag 0: -145.54; 5-day avg: -238.72; 9-day avg: -70.10 Outdoor air pollutants: Lag 0: -105.73; 5-day avg: -176.72; 9-day avg: -41.92

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Delfino et al. **(2009, 200844)** **Period of Study:** Jul-midOct and midOct-Feb of 2005-2006 and 2006-2007 **Location:** Los Angeles, CA	**Health Outcome:** Biomarkers of inflammation **Study Design:** Panel **Statistical Analyses**: Linear mixed effects models adjusted for confounders **Age Groups:** 65+ (84.1 ± 5.60) yr **Sample Description:** 60 subjects with confirmed CAD history, nonsmoker, unexposed to environmental tobacco smoke	**Averaging Time:** 24 h **Mean (SD) unit:** 0.50 (0.25) ppm **Range (min, max):** 0.11, 1.30 **Copollutant:** NO_2, NO_X, O_3, $PM_{0.25}$, $PM_{0.25-2.5}$, $PM_{2.5-10}$, EC_3 OC, BC, OCpri, SOC, PN/cm^3	Increment: NR Regression coefficients (95% CI) Subjects with positive responses: Cu,Zn-SOD (U/g Hb): 1-day avg: 1441 (97, 2786), 3-day avg: 2634 (1416, 3854), 5-day avg: 4227 (2078, 6376), 7-day avg: 3474 (914, 6034), 9-day avg: 2954 (737, 5172) GPx-1 (U/g HB): 1-day avg: -0.97 (-4.45, 2.50), 3-day avg: -2.21 (-6.48, 2.06), 5-day avg: 4.71 (-2.90, 12.33), 7-day avg: 4.20 (-3.29, 11.68), 9-day avg: 4.76 (-1.58, 11.10) Subjects with negative responses: Cu,Zn-SOD (U/g Hb): 1-day avg: -195 (-338, -52), 3-day avg: -242 (-399, -85), 5-day avg: -242 (-440, -44), 7-day avg: -315 (-664, 34), 9-day avg: -176 (-508, 156) GPx-1 (U/g HB): 1-day avg: -0.82 (-1.55, -0.08), 3-day avg: -0.85 (-1.66, -0.04), 5-day avg: -0.84 (-1.88, 0.21), 7-day avg: -1.04 (-2.85, 0.78), 9-day avg: -0.47 (-2.19, 1.26) All subjects: IL-6 (pg/mL): 1-day avg.: 0.35 (0.17, 0.54), 3-day avg.: 0.40 (0.20, 0.61), 5-day avg.: 0.54 (0.27, 0.80), 7-day avg.: 0.34 (-0.06, 0.74), 9-day avg.: 0.31 (-0.07, 0.70) P-selectin (ng/mL): 1-day avg.: 3.33 (0.94, 5.73), 3-day avg.: 3.65 (1.02, 6.29), 5-day avg.: 5.28 (1.86, 8.70), 7-day avg.: 11.2 (5.39, 17.0), 9-day avg.: 10.4 (4.83, 16.0) TNF-RII (pg/mL): 1-day avg: 112 (13, 211), 3-day avg: 136 (29, 243), 5-day avg: 229 (88, 371), 7-day avg: 132 (-86, 349), 9-day avg: 220 (19, 421) TNF-α (pg/mL): 1-day avg: 0.05 (-0.05, 0.16), 3-day avg: 0.09 (-0.03, 0.20), 5-day avg: 0.14 (-0.01, 0.29), 7-day avg: 0.07 (-0.19, 0.33), 9-day avg: 0.14 (-0.11, 0.39) CRP (ng/mL): 1-day avg: 780 (343, 1217), 3-day avg: 739 (255, 1222), 5-day avg: 1117 (485, 1749), 7-day avg: 126 (-800, 1052), 9-day avg: 41 (-840, 923) SOD (U/g Hb): 1-day avg: -62 (-231, 108), 3-day avg: -53 (-244, 138), 5-day avg: -37 (-285, 211), 7-day avg: 98 (-314, 509), 9-day avg: 208 (-173, 590) GPx-1 (U/g Hb): 1-day avg: -0.69 (-1.41, 0.03), 3-day avg: -0.69 (-1.48, 0.11), 5-day avg: -0.56 (-1.60, 0.48), 7-day avg: -0.56 (-2.34, 1.21), 9-day avg: 0.05 (-1.63, 1.72) Effect modification by medication use: TNF-RII (pg/mL): 1-day avg: All subjects: 125 (11, 239), Statins: 48 (-105, 201), No Statins: 199 (47, 352); 3-day avg: All subjects: 161 (39, 283), Statins: 1 (-170, 171), No Statins: 306 (141, 472) ; 5-day avg: All subjects: 257 (100, 413), Statins: 15 (-210, 240), No Statins: 445 (240, 649); 7-dayay avg: All subjects: 176 (-68, 419), Statins: 43 (-297, 382), No Statins: 283 (-23, 589); 9-dayay avg: 265 (41, 489), Statins: 160 (-158, 478), No Statins: 355 (65, 646) sP-selectin (ng/mL): 1-day avg: All subjects: 1.84 (-0.62, 4.30), Clopidogrel: 0.00 (-2.80, 2.81), No Clopidogrel: 1.72 (-0.42, 3.86); 3-day avg: All subjects: 1.90 (-0.79, 4.60), Clopidogrel: -0.67 (-3.95, 2.60), No Clopidogrel: 1.60 (-0.76, 3.96); 5-day avg: All subjects: 2.97 (-0.47, 6.41), Clopidogrel: -0.18

Study	Design	Concentrations	CO Effect Estimates (95% CI)
			(-4.38, 4.01), No Clopidogrel: 3.04 (0.06, 6.01); 7-day avg: All subjects: 6.74 (0.75, 12.73), Clopidogrel: 2.24 (-4.22, 8.71), No Clopidogrel: 6.78 (1.60, 3.96); 9-day avg: All subjects: 6.96 (1.20, 12.72), Clopidogrel: 2.0 (-4.40, 8.48), No Clopidogrel: 5.54 (0.46, 10.6)
Author: Liao et al. (2005, 088677) **Period of Study:** 1996-1998 **Location:** Forsyth County, NC; Selected suburbs of Minneapolis, MN; Jackson, MI	**Health Outcome:** Various measures of hemostasis/ inflammation **Study Design:** Cohort **Statistical Analyses:** Linear regression **Age Groups Analyzed:** 45-64 yr **Sample Description:** 10,208 subjects from the Atherosclerosis Risk in Communities Study	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	Increment: 0.6 ppm Regression coefficients [SE] Lags examined (days): 1 Lag 1: Fibrinogen (mg/dL): -0.16 (0.67) Factor VIII –C (%): 0.45 (0.42) vWF %: -0.29 (0.50) WBC (x 103/mm3): 0.003 (0.017) Albumin (g/dL): -0.018 (0.003)** ** p < 0.01
Author: Ljungman et al. (2009, 191983) **Period of Study:** May 2003-July 2004 **Location:** Athens, Greece; Augsberg, Germany; Barcelona, Spain; Helsinki, Finland; Rome, Italy; Stockholm, Sweden	**Health Outcome:** Plasma Interleukin-6 (IL-6), Fibrinogen **Study Design:** Panel/Field **Statistical Analyses:** Linear Mixed Effects Model **Age Groups Analyzed:** 35-80 yr (mean = 62.2 yr) **Sample Description:** 955 subjects who had experienced MI between 4 mo and 6 yr before start of the study	**Averaging Time:** 24 h **Mean (SD) unit:** **Individual cities:** 0.29-1.48 mg/m^3 **Mean for all cities:** 0.78 mg/m^3 **Range (percentiles):** 25th = 0.56; 75th = 0.90 (for mean of all cities) **Copollutant:** (mean for all cities) NO_2: r = 0.69 PM_{10}: r = 0.47 $PM_{2.5}$: r = 0.55 PNC: r = 0.67	**Increment:** 0.34 mg/m^3 Change of IL-6 % of overall mean per IQ range increase **Genotypes:** 1 1, 1 2, 2 2 IL6 rs2069832 1 1: 2.0 (0.3, 3.6); 1 2: -0.2 (-1.7, 1.3); 2 2: -2.0 (-4.7, 0.8); p-value: 0.03 IL6 rs2069840 1 1: 2.0 (0.3, 3.8); 1 2: 0.4 (-0.9, 1.7); 2 2: -1.2 (-3.4, 1.1); p-value: 0.04 IL6 rs2069845 1 1: 1.9 (0.2, 3.5); 1 2: -0.1 (-1.5, 1.4); 2 2: -1.6 (-4.3, 1.2); p-value: 0.31 FGA rs2070011 1 1: 1.0 (-0.7, 2.7); 1 2: 0.7 (0.6, 2.0); 2 2: 0.4 (-1.9, 2.7); p-value: 0.64 FGB rs1800790 1 1: -0.2 (-1.8, 1.3); 1 2: 2.1 (0.4, 3.8); 2 2: 4.5 (1.1, 8.0); p-value: 0.02
Author: Pekkanen et al. (2000, 013250) **Period of Study:** 1991-1993 **Location:** London, England	**Health Outcome:** Fibrinogen **Study Design:** Cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** 35-55 yr **Sample Description:** 7,205 office workers	**Averaging Time:** 8 h **Mean (SD) unit:** 1.4 mg/m^3 **Range (Min, Max):** Min = NR, Max = 9.9 **Copollutant correlation:** PM_{10}: r = 0.57 NO_2: r = 0.81 SO_2: r = 0.61 O_3: r = -0.45	**Increment:** 1.6 mg/m^3 % Change in fibrinogen concentration [p value] ; **Lags examined:** 0, 1, 2, 3 Lag 0: 1.43 (<0.01); Lag 1: 1.49 (<0.01); Lag 2: 1.59 (<0.01); Lag 3: 1.26 (<0.01) OR for having Fibrinogen above 3.19 g/l [p value] **Lags examined**: 0, 1, 2, 3 Lag 0: 1.17 (0.05); Lag 1: 1.09 (0.31); Lag 2: 1.14 (0.11); Lag 3: 1.22 (<0.01)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Ruckerl et al. (2006, 088754) **Period of Study:** 2000-2001 **Location:** Erfert, Germany	**Health Outcome:** Blood markers of inflammation and coagulation **Study Design:** Panel **Statistical Analyses:** Linear and logistic regression (fixed effects) **Age Groups Analyzed:** 51-76 yr (mean = 66 yr) **Sample Description:** 57 male patients with CHD	**Averaging Time:** 24 h **Mean (SD) unit:** 0.52 mg/m^3 **Range (Min, Max):** 0.11, 1.93 **Copollutant correlation:** NO_2: r = 0.82	**Increment:** 0.27 mg/m^3 **OR Estimate for blood marker** >90th percentile **[Lower CI, Upper CI]** **Lags examined (h):** 0-23, 24-47, 48-71, 5-day avg CRP (C-reactive protein) 0-23: 0.9 (0.7-1.2); 24-47: 1.0 (0.7-1.5); 48-71: 1.5 (1.1-2.1); 5-day avg 1.1 (0.8-1.6) ICAM-1 (Intercellular adhesion molecule 1) 0-23: 0.8 (0.6-1.0); 24-47: 1.5 (1.2-1.9); 48-71: 1.7 (1.3-2.3); 5-day avg 1.2 (1.0-1.6) % of change from the mean of blood marker vWF (von Willebrand factor antigen) 0-23: 4.4 (1.4- 7.5); 24-47: 2.7 (-0.8 to 6.1); 48-71: 2.0 (-1.7 to 5.8); 5-day avg: 4.9 (1.0-8.8) FVII (Factor VII) 0-23: -1.4 (-3.8 to 1.1); 24-47: -2.6 (-4.8 to 0.3); 48-71: -2.8 (-5.1 to -0.4); 5-day avg: -3.0 (-5.5 to -0.4)
Author: Ruckerl et al. (2007, 156931) **Period of Study:** May 2003-July 2004 **Location:** 6 cities across Europe: Athens, Greece; Augsburg, Germany; Barcelona, Spain; Helsinki, Finland; Rome, Italy; Stockholm, Sweden	**Health Outcome:** Interleukin-6, C-reactive protein, Fibrinogen **Study Design:** Panel/Cohort **Statistical Analyses:** Linear regression (mixed effects) **Age Groups Analyzed:** 37-81 yr **Sample Description:** 1,003 MI survivors who had at least 2 valid repeated blood samples	**Averaging Time:** 24 h **Mean (SD) unit:** Athens: 1.48 mg/m^3 Augsburg: 0.58 mg/m^3 Barcelona: 0.59 mg/m^3 Helsinki: 0.31 mg/m^3 Rome: 1.40 mg/m^3 Stockholm: 0.29 mg/m^3 **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** 0.34 mg/m^3 % Change in mean [Lower CI, Upper CI] **Lags examined:** 0, 1, 2, 5-day avg (Pooled estimates) Interleukin-6 Lag 0: 0.57 (-0.63 to 1.79) Lag 1: 0.44 (-0.79 to 1.68); Lag 2: -2.36 (-4.82 to 0.17) 5-day avg: -0.28 (-2.53 to 2.02) C-reactive protein Lag 0: -0.01 (-1.72 to 1.73 Lag 1: -1.51 (-3.30 to 0.32) Lag 2: -2.35 (-6.84 to 2.36); 5-day avg: -0.85 (-.5.37 to 3.90) Fibrinogen Lag 0: 0.24 (-0.54 to 0.92) Lag 1: 0.32 (-0.35 to 1.00); Lag 2: -0.44 (-1.11 to 0.23) 5-day avg: 0.12 (-0.81 to 1.05)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Rudez et al. (2009, 193783) **Period of Study:** January 2005-December 2006 **Location:** Rotterdam, the Netherlands	**Health Outcome:** Platelet aggregation, thrombin generation, Fibrinogen, C-reactive protein **Study Design:** Panel **Statistical Analyses:** Linear regression **Age Groups Analyzed:** Mean = 41 yr **Sample Description:** 40 healthy individuals	**Averaging Time:** 24 h **Median (SD) unit:** 333 µg/m^3 **Range (percentiles):** 25th = 276; 75th = 412 **Copollutant:** PM_{10}: r >0.6 NO: r >0.6 NO_2: r >0.6 O_3: -0.4 ≥ r ≥ -0.6	**Increment:** NR **Estimated Changes** [Lower CI, Upper CI] Platelet Aggregation Parameters Maximal Platelat Aggregation: D0-6: -3.6 (-9.3, 2.1); D0-12: -4.7 (-11.0, 1.5); D0-24: -2.6 (-7.9, 2.7); I24-48: -1.1 (-7.2, 4.9); I48-72: 8.4 (2.5, 14.3); I72-96: -0.1 (-5.1, 5.0); D+I0-96: 9.5 (1.6, 17.4) Late Aggregation: D0-6: 10.5 (0.8, 20.3); D0-12: 11.6 (1.2, 21.9); D0-24: 11.2 (1.4, 21.0); I24-48: 7.5 (-2.2, 17.1); I48-72: 18.1 (8.4, 27.8); I72-96: 4.2 (-5.5, 13.9); D+I0-96: 20.4 (8.4, 32.4) Thrombin Generation ETP D0-6: -1.51 (-3.7, 0.80); D0-12: -1.1 (-3.4, 1.1); D0-24: -1.5 (-3.9, 0.9); I24-48: -0.7 (-3.4, 2.0); I48-72: 0.8 (-1.9, 3.4); I72-96: 3.5 (0.8, 6.2); D+I0-96: 0.8 (-2.7, 4.3) Peak D0-6: -2.5 (-6.3, 1.3) D0-12: -1.9, (-5.7, 1.9); D0-24: -3.3 (-7.3, 0.7); I24-48; -1.3 (-6.1, 3.6); I48-72: -0.5 (-5.0, 4.0) I72-96: 3.8 (-0.8, 8.4) D+I0-96: -1.7 (-7.5, 4.2) Lag Time D0-6: 1.0 (-0.5, 2.5); D0-12: 1.0 (-0.5, 2.5); D0-24: 1.6 (0.1, 3.1); I24-48; 0.4 (-1.3, 2.2); I48-72: -1.0 (-2.7, 0.7); I72-96: -1.5 (-3.2, 0.2); D+I0-96: 0.1 (-2.1, 2.2) Inflammatory Markers Fibrinogen I24-48; 0.0 (-1.7, 1.8); I48-72: 0.0 (-1.8, 1.9) I72-96: -0.1 (-1.9, 1.7) CRP I24-48; 3.2 (-6.4, 12.8); I48-72: -1.9 (-12.5, 8.7); I72-96: -4.5 (-15.3, 6.3)
Author: Steinvil et al. (2008, 188893) **Period of Study:** 2003-2006 **Location:** Tel Aviv, Israel	**Health Outcome:** Various measures of inflammation sensitive biomarkers **Study Design:** Cohort **Statistical Analyses:** Linear regression **Age Groups Analyzed:** Mean = 46 yr **Sample Description:** 3,659 subjects living within 11 km of monitoring site	**Averaging Time:** 24 h **Mean (SD) unit:** 0.8 ppm **Range (percentiles):** 25th = 0.7; 75th = 1.0 **Copollutant:** correlation PM_{10}: r = 0.75 NO_2: r = 0.857 SO_2: r = 0.671 O_3: r = -0.656	**Increment:** 0.3 ppm **Regression co-efficient** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3, 4, 5, 6, 7, last wk avg Fibrinogen: Men Lag 0: -3.3 (-6.1 to -0.6); Lag 1: -2.6 (-5.5 to 0.4); Lag 2: -3.4 (-6.6 to -0.3); Lag 3: -3.4 (-6.5 to -0.2); Lag 4: -5.9 (-8.9 to -2.9); Lag 5: -4.7 (-7.8 to -1.6); Lag 6: -2.0 (-5.1 to 1.0); Lag 7: -2.7 (-5.7 to 0.2); Last wk avg: -7.7 (-12.1 to -3.3) **Notes:** No effect on fibrinogen among women. CO had no effect on CRP among men and no effect on CRP and WBC among women for all Lag times examined.
VARIOUS MEASURES OF CARDIOVASCULAR HEALTH			
Author: Briet et al. (2007, 093049) **Period of Study:** NR **Location:** Paris, France	**Health Outcome:** Endothelial function, Reactive Hyperemia **Study Design:** Case-crossover **Statistical Analyses:** Multiple regression models **Age Groups Analyzed:** 18-35 yr **Sample Description:** 40 healthy white male nonsmokers	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** $PM_{2.5}$, PM_{10}, NO, NO_2, SO_2	**Increment:** NR β-Coefficient [Lower CI, Upper CI] **Flow-mediated Brachial Artery Dilatation:** -0.68 (-1.22, -0.15) **Small Artery Reactive Hyperemia:** 10.46 (1.73, 19.31)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Nautiyal et al. (2007, 190301) **Period of Study:** August 1999-May 2000 **Location:** Mandi Gobindgarh, India Morinda, India	**Health Outcome:** Various measures of cardiovascular health via ECG (Minnesota Code) **Study Design:** Cross-sectional **Statistical Analyses:** NR **Age Groups Analyzed:** +15 yr **Sample Description:** 200 total survey participants (100/town)	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** Morinda Pure residential Site: 0-1 ppm GT Road Site: 2-3 ppm Mandi Gobindgarh Mixed Habitat Site: 0-3 ppm GT Road Site: 1-3 ppm Co**pollutant:** $PM_{2.5}$, PM_{10}, NO_X, SO_X	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] **Lags examined:** NR No quantitative results presented
Author: Wellenius et al. (2007, 092830) **Period of Study:** February 2002-March 2003 **Location:** Boston, MA	**Health Outcome:** Congestive heart failure **Study Design:** Cohort (retrospective) **Statistical Analyses:** Linear mixed models **Age Groups Analyzed:** 33-88 yr. Tai Chi Group mean age (n=14): 66 ± 13 yr. Control Group mean age (n=14): 63 ± 14 yr. **Sample Description:** 28 patients with CHF and impaired systolic function	**Averaging Time:** 24 h **Mean (SD) unit:** 0.44 ppm **Range (IQ):** 0.20 ppm **Copollutant:** $PM_{2.5}$: r = 0.35 NO_2, SO_2, O_3, BC	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] **Lags examined:** 0, 1, 2, 3 Results presented graphically

Table C-2. Studies of CO exposure and cardiovascular hospital admissions and ED visits.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
STROKE			
Author: Chan et al. (2006, 090193) **Period of Study:** 1997-2002 **Location:** Taipei, Taiwan	**ED Visits** **Health Outcome** (ICD9): Cerebrovascular disease (430-437); Strokes (430-434); Hemorrhagic stroke (430-432); Ischemic stroke (433-434) **Study Design:** Time-series **Statistical Analyses:** GAM **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 8 h **Mean (SD) unit:** 1.7 ppm **Range (Min, Max):** 0.6, 4.4 **Copollutant:** correlation O_3: r = 0.30 SO_2:r = 0.63 NO_2: r = 0.77 $PM_{2.5}$: r = 0.44 PM_{10}: r = 0.47	**Increment:** 0.8 ppm **OR Estimate** [Lower CI, Upper CI] **Lags (days) examined** 0, 1, 2, 3 Cerebrovascular disease: Lag 2, 1.03 (1.01, 1.06) Stroke: Lag 2, 1.03 (1.01, 1.05) Ischemic and Hemorrhagic stroke: not significant. Cerebrovascular 2 pollutant model: CO + O_3: Lag 2, 1.03 (1.01-1.05) CO + $PM_{2.5}$: Lag 2, 1.02 (1.00-1.04) CO + PM_{10}: Lag 2, 1.03 (1.01-1.05)
Author: Henrotin et al. (2007, 093270) **Period of Study:** 1994-2004 **Location:** Dijon, France	**Health Outcome** (ICD9 or ICD10): Stroke (Ischemic & Hemorrhagic) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** ≥ 40 yr **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 683 μg/m^3 **Range (Min, Max):** 0, 4014 **Copollutant:** NR	**Increment:** 10 μg/m^3 **OR Estimate [Lower CI, Upper CI]** **Lags (days) examined:** 0, 1, 2, 3. Ischemic: Lag 0: 0.999 (0.997-1.001) Lag 1: 0.998 (0.997-1.001) Lag 2: 0.999 (0.998-1.001) Lag 3: 1.000 (0.998-1.001) Hemorrhagic: Lag 0: 1.000 (0.996-1.004) Lag 1: 1.001 (0.997-1.005) Lag 2: 0.999 (0.995-1.004) Lag 3: 0.998 (0.994-1.002) Also not significant when stratified by sex.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Maheswaran et al. (2005, 090769) **Period of Study:** 1994-1998 **Location:** Sheffield, UK	**Health Outcome** (ICD9 or ICD10): Stroke deaths (ICD9: 430-438); Stroke Hospital admissions (ICD10: I60-I69) **Study Design:** Ecological **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** ≥ 45 yr **Sample Description:** 1,030 census districts	**Averaging Time:** NR **Mean (SD) unit:** Quintiles **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR – Quintiles of exposure **RR Estimate** [Lower CI, Upper CI] Adjusted for sex, age, deprevation, smoking. Quintiles: 2nd: 1.04 (0.94-1.16) 3rd: 1.01 (0.91-1.13) 4th: 1.10 (0.99-1.23) 5th: 1.11 (0.99-1.25) Adjusted for sex, age: 2nd: 1.11 (1.01-1.22) 3rd: 1.15 (1.04-1.27) 4th: 1.29 (1.17-1.42) 5th: 1.37 (1.24-1.52)
Author: Tsai et al. (2003, 080133) **Period of Study:** 1997-2000 **Location:** Kaohsiung, Taiwan	**Study Design:** Case-crossover **Health Outcome (ICD9 or ICD10):** Cerebrovascular diseases: ICD9: 430 to 438 (Subarachnoid hemorrhagic stroke 430, Primary intracerebral hemorrhage (PIH): 431-432, Ischemic stroke (IS): 433-435). **Statistical Analyses:** NR **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 0.79 ppm **Range (Min, Max):** 0.24, 1.72 **Copollutant:** NR	**Increment:** 0.8 ppm (IQR) **RR Estimate** [Lower CI, Upper CI] **Lag (days):** 0-2 >20ºC PIH: OR 1.21 (1.09-1.34) IS: OR 1.21 (1.14-1.28) <20ºC PIH: OR 1.18 (0.80-0.72) IS: OR 1.77 (1.31-2.39) Notes: 2-pollutant models: PIH results persisted when adjusting for SO_2 and O_3 IS results persisted when controlling for PM_{10}, SO_2 and O_3
Author: Villeneuve et al. (2006, 090191) **Period of Study:** 1992-2002 **Location:** Edmonton, Canada	ED Visits (within 5 hospitals) **Health Outcome (ICD9):** Stroke (430-438); Ischemic (434-436) Hemorrhagic (430-432); Transient Ischemic Attack (435) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 65+ yr **Sample Description:** 12,422 visits	**Averaging Time:** 24 h **Mean (SD) unit:** 0.8 ppm **Range (percentiles):** 25th = 0.5; 75th = 1.0 **Copollutant correlation:** O_3: r = -0.54 $PM_{2.5}$: r = 0.43 PM_{10}: r = 0.30	**Increment:** 0.5 ppm **OR Estimate** [Lower CI, Upper CI] **Lags (days) examined:** 0, 1 & 0-2 Ischemic (April-Sept) Lag 0: 1.16 (1.00, 1.33) Lag 1: 1.17 (1.01, 1.36) Lag 0-2: 1.32 (1.09, 1.60) Notes: - Not significant for all seasons or Oct-Mar. - Hemorrhagic: Not significant for all seasons or Oct-Mar, Apr-Sept. - Transient Ischemic Attack: Not significant for all seasons or Oct-Mar, Apr-Sept.
Author: Wellenius et al. (2005, 088685) **Period of Study:** NR **Location:** 9 U.S. cities: Chicago, Detroit, Pittsburgh, Cleveland, Birmingham, New Haven, Seattle, Minneapolis, Salt Lake City	ED Visits **Health Outcome:** Stroke among Medicare beneficiaries: (Ischemic, hemorrhagic) **Study Design:** Time-series **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** ≥ 65 yr **Sample Description:** 155,503 visits	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (percentiles):** 25th = 0.73; 50th = 1.02; 75th = 1.44 (ppm) **Copollutant:** correlation PM_{10}: r = 0.43	**Increment:** 0.71 ppm **% Change** [Lower CI, Upper CI] **Lag:** 0 Ischemic: 2.83 (1.23-4.46) Hemorrhagic: -1.61 (-4.79 to 1.68)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
ISCHEMIC HEART DISEASE			
Author: D'Ippoliti et al. (2003, 074311) **Period of Study:** 1995-1997 **Location:** Rome, Italy	Hospital Admissions **Health Outcome (ICD9):** MI (410) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 18+ yr **Sample Description:** 6,531 patients.	**Averaging Time:** 24 h **Mean (SD) unit:** 4.4 mg/m^3 **Range (percentiles):** 25th = 2.8; 75th = 4.3 **Copollutant:** correlation TSP: r = 0.35 SO_2: r = 0.56 NO_2: r = 0.31	**Increment:** 1 mg/m^3 **OR Estimate** [Lower CI, Upper CI] ; lag: **Lags examined (days):** 0, 1, 2, 3, 4, 0-2 Acute MI Lag 0: 1.021 (0.988-1.054) Lag 1: 1.020 (0.988-1.054) Lag 2: 1.033 (1.001-1.066) Lag 3: 1.010 (0.982-1.040) Lag 4: 1.025 (0.996-1.055) Lag 0-2: 1.044 (1.000- .089
Author: Hosseinpoor et al. (2005, 087413) **Period of Study:** 1996-2001 **Location:** Tehran, Iran	**Health Outcome:** Angina Pectoris (ICD9: 413; ICD10: I20) **Study Design:** Time series **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 10.8 mg/m^3 **Range (Min, Max):** 1.6, 57.8 **Copollutant:** NR	**Increment:** 1 mg/m^3 **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3 Lag 1: 1.00957 (1.00600-1.01315)
Author: Lanki et al. (2006, 089788) **Period of Study:** 1994-2000 **Location:** 5 European cities: Augsburg, Germany Barcelona, Spain Helsinki, Finland Rome, Italy Stockholm, Sweden	**Health Outcome:** First AMI (ICD9: 410; ICD10: I21, I22) **Study Design:** Time series **Statistical Analyses:** Poisson regression (GAM) **Age Groups Analyzed:** 35+ yr **Sample Description:** 26,854 Hospital Admissions	**Averaging Time:** 24 h **Mean (SD) unit:** NR Unit: mg/m^3 **Range (percentiles):** Augsburg, Germany 25th = 0.7; 75th = 1.1 Barcelona, Spain 25th = 0.6; 75th = 1.4 Helsinki, Finland 25th = 0.3; 75th = 0.5 Rome, Italy 25th = 1.7; 75th = 2.9 Stockholm, Sweden 25th = 0.3; 75th = 0.5 **Copollutant:** correlation PM_{10}: r = 0.21 – 0.56 NO_2: r = 0.43 – 0.75 O_3: r = -.023 – 020	**Increment:** 0.2 mg/m^3 **RR Estimate** [Lower CI, Upper CI] ; lag: **Lags examined:** 0, 1, 2, 3 All 5 cities: Lag 0: 1.005 (1.000-1.010) Lag 1: 1.002 (0.996-1.007) Lag 2: 1.002 (0.997-1.007) Lag 3: 0.998 (0.992-1.003) 3 cities with Hospital Discharge Register(HDR): Lag 0: 1.007 (1.001-1.012) Lag 1: 1.002 (0.996-1.008) Lag 2: 1.003 (0.998-1.009) Lag 3: 1.004 (0.988-1.020) 3 cities with HDR – ≤ 75years Fatal: Lag 0: 1.027 (1.006-1.048) Lag 1: 1.021 (1.000-1.042) Lag 2: 1.018 (0.997-1.039) Lag 3: 1.015 (0.994-1.037) Non-Fatal: Lag 0: 1.001 (0.995-1.008) Lag 1: 1.000 (0.994-1.007) Lag 2: 1.004 (0.998-1.011) Lag 3: 0.999 (0.992-1.006) 3 cities with HDR – ≥ 75years Fatal: Lag 0: 1.009 (0.992-1.006) Lag 1: 1.001 (0.985-1.018) Lag 2: 1.006 (0.990-1.023) Lag 3: 1.000 (0.983-1.017) Non-Fatal: Lag 0: 1.015 (1.004-1.086) Lag 1: 1.006 (0.995-1.017) Lag 2: 0.995 (0.983-1.006) Lag 3: 0.998 (0.987-1.009)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Lee et al. (2003, 095552) **Period of Study:** 1997-1999 **Location:** Seoul, Korea	**Study Design:** Time-series **Health Outcome (ICD9 or ICD10):** Angina: ICD10: 120 AMI: ICD10: I21-I23 Other Acute IHDs: ICD10: I24 **Statistical Analyses:** Poisson regression, GAM **Age Groups Analyzed:** 64+ yr **Sample Description:** 822 days	**Averaging Time:** Daily max **Mean (SD) unit:** 1.8 ppm **Range (percentiles):** 25th = 1.2 75th = 2.2 **Copollutant:** correlation PM_{20}: 0.60 SO_2: 0.81 NO_2: 0.79 O_3: -0.39	**Increment:** 1 ppm (IQR) **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3, 4, 5, 6 All yr: Lag 5: All ages: 0.94 (0.91 0.98) Lag 5: 64+ age: 1.07 (1.01-1.13) Summer: Lag 5: All ages: 1.19 (1.02-1.38) Lag 5: 64+ age: 1.60 (1.27-2.03) 2-pollutant model: Lag 5: 64+ age: CO + PM_{10}: 1.04 (0.98-1.11)
Author: Maheswaran et al. (2005, 090769) **Period of Study:** 1994-1998 **Location:** Sheffield, UK	Emergency Hospital Admission **Health Outcome (ICD9):** CHD (410-414) **Study Design:** Ecological **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** 45+ yr **Sample Description:** 11,407 Emergency Hospital Admissions for CHD in patients 45+ yr (within 1,030 census districts)	**Averaging Time:** NR **Mean (SD) unit:** Quintiles **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NA **RR Estimate** [Lower CI, Upper CI] Lowest quintile reference category Adjusted for sex, age, deprivation, smoking: 2nd: 0.97 (0.89-1.07) 3rd: 0.94 (0.86-1.04) 4th: 0.96 (0.97-1.06) 5th: 0.88 (0.79- 0.98) Adjusted for sex, age: 2nd: 1.09 (1.00-1.19) 3rd: 1.15 (1.05-1.26) 4th: 1.19 (1.09-1.30) 5th: 1.20 (1.09-1.32)
Author: Mann et al. (2002, 036723) **Period of Study:** 1988-1995 **Location:** Southern California	**Health Outcome (ICD9):** IHD (IHD) (410-414); MI (410) **Study Design:** Time series **Statistical Analyses:** Poisson regression, GAM **Age Groups Analyzed:** All **Sample Description:** 54,863 IHD admissions among Southern California Kaiser- Permanente members (within 20km of monitor)	**Averaging Time:** 8 h **Mean (SD) unit:** 2.07 ppm **Range (Min, Max):** 0.30, 11.8 **Copollutant:** correlation Ranging across 7 regions: NO_2: r = 0.64, 0.86 O_3: r = -0.37, 0.28 PM_{10}: r = 0.15, 0.40	**Increment:** 1 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 2 ma, 3 ma, 4 ma With arrythmia: Lag 0: 2.99 (1.80-4.99) Lag 1: 1.51 (0.37-2.66) Lag 2: 1.26 (0.15-2.38) 2 ma: 2.66 (1.40-3.94) 3 ma: 2.59 (1.27-3.92) 4ma: 2.25 (0.90-3.63) With CHF: Lag 0: 3.60 (1.620-5.63) Lag 1: 3.34 (1.48-5.22) Lag 2: 1.90 (0.11-3.72) 2 ma: 4.23 (2.13-6.37) 3 ma: 4.14 (1.96-6.37) 4 ma: 4.07 (1.81-6.38) Without secondary diagnosis: Lag 0: 1.62 (0.65-2.59) Lag 1: 1.45 (0.54-2.37) Lag 2: 0.92 (0.04-1.82) 2 ma: 1.83 (0.80-2.86) 3 ma: 1.79 (0.72-2.87) 4 ma: 1.82 (0.71-2.94)
Author: Szyszkowicz (2007, 193793) **Period of Study:** 1997-2003 **Location:** Montreal, Canada	**Study Design:** Time-series **Health Outcome (ICD9 or ICD10):** ED Visits. IHD: ICD9: 410-414 **Statistical Analyses:** Poisson regression (GLMM) **Age Groups Analyzed:** All **Sample Description:** 4,979 ED Visits	**Averaging Time:** 24 h **Mean (SD) unit:** 0.5 ppm **Range (Min, Max):** 0.1, 3.1 **Copollutant:** NR	**Increment:** 0.2 ppm **% Change** [Lower CI, Upper CI] ; lag: **Lags examined (days):** 0, 1 All Patients: Lag 0: 5.4 (2.3-8.5) Males: Lag 0: 7.5 (3.6-11.6) Females: Lag 0: 2.7 (-2.0 to 7.6) Ages ≥ 64 All Patients: Lag 0: 4.9 (1.3-8.7) Males: Lag 0: 7.5 (2.6-12.6) Females: Lag 0: 2.4 (-3.0 to.0) Lag 1 not significant for all results

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: von Klot et al. (2005, 088070) **Period of Study:** 1992-2001 **Location:** 5 European cities: Augsburg, Germany Barcelona, Spain Helsinki, Finland Rome, Italy Stockholm, Sweden	**Health Outcome:** Hospital cardiac (mi), angina, dysrythmia, heart failure) re-admissions **Study Design:** Prospective Cohort **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** All **Sample Description:** 22,006 survivors of first MI	**Averaging Time:** 24 h **Unit:** mg/m^3 **Mean (SD) unit:** Augsburg, Germany: 0.93 Barcelona, Spain: 1.00 Helsinki, Finland: 0.42 Rome, Italy: 2.21 Stockholm, Sweden: 0.43 **Range (Min, Max):** NR **Copollutant:** correlation PM_{10}: r = 0.21 – 0.57 NO_2: r = 0.44 – 0.75 O_3: r = -.027 – 0.47	**Increment:** 0.2 mg/m^3 (0.172 ppm) **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3 Lag 0: MI:1.022 (0.998-.047) Angina: 1.009 (0.992-.02) Cardiac: 1.014 (1.001-.026)
HEART FAILURE			
Author: Lee et al. (2007, 090707) **Period of Study:** 1996-2004 **Location:** Kaohsiung City, Taiwan	Hospital Admissions **Health Outcome (ICD9):** CHF (428) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 13,475 Hospital Admissions (63 Hospitals)	**Averaging Time:** 24 h **Mean (SD) unit:** 0.76 ppm **Range (Min, Max):** 0.14, 1.72 **Copollutant:** NR	**Increment:** 0.31 ppm **OR Estimate** [Lower CI, Upper CI] **Lag examined (days):** 0-2 ≥ 25°C: 1.19 (1.09-1.31) <25°C: 1.39 (1.24-1.54) Adjusted for PM_{10}: ≥ 25°C; 1.15 (1.04-1.27) <25°C; 1.21 (1.206-1.38) Adjusted for SO_2: ≥ 25°C: 1.23 (1.11-1.36) <25°C: 1.39 (1.24-1.55) Adjusted for NO_2: ≥ 25°C: 1.22 (1.08-1.39) <25°C: 0.94 (0.81-1.10) Adjusted for O_3: ≥ 25°C: 1.17 (1.07-1.28) <25°C: 1.36 (1.22-1.51)
Author: Symons et al. (2006, 091258) **Period of Study:** 2002 (April-November) **Location:** Johns Hopkins Bayview Medical Center, Baltimore, MD	Hospital Admissions **Health Outcome:** NR **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 398 Hospital Admissions for CHF	**Averaging Time:** 24 h **Mean (SD) unit:** 0.4 ppm **Range (Min, Max):** 0.1, 1.0 **Copollutant:** NR	**Increment:** 0.2 ppm **OR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3, cum 1, cum 2, cum 3 Lag 0: 0.86 (0.67-1.11) Lag 1: 0.90 (0.70-1.17) Lag 2: 0.96 (0.73-1.26) Lag 3: 0.88 (0.67-1.16) Cum. Lag1: 0.82 (0.60-1.13) Cum. Lag2: 0.80 (0.54-1.17) Cum. Lag3: 0.27 (0.46-1.14)
Author: Wellenius et al. (2005, 087483) **Period of Study:** 1987-1999 **Location:** Pittsburgh, PA	Hospital Admissions **Health Outcome (ICD9):** CHF (428, 428.1) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 65+ yr **Sample Description:** 54,019 Hospital Admissions among Medicare beneficiaries	**Averaging Time:** 24 h **Mean (SD) unit:** 1.03 ppm **Range (percentiles):** 25th = 0.68; 75th = 1.23 **Copollutant:** correlation PM_{10}: r = 0.57 NO_2: r = 0.70 O_3: r = -0.25 SO_2: r = 0.54	**Increment:** 0.55 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3 Lag 0: Single pollutant model: 4.55 (3.33-5.79) Adjusted for PM_{10}: 5.18 (3.49-6.89) Adjusted for NO_2: 4.84 (3.06-6.66) Adjusted for O_3: 4.35 (3.08-5.64) Adjusted for SO_2: 4.51 (3.15-5.90)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Yang (2008, 157160) **Period of Study:** 1996-2004 **Location:** Taipei, Taiwan	Hospital Admissions **Health Outcome:** CHF **Study Design:** Case-crossover **Statistical Analyses:** NR **Age Groups Analyzed:** NR **Sample Description:** 24,240 CHF HA from 47 hospitals	**Averaging Time:** 24 h **Mean (SD) unit:** 1.26 ppm **Range (Min, Max):** 0.12, 3.66 **Copollutant:** PM_{10}, NO_2, O_3, SO_2	**Increment:** NR **OR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2 **Single Pollutant Model** Warm days (>20o C): 1.24 (1.16, 1.33) Cool days (<20o C): 1.05 (0.96, 1.15) **Two Pollutant Models** Warm days (≥20°C) Adjusted for PM_{10}: 1.16 (1.08, 1.26) Adjusted for NO_2: 1.02 (0.92, 1.13) Adjusted for O_3: 1.25 (1.17, 1.34) Adjusted for SO_2: 1.32 (1.22, 1.42) Cool days (<20°C) Adjusted for PM_{10}: 1.09 (0.97, 1.21) Adjusted for NO_2: 1.07 (0.92, 1.25) Adjusted for O_3: 0.89 (0.80, 0.99) Adjusted for SO_2: 1.03 (0.92, 1.16)
CARDIOVASCULAR DISEASES – NON-SPECIFIC			
Author: Ballester et al. (2001, 013257) **Period of Study:** 1994-1996 **Location:** Valencia, Spain	ED Visits **Health Outcome** (ICD9: CVD (390-459); Heart diseases (410-414, 427, 428); cerebrovascular disease (430-438) **Study Design:** Time series **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 6.2 mg/m^3 **Range (Min, Max):** 0.6, 17.8 **Copollutant:** correlation BS: r = 0.64 NO_2: r = 0.03 SO_2: r = 0.74 O_3: r = -0.26	**Increment:** 1 mg/m^3 **RR Estimate** [Lower CI, Upper CI] ; lag: **Lags examined (days):** 0, 1, 2, 3, 4, 5 All cardiovascular: Lag 2: 1.0077 (0.9912-1.0138) Heart Disease: Lag 1: 1.0092 (0.9945-1.0242) Cerebrovascular Disease: Lag 1: 0.9874 (0.9646-1.0107)
Author: Ballester et al. (2006, 088746) **Period of Study:** 1995-1999 **Location:** 14 Cities in Spain	**Health Outcome** (ICD9: All CVD (390-459);Heart diseases (410-414, 427, 428) **Study Design:** Time series **Statistical Analyses:** GAM **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 8 h **Mean (SD) unit:** Range across 14 cities, 1.4-2.8 mg/m^3 **Range (percentiles):** 10th = 0.4-1.7; 90th = 2.0-3.9 **Copollutant:** NR	**Increment:** 1 mg/m^3 **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0-1 All CVD: Lag 0-1: 2.06 (0.65-3.48) Heart Disease: Lag 0-1: 4.15 (1.31-7.08)
Author: Barnett et al. (2006, 089770) **Period of Study:** 1998-2001 **Location:** Brisbane, Canberra, Melbourne, Perth, Sydney Australia Auckland & Christchurch, New Zealand	Hospital Admissions with CVDs **Health Outcome** (ICD9: Arrythmia (247); Cardiac Disease (390-429); Cardiac Failure (428); IHD (410-413); MI (410); Total CVD (390-459) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed**: 15-64 yr & ≥ 65 yr **Sample Description:** NR	**Averaging Time:** 8 h **Mean (SD) unit:** ppm Brisbane: 1.7 Canberra: 0.9 Melbourne: 1.0 Perth: 1.0 Sydney: 0.8 Auckland: 2.1 Christchurch: 0.5 **Range (Min, Max):** ppm Brisbane: 0.0, 7.0 Canberra: 0.0, 5.8 Melbourne: 0.1, 8.0 Perth: 0.1, 4.0 Sydney: 0.0, 4.5 Auckland: 0.2, 7.9 Christchurch: 0.0, 5.4 **Copollutant** NR	**Increment:** 0.9 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0-1 15-64 yr Arrythmia: 2.5 (0.1-4.9) Cardiac: 1.7 (0.5-2.9) Cardiac Failure: 4.2 (0.6-7.8) IHD: 1.6 (-0.6 to 3.9) MI: 1.8 (-0.7 to 4.3) Total CVD: 1.2 (0.3-2.1) ≥ 65 yr Arrythmia: 0.1 (-1.8 to 2.1) Cardiac: 2.8 (1.3-4.4) Cardiac Failure: 6.0 (3.5-8.5) IHD: 2.3 (0.9-3.8) MI: 2.9 (0.8-4.9) Total CVD: 2.2 (0.9-3.4)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Bell et al. (2009, 193780) **Period of Study:** 1999-2005 **Location:** 126 U.S. urban counties	Hospital Admissions with CVDs **Health Outcome (ICD9):** Cardiac failure (428); cerebrovascular events (430-438); heart rhythm disturbances (426-427); ihd (410-414,429); peripheral vascular disease (440-448) **Study Design:** Time series **Statistical Analyses:** Log-linear over-dispersed Poisson regression **Age Groups Analyzed:** ≥ 65 yr **Sample Description:** >9.3 million Medicare subjects	**Averaging Time:** 1 h **Mean (SD) unit**: 1.6 ppm **Median (SD) unit:** 1.3 ppm **Median Range** (Min, Max): 0.2, 9.7 **Copollutant:** $PM_{2.5}$: r = 0.26 NO_2: r = 0.56 EC: r = 0.48	**Increment:** 1 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0-2 Lag 0: Single pollutant model: 0.96 (0.79-1.12) Adjusted for $PM_{2.5}$: 0.76 (0.57-0.96) Adjusted for NO_2: 0.55 (0.36-0.74) Adjusted for EC: 0.97 (0.38-1.57)
Author: Chang et al. (2005, 080086) **Period of Study:** 1997-2001 **Location:** Taipei, Taiwan	**Health Outcome (ICD9):** CVD Hospital Admissions (410-429) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 74,509 CVD hospital admissions (47 Hospitals)	**Averaging Time:** 24 h **Mean (SD) unit:** 1.37 ppm **Range (Min, Max):** 0.37, 3.66 **Copollutant:** NR	**Increment:** 0.49 ppm **OR Estimate** [Lower CI, Upper CI] **Lag examined (days):** 0-2 ≥ 20°C: 1.090 (1.064-1.118) <20°C: 0.984 (0.927-1.044) Adjusted for PM_{10}: ≥ 20°C: 1.171 (1.132-1.211) <20°C: 0.946 (0.892-1.003) Adjusted for SO_2: ≥ 20°C: 1.232 (1.194-1.272) <20°C: 1.098 (1.034-1.165) Adjusted for NO_2: ≥ 20°C: 1.048 (1.003-1.095 <20°C: 0.983 (0.914-1.058) Adjusted for O_3: ≥ 20°C: 1.196 (1.161-1.232) <20°C: 1.092 (1.031-1.157)
Author: Filhol. (2008, 190260) **Period of Study:** January 2001-July 2003 **Location:** Sao Paulo, Brazil	ED Visits **Health Outcome (ICD10):** Hypertension and Cardiac Ischemic Disease (I10-I25) **Study Design:** Time series **Statistical Analyses:** Linear Poisson regression models **Age Groups Analyzed:** >18 yr **Sample Description:** 45,000 Cardiovascular emergency room visits from diabetic and non-diabetic patients (tertiary referral teaching hospital)	**Averaging Time:** 8 h **Mean (SD) unit:** 2.7 ppm **Range (Min, Max):** 0.7, 12.1 **Copollutant:** correlation PM_{10}: r = 0.69 NO_2: r = 0.58 SO_2: r = 0.52 O_3: r = 0.07	**Increment:** 1.2 ppm **Regression Coefficients** [SEM] **Lags examined (days):** 0, 1, 2 **CVD Visits/Diabetes:** Lag 0: 0.0575 (0.0410) Lag 1: - 0.0056 (0.0418) Lag 2: -0.0324 (0.0426) 2-day moving avg: 0.0324 (0.0470) 3-day moving avg: 0.0074 (0.0528) 4-day moving avg: -0.0025 (0.0582) **CVD Visits/Non-Diabetes:** Lag 0: 0.0286 (0.0095) Lag 1: 0.0098 (0.0091) Lag 2: 0.0102 (0.0089) 2-day moving avg: 0.0271 (0.0108) 3-day moving avg: 0.0281 (0.0120) 4-day moving avg: 0.0306 (0.0131)
Author: Fung et al. (2005, 074322) **Period of Study:** 1995-2000 **Location:** Windsor, Ontario, Canada	Hospital Admissions of CVDs **Health Outcome (ICD9):** CHF (428); IHD (410-414); dysrythmias (427) **Study Design:** Time series Statistical Analyses: GLM **Age Groups Analyzed:** All **Sample Description:** 11,632 Cardiac hospital admissions	**Averaging Time:** 24 h **Mean (SD) unit:** 1.3 ppm **Range (Min, Max):** 0.0, 11.8 **Copollutant:** correlation PM_{10}: r = 0.21 NO_2: r = 0.38 SO_2: r = 0.16 O_3: r = 0.10	**Increment:** 1.2 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0, 0-1, 0-2 <65 yr Lag 0: -3.1 (-7.4 to 1.4) Lag 0-1: -2.7 (-8.1 to 3.0) Lag 0-2: -0.5 (-6.7 to 6.0) ≥ 65 yr Lag 0: 0.5 (-2.2 to 3.3) Lag 0-1: 2.3 (-1.1 to 5.9) Lag 0-2: 2.8 (-1.1 to 7.0)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Jalaludin et al. (2006, 189416) **Period of Study:** 1997-2001 **Location:** Sydney, Australia	ED Visits **Health Outcome (ICD9):** All cardiovascular (390-459); cardiac disease (390-429); IHD (410-413); cerebrovascular or stroke (430-438) **Study Design:** Time series **Statistical Analyses:** GLM & GAM **Age Groups Analyzed:** 65+ yr **Sample Description:** NR	**Averaging Time:** 8 h **Mean (SD) unit:** 0.82 ppm **Range (Min, Max):** 0.02, 4.63 **Copollutant:** correlation PM_{10}: r = 0.31 NO_2: r = 0.71 SO_2: r = 0.51 O_3: r = 0.19	**Increment:** 0.69 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2, 3, 0-1 All Cardiovascular: Lag 0: 2.32 (1.45-3.19) Lag 1: 1.33 (0.47-2.20) Lag 0-1: 2.35 (1.39-3.32) Cardiac Disease: Lag 0: 2.52 (1.50-3.54) Lag 1: 1.85 (0.83-2.88) Lag 2: 1.11 (0.0-2.15) Lag 0-1: 2.85 (1.71-4.01) IHD: Lag 0: 2.83 (1.22-4.48) Lag 1: 1.58 (0.01-3.19) Lag 0-1: 2.86 (1.07-4.68) Stroke: No results were significant for Stroke. All CVD: Cool period: Lag 0: 3.26 (2.00-4.53) Cardiac Disease: Cool period: Lag 0: 3.43 (1.95-4.93) IHD: Cool period: Lag 0: 3.64 (1.28-6.06) Warm period: Lag 0: 2.29 (0.01-4.62) Stroke: Cool period: Lag 0: 3.54 (0.78-6.37) Notes: Cool: May to October Warm: November to April
Author: Koken et al. (2003, 049466) **Period of Study:** 1993-1997 **Location:** Denver, CO	Hospital Admissions for CVD **Health Outcome (ICD9:** MI (410-410.92); coronary atherosclerosis (414-414.05); pulmonary heart disease (416-416.9); cardiac dysrythmia (427-427.9); CHF (428) **Study Design:** Time series **Statistical Analyses:** GLM **Age Groups Analyzed:** >65 yr **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 0.9 ppm **Range (Min, Max):** 0.3, 1.6 **Copollutant:** correlation PM_{10}: r = 0.25 NO_2: r = 0.73 SO_2: r = 0.21 O_3: r = -0.40	**Increment:** 0.3 ppm **% Change** [Lower CI, Upper CI] **Lags examined (days):** 1, 2, 3, 4 CHF: Lag 3: 10.5 (0.1-22.0) CO not significantly associated with other Lag periods.
Author: Linn et al. (2000, 002839) **Period of Study:** 1992-1995 **Location:** Los Angeles, CA	**Health Outcome:** Hospital Admissions for Cardiovascular, Cerebrovascular, Pulmonary. **Study Design:** Time series **Statistical Analyses:** Ordinary least squares regression; Poisson regression **Age Groups Analyzed:** >30 yr **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** Winter: 1.7; Spring: 1.0; Summer: 1.2; Fall: 2.1 **Range (Min, Max):** Winter: 0.5, 5.3; Spring: 0.4, 2.2; Summer: 0.3, 2.7; Fall: 0.2, 4.3 **Copollutant: correlation** Winter: PM_{10}: r = 0.78; NO_2: r = 0.89; O_3: r = -0.43; Spring: PM_{10}: r = 0.54; NO_2: r = 0.92; O_3: 0.29 Summer: PM_{10}: r = 0.72; NO_2: r = 0.94; O_3: 0.03 Fall: PM_{10}: r = 0.58; NO_2: r = 0.84; O_3: r = -0.36	**Increment:** 1 ppm Co-efficient [SE] **Lags examined (lags):** 0, 1 Lag 0: Cardiovascular All: 0.032 (0.003)* (e.g. 3.2% increase) Winter: 0.038 (0.006)* Spring: 0.010 (0.015) Summer: 0.035 (0.014)* Fall: 0.027 (0.006)* Cerebrovascular All: 0.009 (0.007) Winter: -0.008 (0.014) Spring: 0.107 (0.033)* Summer: 0.030 (0.033) Fall: 0.008 (0.012) MI All: 0.040 (0.009) * CHF All: 0.025 (0.009)* Cardiac Arrythmia All: 0.023 (0.009)* Stroke All: 0.044 (0.009)* Notes:* $p < 0.05$

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Metzger et al. (2004, 044222) **Period of Study:** 1993-2000 **Location:** Atlanta, GA	ED Visits (from 31 hospitals) **Health Outcome (ICD9:** Cardiovascular: IHD (410-414); Acute MI (410); Dysrythmia (427); Cardiac Arrest (427.5); CHF (428); Peripheral Vascular & Cereberovascular Disease (PVCD) (433-437, 440, 443, 444, 451-453); Atherosclerosis (440); Stroke (436) **Study Design:** Case-crossover **Statistical Analyses:** Poisson regression (GLM) **Age Groups Analyzed:** All **Sample Description:** 4,407,535 visits	**Averaging Time:** 1 h **Median (SD) unit:** 1.5 ppm **Range (percentiles):** 10th = 0.5; 90th = 3.4 **Copollutant:** correlation PM_{10}: r = 0.47 NO_2: r =0.68 SO_2: r =0.26 O_3: r =0.20	**Increment:** 1 ppm RR Estimate [Lower CI, Upper CI] **Lags examined (days):** 0-2ma All CVD: 1.017 (1.008-1.027) Dysrythmia: 1.012 (0.993-1.031) CHF: 1.010 (0.988-1.032) IHD: 1.016 (0.999-1.034) PVCD: 1.031 (1.010-1.052)
Author: Peel et al. (2007, 090442) **Period of Study:** 1993-2000 **Location:** Atlanta, GA	ED Visits (from 31 hospitals) **Health Outcome (ICD9:** Cardiovascular: IHD (410-414); Dysrythmia (427); CHF (428); PVCD (433-437, 440, 443, 444, 451-453) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 4,407,535 visits	**Averaging Time:** 1-h **Mean (SD) unit:** 1.8 ppm **Range (SD):** SD: 1.2 **Copollutant:** NR	**Increment:** 1.2 ppm OR Estimate [Lower CI, Upper CI] **Lags examined (days):** 0-2ma IHD: Without Diabetes: 1.023 (1.004-1.420) Without CHF: 1.024 (1.006-1.042) Dysrythmias: With Hypertension: 1.065 (1.015-1.118) PVCD: With Hypertension: 1.038 (1.004-1.074) Without Hypertension: 1.027 (1.002-1.054) With Diabetes: 1.065 (1.012-1.121) Without Diabetes: 1.025 (1.003-1.048) With COPD: 1.113 (1.027-1.205) Without COPD: 1.026 (1.004-1.047) Without CHF: 1.029 (1.008-1.051) With Dysrythmias: 1.072 (1.011-1.138) Without Dysrythmias: 1.026 (1.004-1.048) CHF: With COPD: 1.058 (1.003-1.115)
Author: Slaughter et al. (2005, 073854) **Period of Study:** 1995-2001 **Location:** Spokane, WA	Health Outcome (ICD9: Cardiac Hospital Admissions: (390-459) **Study Design:** Time series **Statistical Analyses:** Poisson regression (GLM & GAM) **Age Groups Analyzed:** All **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 0.42-1.82 **Range (Min, Max):** NR **Copollutant correlation:** PM_{10}: r = 0.32 $PM_{2.5}$: r = 0.62	**Increment:** NR **RR Estimate [Lower CI, Upper CI] ;** lag: **Lags examined (days):** 1, 2, 3 No significant association. Results not reported.
Author: Tolbert et al. (2007, 090316) **Period of Study:** 1993-2004 **Location:** Atlanta, GA	ED Visits (from 41 hospitals) **Health Outcome (ICD9):** IHD (410-414), cardiac dysrhythmias (427), CHF (428), peripheral vascular and cerebrovascular diseases (433-437, 440, 443-445 and 451-453) **Study Design:** Time series **Statistical Analyses:** Poisson generalized linear model **Age Groups Analyzed:** NR **Sample Description:** 10,234,490 ED Visits (238,360 CVD group)	**Averaging Time:** 1 h **Mean (SD) unit:** 1.6 ppm **Range (Min, Max):** 0.1, 7.7 **Copollutant:** PM_{10}: r = 0.51 NO_2: r =0.70 SO_2: r =0.28 O_3: r =0.27 $PM_{2.5}$: r = 0.47	**Increment:** NR RR Estimate [Lower CI, Upper CI] **Lags examined (days):** 1, 2, 3 Single-Pollutant Model 3-day ma: 1.020 (1.010, 1.030) Results for multi-pollutant models presented graphically

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Yang et al. (2004, 094376) **Period of Study:** 1997-2000 **Location:** Kaohsiung City, Taiwan	**Health Outcome (ICD9:** CVDs (410-429) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All **Sample Description:** 29,661 Cardiovascular hospital admissions (63 hospitals)	**Averaging Time:** 24 h **Mean (SD) unit:** 0.79 ppm **Range (Min, Max):** 0.24, 1.72 **Copollutant:** NR	**Increment:** 0.28 ppm OR Estimate [Lower CI, Upper CI] **Lag examined (days):** 0-2 ≥ 25°C: 1.264 (1.205-1.326) <25°C: 1.448 (1.357-1.545) Adjusted for PM_{10}: ≥ 25°C: 1.206 (1.146-1.270) <25°C: 1.314 (1.213-1.423) Adjusted for SO_2: ≥ 25°C: 1.406 (1.327-1.489) <25°C: 1.3450 (1.352-1.555) Adjusted for NO_2: ≥ 25°C: 1.246 (1.166-1.332) <25°C: 0.905 (0.819-0.999) Adjusted for O_3: ≥ 25°C: 1.250 (1.191-1.311) <25°C: 1.447 (1.356-1.545)

Table C-3. Studies of CO exposure and neonatal and postneonatal outcomes.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Bell et al. (2007, 091059) **Period of Study:** 1999-2002 **Location:** Connecticut and Massachusetts	**Health Outcome:** Birth weight and LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 358,504 full-term live singleton births (32-44 wk)	**Averaging Time:** 24 h **Mean (SD) unit:** 0.65 ppm (0.18) **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** Interquartile range – 0.30 ppm Regression co-efficient for birth weight (g) [Lower CI, Upper CI] Entire pregnancy: -16.2 (-19.7 to -12.6) Stratified by race. Black mother: -10.9 (-20.2 to -1.6) White mother: -17.5 (-21.3 to -13.7) OR for LBW [Lower CI, Upper CI] Entire pregnancy: 1.028 (0.983-1.074)
Author: Brauer et al. (2008, 156292) **Period of Study:** 1999-2004 **Location:** Vancouver, Canada	**Health Outcome:** LBW, PTB and SGA **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 70,249 live singleton births	**Averaging Time:** LUR model **Mean (SD) unit:** 633 $\mu g/m^3$ **Range (Min, Max):** 124, 1409 **Copollutant: correlation:** PM_{10}: r = 0.73 NO_2: r = 0.75 SO_2: r = 0.82 O_3: r = -0.39	**Increment:** 100 $\mu g/m^3$ OR for SGA [Lower CI, Upper CI] ; Entire pregnancy: 1.06 (1.03-1.08) OR for term LBW [Lower CI, Upper CI] ; Entire pregnancy: 1.02 (0.96-1.09) OR PTB [Lower CI, Upper CI] ; Entire pregnancy: 1.16 (1.01-1.33)
Author: Chen et al. (2002, 024945) **Period of Study:** 1991-1999 **Location:** Northern Nevada	**Health Outcome:** Birth weight & LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 39,338 full term live singleton births (37-44 wk)	**Averaging Time:** 8 h **Mean (SD) unit:** 0.98 ppm **Range (Min, Max):** 0.25, 4.87 **Copollutant:** NR	**Increment:** NR Regression co-efficient for birth weight (g) [SE] Trimesters: First: -1.02 (6.68) Second: -0.07 (6.58) Third: -3.95 (6.76) Entire pregnancy: -8.28 (14.9) **Notes:** CO not associated with LBW

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Conceicao et al. (2001, 016628) **Period of Study:** 1994-1997 **Location:** Sao Paulo, Brazil	**Health Outcome:** Child mortality, under 5 yr of age **Study Design:** Time series **Statistical Analyses:** Poisson regression (GAM) **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 4.4 ppm (2.2) **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR Regression co-efficient for Child mortality – under 5 yr of age [SE] ; **Lags examined:** 0, 1, 2, 3 Lag 2: 0.0306 (0.0076) ($p < 0.01$) Lag chosen for best fitting model
Author: Gilboa et al. (2005, 087892) **Period of Study:** 1997-2000 **Location:** Texas	**Health Outcome:** Birth defects (heart defects and orofacial clefts) **Study Design:** Case control **Statistical Analyses:** Conditional Logistic regression **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** Exposure categories (ppm):<0.4; 0.4 – 0.5; 0.5 – 0.7; >0.7 OR for Birth Defects [Lower CI, Upper CI] ; Exposure period: wk 3 to 8 of pregnancy Conotruncal defects: 1.00; 1.38 (0.97-1.97); 1.17 (0.81-1.70); 1.46 (1.03-2.08) Tetralogy of Fallot: 1.00; 0.92 (0.52-1.62); 1.27 (0.75-2.14); 2.04 (1.26-3.29) Notes: CO was not associated with the following defects: Aortic artery and valve, atrial septal, pulmonary artery and valve, ventricular septal, endocardial cushion and mitral valve , cleft lip, cleft palate, aortic valve stenosis, coarctation of the aorta, ostium secundum.
Author: Gouveia et al. (2004, 055613) **Period of Study:** 1997 **Location:** Sao Paulo, Brazil	**Health Outcome:** Birth weight & LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 179,460 live singleton term births (>37 wk)	**Averaging Time:** 8 h **Mean (SD) unit:** 3.7 ppm **Range (Min, Max):** 1.1, 11.4 **Copollutant:** NR	**Increment:** 1 ppm Regression co-efficient for birth weight (g) [Lower CI, Upper CI] Trimesters: First: -23.1 (-41.3 to -4.9) Second: 3.2 (-18.2 to 24.5) Third: 1.9 (-18.2 to 22.0) OR for LBW) [Lower CI, Upper CI] 4th quartile exposure (compared to lowest quartile): First: 1.02 (0.82-1.27); Second: 1.07 (0.88-1.30); Third: 0.93 (0.76-1.12)
Author: Ha et al. (2001, 019390) **Period of Study:** 1996-1997 **Location:** Seoul, South Korea	**Health Outcome:** LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression (GAM) **Age Groups Analyzed:** NA **Sample Description:** 276 763 full-term live singleton births (>37 wk)	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** Percentiles: 25th: 0.99 ppm 75th: 1.41 ppm **Copollutant correlation:** TSP: r = 0.73 NO_2: r = 0.75 SO_2: r = 0.82 O_3: r = -0.39	**Increment:** 0.42 ppm RR for LBW [Lower CI, Upper CI] Trimesters: First: 1.08 (1.04, 1.12) Third: 0.91 (0.87, 0.96)
Author: Ha et al. (2003, 042552) **Period of Study:** 1995-1999 **Location:** Seoul, South Korea	**Health Outcome:** Post-neonatal mortality (1 mo-1 yr) (also looked at older age groups) **Study Design:** Time series **Statistical Analyses:** Poisson regression (GAM) **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 1.2 ppm **Range (Min, Max):** 0.39, 3.38 **Copollutant correlation:** PM_{10}: r = 0.63 NO_2: r = 0.72 SO_2: r = 0.75 O_3: r = -0.46	**Increment:** 0.57 ppm RR for Post–neonatal mortality (1 mo-1 yr) [Lower CI, Upper CI] **Lags examined:** 0 Total mortality: Lag 0: 1.020 (0.976-1.067) Respiratory mortality: Lag 0: 1.388 (1.009-1.911)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Hajat et al. (2007, 093276) **Period of Study:** NR **Location:** Birmingham, Bristol, Leeds, Liverpool, London, Manchester, Middlesbrough, Newcastle, Nottingham, Sheffield England	**Health Outcome:** Neonatal and postneonatal mortality **Study Design:** Time series **Statistical Analyses:** Poisson regression (GLM) **Age Groups Analyzed:** NA **Sample Description:** 22,288 total infant deaths between 1990 and 2000	**Averaging Time:** 3 days **Mean (SD) unit:** (mg/m^3) Birmingham: 0.64; Bristol: 1.01; Leeds: 0.73; Liverpool: 0.51; London: 0.77; Manchester: 0.63; Middlesbrough: 0.37; Newcastle: 0.67; Nottingham: 0.62; Sheffield: 0.60 **Range (Min, Max):** Birmingham: 0.4, 0.8; Bristol: 0.6, 1.2; Leeds: 0.5, 0.9; Liverpool: 0.3, 0.6; London: 0.5, 0.9; Manchester: 0.4, 0.7; Middlesbrough: 0.2, 0.4; Newcastle: 0.5, 0.8; Nottingham: 0.4, 0.7; Sheffield: 0.3, 0.7 **Copollutant:** SO_2, NO_2, NO, O_3, PM_{10}	**Increment:** 1 mg/m^3 **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0, 1, 2 All infant deaths: 1.02 (0.96, 1.09) Neonatal deaths: 0.99 (0.92, 1.07) Post-neonatal deaths: 1.09 (0.94, 1.25) City-specific results of all infant mortality displayed graphically
Author: Huynh et al. (2006, 091240) **Period of Study:** 1999-2000 **Location:** California	**Health Outcome:** PTB (24-36 wk gestation) **Study Design:** Case-control **Statistical Analyses:** Conditional Logistic regression **Age Groups Analyzed:** Cases = 24- to 36-wk gestation; Controls = 39- to 44-wk **Sample Description:** 10,673 PTBs (cases); 32,119 term births (controls)	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** 1 ppm Exposure level – Quartiles of exposure for first mo and last two wk of gestation (mg/m^3) First: <0.61; Second: 0.61 – 0.82; Third: 0.82 – 1.07; Fourth: >1.07 Quartiles for entire pregnancy and last two wk of pregnancy were similar. OR for PTB [Lower CI, Upper CI] First mo of gestation: Per 1 ppm increase: 1.10 (0.99-1.20) Second quartile: 0.94 (0.88-1.01) Third quartile: 1.04 (0.97-1.11) Fourth quartile: 1.05 (0.96-1.14) Last two wk of gestation: Per 1 ppm increase: 1.00 (0.93-1.09) Second quartile: 1.03 (0.97-1.10) Third quartile: 1.04 (0.97-1.12) Fourth quartile: 0.99 (0.91-1.08) Entire pregnancy: Per 1 ppm increase: 1.06 (0.95-1.18) Second quartile: 0.97 (0.91-1.04) Third quartile: 0.99 (0.92-1.05) Fourth quartile: 1.02 (0.94-1.09) Lowest quartile used as reference group
Author: Hwang and Jaakkola (2008, 193794) **Period of Study:** 2001-2003 **Location:** Taiwan	**Health Outcome:** Oral clefts (with or without palate) **Study Design:** Case control **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 6,530 cases from 721,289 newborns	**Averaging Time:** 8 h **Mean (SD) unit:** 0.69 (0.4) **Range (Min, Max):** 0.25, 2.7 **Copollutant correlation:** PM_{10}: r = -0.19 NO_X: r = 0.82 SO_2: r = 0.24 O_3: r = -0.19	**Increment:** 100 ppb **RR for oral cleft** [Lower CI, Upper CI] Month 1: 1.00 (0.96-1.04) Month 2: 1.00 (0.96-1.03) Month 3: 1.00 (0.96-1.03)
Author: Jalaludin et al. (2007, 156601) **Period of Study:** 1998-2000 **Location:** Sydney, Australia	**Health Outcome:** PTB **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 123,840 full term live singleton births (<42 wk)	**Averaging Time:** 8 h **Mean (SD) unit:** 0.9 ppm (0.68) **Range (Min, Max):** NR **Copollutant correlation:** PM_{10}: r = 0.28 NO_2: r = 0.60 SO_2: r = 0.24 O_3: r = -0.21	**Increment:** 1 ppm **RR for PTB** [Lower CI, Upper CI] First mo: All of Sydney: 0.89 (0.84-0.95) Within 5km of site: 1.03 (0.68-1.54) First trimester: All of Sydney: 0.77 (0.71-0.83) Within 5km of site: 1.24 (0.81-1.91) 1 mo prior to birth: All of Sydney: 0.96 (0.88-1.04) Within 5km of site: 1.00 (0.86-1.15) 3 mo prior to birth: All of Sydney: 0.99 (0.90-1.09) Within 5km of site: 1.11 (0.94-1.31)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Lee et al. (2003, 043202) Period of Study: 1996-1998 **Location:** Seoul, South Korea	**Health Outcome:** LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 388,105 full-term live singleton births (37-44 wk)	**Averaging Time:** 24 h **Mean (SD) unit:** 1.2 ppm **Range (Min, Max):** 0.4, 3.4 **Copollutant correlation:** PM_{10}: r = 0.47 NO_2: r = 0.77 SO_2: r = 0.79	**Increment:** 0.5 ppm **OR for LBW** [Lower CI, Upper CI] First: 1.04 (1.01-1.07) Second: 1.03 (1.00-1.06) Third: 0.96 (0.93-0.99) Entire pregnancy: 1.05 (1.01-1.09)
Author: Leem et al. (2006, 089828) **Period of Study:** 2001-2002 **Location:** Incheon, Korea	**Health Outcome:** PTB **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 52,113 live singleton births	**Averaging Time:** Kriging was used to estimate exposure **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant correlation:** PM_{10}: r = 0.27 NO_2: r = 0.63 SO_2: r = 0.31	**Increment:** Exposure level – Quartiles of exposure for first trimester (mg/m^3) First: 0.47-0.63; Second: 0.6 -0.77; Third: 0.78-0.90; Fourth: 0.91-1.27 - exposure groups for third trimester was similar OR for PTB [Lower CI, Upper CI] First Trimester: Second quartile: 0.92 (0.81-1.05) Third quartile: 1.14 (1.01-1.29) Fourth quartile: 1.26 (1.11-1.44) Third Trimester: Second quartile: 1.07 (0.95-1.21) Third quartile: 1.07 (0.94-1.22) Fourth quartile: 1.16 (1.01-1.34) Lowest quartile used as reference group.
Author: Lin et al. (2004, 095787) **Period of Study:** 1998-2000 **Location:** Sao Paulo, Brazil	**Health Outcome:** Neonatal death (within first 28 days of life) **Study Design:** Time series **Statistical Analyses:** Poisson regression (GAM) **Age Groups Analyzed:** NA Sample Description: NR	**Averaging Time:** 24 h **Mean (SD) unit:** 2.83 ppm **Range (Min, Max):** 0.54, 10.25 **Copollutant correlation:** PM_{10}: r = 0.71 NO_2: r = 0.67 SO_2: r = 0.55 O_3: r = 0.03	**Increment:** NR Regression coefficent for neonatal death [SE] **Lags examined:** 0 Lag 0: 0.0061 (0.0110)
Author: Lin et al. (2004, 089503) **Period of Study:** 1995-1997 **Location:** Taipei & Kaoshiung, Taiwan	**Health Outcome:** LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 92,288 full-term live singleton births (>37 wk) within 3 km of monitoring site.	**Averaging Time:** 24 h **Mean (SD) unit:** Taipei (avg over 5 sites) 0.84-1.31 Kaohsiung (avg over 5 sites) 5.56-10.05 **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** Exposure groups M = Median exposure 1.1-14.2 ppm H = High exposure >14.2 ppm OR for LBW [Lower CI, Upper CI] Trimesters: First: M 1.01 (0.89, 1.16), H 0.90 (0.75, 1.09) Second: M 1.02 (0.90, 1.16), H 1.00 (0.82, 1.22) Third: M 0.88 (0.77, 1.00), H 0.86 (0.71, 1.03) Entire pregnancy: M 0.89 (0.77, 1.01), H 0.77 (0.63, 0.94) **Notes:** Cut off for exposures groups for second and third trimester were similar to those presented above.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Liu et al. (2003, 089548) **Period of Study:** 1985-1998 **Location:** Vancouver, BC, Canada	**Health Outcome:** PTB, IUGR, LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 229,085 live singleton births	**Averaging Time:** 24 h **Mean (SD) unit:** 1.0 ppm **Range (Min, Max):** 25th: 0.7; 75th: 1.2 **Copollutant:** NR	**Increment:** 1.0 ppm OR for LBW [Lower CI, Upper CI] Month of pregnancy: First mo: 1.01 (0.93-1.09) Last mo: 0.96 (0.88-1.04) OR for PTB [Lower CI, Upper CI] First mo: 0.95 (0.89-1.01) Last mo: 1.08 (1.01-1.15) OR for IUGR [Lower CI- Upper CI] First mo: 1.06 (1.01-1.10) Last mo: 0.98 (0.94-1.03) Trimester 1: 1.05 (1.00-1.10) Trimester 2: 0.97 (0.92-1.01) Trimester 3: 0.97 (0.93-1.02)
Author: Liu et al. (2007, 090429) **Period of Study:** 1995-2000 **Location:** Calgary, Edmonton, and Montreal, Canada	**Health Outcome:** IUGR **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 386,202 live singleton births	**Averaging Time:** 24 h **Mean (SD) unit:** 1.1 ppm **Range (Min, Max):** 25th: 0.6; 75th: 1.3 **Copollutant correlation:** $PM_{2.5}$: r = 0.31 NO_2: r = 0.71 SO_2: r = 0.21 O_3: r = -0.42	**Increment:** 1 ppm **RR for LBW** [Lower CI, Upper CI] **Notes:** CO was associated with an increased risk of IUGR of approximately 16% and 23% in the first and nine mo of pregnancy. (All results presented in Figures)
Author: Maisonet et al. (2001, 016624) **Period of Study:** 1994-1996 **Location:** Northeastern USA	**Health Outcome:** Live birth weight **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 89,557 live singleton term births (37-44 wk)	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Range (Min, Max):** Percentiles: 25th: 0.93 ppm; 75th: 1.23 ppm **Copollutant:** NR	**Increment:** 1 ppm **OR for LBW [Lower CI, Upper CI]** Trimester: First: 1.08 (0.91-1.28); Second: 1.14 (0.83-1.58); Third: 1.31 (1.06-1.62) Stratified results among African-Americans: First: 1.43 (1.18-1.74); Second: 1.27 (0.87-1.86); Third: 1.75 (1.50-2.04) **Notes**: CO had no effect on whites or Hispanics
Author: Mannes et al. (2005, 087895) **Period of Study:** 1998-2000 **Location:** Sydney, Australia	**Health Outcome:** Birth weight and SGA **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 138,056 full-term all singleton births (including stillbirths) (at least 20-wk gestation)	**Averaging Time:** 8 h **Mean (SD) unit:** 0.8 ppm **Range (Min, Max):** 0.0, 4.6 **Copollutant: correlation** PM_{10}: r = 0.26 NO_2: r = 0.57 O_3: r = -0.20	**Increment:** 1 ppm Regression coefficients for birth weight (g) [Lower CI, Upper CI] All births: First trimester: 1.86 (-8.31 to 12.03) Second trimester: -10.72 (-23.09 to 1.65) Third trimester: -6.63 (-18.57 to 5.31) One mo prior to birth: -15.28 (-25.59 to -4.97) Births within 5 km of monitor: First trimester: -8.56 (-28.60 to 10.68) Second trimester: -28.87 (-50.98 to -6.76) Third trimeste: -22.88 (-44.58 to -1.18) One mo prior to birth: -10.41 (-30.03 to 9.21) OR for SGA [Lower CI, Upper CI] All births: First trimester: 0.95 (0.88-1.04) Second trimester: 0.99 (0.90-1.10) Third trimester: 1.01 (0.91-1.11) One mo prior to birth: 1.06 (0.98-1.16) Births within 5km of monitor: First trimester 0.99 (0.86-1.14) Second trimester: 1.06 (0.90-1.25) Third trimester: 1.05 (0.90-1.23) One mo prior to birth: 1.10 (0.96-1.27)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Medeiros et al. (2005, 089824) **Period of Study:** 1998-2000 **Location:** Sao Paulo, Brazil	**Health Outcome:** Birth weight and LBW **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 311,735 full-term live singleton births (37-41 wk)	**Averaging Time:** 24 h **Mean (SD) unit:** Daily mean shown in Figure (see paper) **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** 1 ppm **Regression coefficient for birth weight (g) [Lower CI, Upper CI]** Trimesters: First: -11.9 (-15.5 to -8.2); Second: 4.9 (0.5-9.3); Third: 12.1 (7.6-16.6) OR for LBW [Lower CI, Upper CI] 4th quartile exposure (compared to lowest quartile) First: 0.98 (0.91-1.06); Second: 0.97 (0.90-1.05); Third: 1.03 (0.96-1.11)
Author: Mortimer et al. (2008, 187280) **Period of Study:** November 2000-April 2005 **Location:** Central Valley of Californinia	**Health Outcome:** Allergic sensitization **Study Design:** Cohort **Statistical Analyses:** Chi-square tests **Age Groups Analyzed:** 6-11 yrs. **Sample Description:** 170 children with asthma from the FACES-LiTE study	**Averaging Time:** 8 h **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** Entire Prenatal: PM_{10}: r = 0.32 NO_2: r = 0.74 O_3: r = -0.40 Trimester 2: PM_{10}: r = 0.32 NO_2: r = 0.68 O_3: r = -0.26	**Increment:** NR Trimester specific results presented graphically Single-pollutant Model for "sensitized to at least one outdoor allergen" **OR adjusted for yr of birth and sex [Lower CI, Upper CI]** Entire Pregnancy 24-h avg: 1.45 (1.02, 2.07) Daily max: 1.53 (1.01, 2.33) 8-h max: 1.55 (1.01, 2.37) 2nd Trimester 24-h avg: 1.52 (0.93, 2.47) Daily max: 1.50 (0.92, 2.45) 8-h max: 1.45 (0.90, 2.35) Coefficient adjusted for yr of birth and sex [SE] Entire Pregnancy 24-h avg: 1.33 (0.68) Daily max:0.54 (0.27) 8-h max: 0.84 (0.42) 2nd Trimester 24-h avg: 0.57 (0.34) Daily max: 0.21 (0.13) 8-h max: 0.32 (0.21)
Author: Parker et al. (2005, 087462) **Period of Study:** 2000 **Location:** California	**Health Outcome:** Birth weight & SGA **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 18,247 full-term live singleton births (40 wk) within 5 mi of a monitor	**Averaging Time:** 24 h **Mean (SD) unit:** 0.78 ppm **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** Quartiles of exposure for first trimester First: <0.57; Second: 0.57-0.76 ; Third: 0.76- 0.93; Fourth: >0.93 - exposure groups for other trimesters were similar Regression co-efficient for birth weight (g) [Lower CI, Upper CI] Trimesters: 4th quartile exposure (compared to lowest quartile) First: -7.3 (-29.7 to 15.0); Second: 14.2 (-8.9 to 37.3); Third: -8.4 (-32.2 to 15.3); Entire pregnancy: -20.5 (-40.1 to -0.8) OR for SGA [Lower CI, Upper CI] 4th quartile exposure (compared to lowest quartile) First: 0.91 (0.76-1.09); Second: 0.80 (0.66-0.97); Third: 0.90 (0.75-1.10); Entire pregnancy: 0.95 (0.81-1.12)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Ritz et al. (2000, 012068) **Period of Study:** 1989-1993 **Location:** Southern California	**Health Outcome:** PTB **Study Design:** Retrospective Cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** Eligible study subjects were singletons born at 26- to 44-wk gestation **Sample Description:** 97,518 neonates born in Southern California	**Averaging Time:** 6-9 a.m. **Mean (SD) unit:** 2.70 ppm **Range (Min, Max):** 0.36, 9.12 **Copollutant correlation:** PM_{10}: r = 0.37 NO_2: r = 0.60 O_3: r = -0.44	**Increment:** 3 ppm **RR for PTB [Lower CI, Upper CI]** Adjusted for various risk factors and season of birth and conception 6 wk prior to birth: 1.04 (0.99-1.10) 1st mo of pregnancy: 1.04 (0.99-1.09) Adjusted for various risk factors 6 wk prior to birth: 1.06 (1.02-1.10) 1st mo of pregnancy: 1.01 (0.97-1.04)
Author: Ritz et al. (2002, 023227) **Period of Study:** 1987-1993 **Location:** Southern California	**Health Outcome:** Birth defects (heart defects and orofacial clefts) **Study Design:** Case control **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** Exposure categories: ppm <1.14; 1.14-1.57; 1.57- 2.39; >2.39 **OR for Birth defects [Lower CI, Upper CI]:** Period of exposure: Second mo of pregnancy. Aortic artery and valve defects: 1.00 (ref group); 1.10 (0.73-1.66); 1.25 (0.74-2.13); 0.93 (0.47-1.85) Pulmonary artery and valve anomalies: 1.00 (ref group); 1.09 (0.69-1.73); 0.92 (0.50-1.70); 1.00 (0.46-2.17) Ventricular septal defects: 1.00 (ref group); 1.62 (1.05-2.48); 2.09 (1.19-3.67); 2.95 (1.44-6.05) Conotruncal defects: 1.00 (ref group); 0.79 (0.47-1.32); 0.73 (0.36-1.47); 0.95 (0.38-2.38) **Notes:** Results also presented for more specific defects, however CO showed no association (see paper Table 3.). CO not associated with orofacial clefts)
Author: Ritz et al. (2006, 089819) **Period of Study:** 1989-2000 **Location:** Southern California	**Health Outcome:** Postneonatal mortality (28 days to 1 yr); all causes; SIDS **Study Design:** Case control **Statistical Analyses:** Conditional Logistic regression **Sample Description:** Mothers residing within 16 km of monitoring site	**Averaging Time:** 24 h **Mean (SD) unit:** 1.63 ppm **Range (Min, Max):** 0.38, 3.44 **Copollutant:** correlation PM_{10}: r = 0.33 NO_2: r = 0.72 O_3: r = -0.57	**Increment:** 1 ppm OR for Post-neonatal death [Lower CI, Upper CI] Exposure period: 2 wk prior to death, 1 mo prior to death, 2 mo prior to death, 6 mo prior to death All causes: 2 wk prior to death: 1.14 (1.03-1.25) 2 mo prior to death: 1.11 (1.06-1.16) SIDS: 2 mo prior to death: 1.19 (1.10-1.28) Term/normal weight births 2 mo prior to death: All causes: 1.12 (1.05-1.19) SIDS: 1.17 (1.07-1.29) Respiratory: 1.14 (0.95-1.36) Preterm &/or LBW births 2 mo prior to death: All causes: 1.12 (1.01-1.25) SIDS: 1.46 (1.09-1.94) Respiratory: 1.03 (0.83-1.27) Notes: These results did not persist in multipollutant models (CO, NO_2, PM_{10}, O_3)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Ritz et al. (2007, 096146) Period of Study: January-December 2003 **Location:** Los Angeles, CA	**Health Outcome:** PTB **Study Design:** Nested case-control **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** A survey of 2,543 of 6,374 women sampled from a cohort of 58,316 eligible births in Los Angeles county.	**Averaging Time:** 24 h **Mean (SD) unit:** NR **Copollutant correlation:** TSP: r = 0.73 NO_2: r = 0.75 SO_2: r = 0.82 O_3: r = -0.39	**Increment: Exposure categories (ppm):** Less than 0.58: 0.59-0.91; 0.92-1.25; >1.25 RR for LBW [Lower CI, Upper CI] First trimester: 1.00 (Ref group); 1.17 (1.08-1.26); 1.15 (1.05-1.26); 1.25 (1.12-1.38) 6 wk prior to birth 1.00 (Ref group); 1.00 (0.93-1.08); 1.08 (0.98-1.20); 1.03 (0.93-1.14) Entire pregnancy: 1.00 (Ref group); 0.76 (0.70-0.82); 0.84 (0.77-0.91); 1.03 (0.91-1.17)
Author: Salam et al. (2005, 087885) **Period of Study:** 1975-1987 **Location:** California	**Health Outcome:** Birth weight, LBW , IUGR **Study Design:** Retrospective cohort **Statistical Analyses:** Linear and logistic regression **Age Groups Analyzed:** NA **Sample Description:** 3,901 infants from the California Children's Health Study	**Averaging Time:** 24-h **Mean (SD) unit:** 1.8 ppm (0.9) (Entire pregnancy) **Range:** NR **Copollutant: correlation** PM_{10}: r = 0.41 NO_2: r = 0.69 O_3: r = -0.27	**Increment:** Entire pregnancy 1.2 ppm Trimesters: First: 1.4 ppm; Second: 1.4 ppm; Third: 1.3 ppm **Regression co-efficient for birth weight (g) [Lower CI, Upper CI]** Trimesters: First: -21.7 (-42.3 to -1.1); Second: 11.3 (-9.7 to 32.3); Third: 11.8 (-8.4 to 32.1); Entire pregnancy: 2.2 (-20.1 to 24.4) OR for LBW [Lower CI, Upper CI] Trimesters: First: 1.0 (0.7-1.5); Second: 0.9 (0.6-1.3); Third: 0.7 (0.5-1.1); Entire pregnancy: 0.8 (0.6-1.3) OR for IUGR [Lower CI, Upper CI] Trimesters: First: 1.2 (1.0-1.4); Second: 1.0 (0.9-1.1); Third: 1.0 (0.8-1.1); Entire pregnancy: 1.0 (0.9-1.2)
Author: Son et al. (2008, 190323) **Period of Study:** NR **Location:** Seoul, Korea	**Health Outcome:** Postneonatal mortality from all causes **Study Design:** Case crossover and time series **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** NA **Sample Description:** 1,286 first-born birth and infant death records from 1999-2003 (only postneonatal deaths)	**Averaging Time:** 8 h **Mean (SD) unit:** 1.01 ppm **Range (Min, Max):** 0.29, 3.54 **Copollutant:** PM_{10}, NO_2, O_3, SO_2	**Increment**: NR **RR Estimate** [Lower CI, Upper CI] **Lags examined (days):** 0-7 Time Series: 1.323 (1.077, 1.625) Case-crossover(1:6): 1.029 (0.833, 1.271) CLR Analyses using different control selection schemes 1:2: 1.076 (0.839, 1.379) 1:4: 0.981 (0.784, 1.228) 1:6: 1.029 (0.833, 1.271)
Author: Strickland et al. (2009, 190324) **Period of Study:** NR **Location:** Atlanta, GA	**Health Outcome:** Cardiovascular malformations **Study Design:** Retrospective cohort **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** NA **Sample Description:** Pregnancies reaching at least 20-wk gestation that were conceived during January 1, 1986-March 12, 2003	**Averaging Time:** 24-h **Mean (SD) unit:** By season of conception: March-May: 0.9 ppm June-August: 0.8 ppm Sept.-Nov.: 0.9 ppm Dec.-Feb.: 0.7ppm By yr of conception: 1986-1991: 0.7 ppm 1992-1997: 0.8 ppm 1998-2003: 0.7 ppm **Range (IQR):** 0.3 **Copollutant:** PM_{10} (24 h): r = 0.32 NO_2 (24 h): r = 0.41 O_3 (8 h): r = 0.07 SO_2 (24 h): r = 0.23	**Increment:** NR **RR Estimate** [Lower CI, Upper CI] Atrial septal defect, secundum: 1.16 (0.67, 2.00) Coarctation of the aorta: 1.15 (0.65, 2.06) Hypoplastic left heart syndrome: 0.82 (0.37, 1.84) Patent ductus arteriosus: 1.39 (0.72, 2.68) Pulmonary stenosis, valvar: 0.97 (0.53, 1.75) Tetralogy of Fallot: 1.09 (0.59, 2.00) Transposition of the great arteries: 1.29 (0.58, 2.85) Ventricular septal defect, muscular: 1.08 (0.77, 1.50) Ventricular septal defect, perimembranous: 1.06 (0.67, 1.68) Conotruncal defect: 1.22 (0.81, 1.85) Left ventricular outflow tract defect: 1.09 (0.70, 1.68) Right ventricular outflow tract defects: 0.73 (0.44, 1.22)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Tsai et al. (2006, 090709) **Period of Study:** 1994-2000 **Location:** Kaoshiung, Taiwan	**Health Outcome:** Postneonatal death (27 days-1 yr old) **Study Design:** Case crossover **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** 8.27 ppm x10 **Range (Min, Max):** 2.26, 17.7 **Copollutant**: NR	**Increment: Interquartile range:** 0.31 ppm OR for Post-neonatal mortality [Lower CI, Upper CI] **Lag examined:** 0-2 Lag 0-2: 1.051 (0.304-3.630)
Author: Wilhelm et al. (2005, 088668) **Period of Study:** 1994-2000 **Location:** Los Angeles, CA	**Health Outcome:** Term LBW and PTB **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** NA **Sample Description:** 518,254 births within 4 mi of a monitoring station. Varied according to analyses.	**Averaging Time:** 24 h **Mean (SD) unit**: Trimester 1: 1.42 ppm Results for third trimester and 6 wk prior to birth were similar to first trimester **Range (Min, Max):** 0.26, 2.82 **Copollutant correlation:** First Trimester: PM_{10}: r = 0.12 $PM_{2.5}$: r = 0.57 NO_2: r = 0.81 SO_2: r = -0.31	**Increment:** 1 ppm **RR for PTB** [Lower CI, Upper CI] First trimester: <1 mile: 1.06 (1.00-1.12) 1-2 miles: 1.06 (1.03-1.10) 2-4 miles: 1.08 (1.06-1.09) ZIP code level: 1.04 (1.01-1.07) 6 wk prior to birth: <: 1.04 (0.98-1.09) 1-2 miles: .04 (1.01-1.08) 2-4 miles: 1.01 (0.99-1.02) ZIP code level: 1.03 (1.00-1.06) **Notes:** All results above did not persist in multipollutant model (CO, NO_2, O_3, PM_{10}) OR for term LBW [Lower CI, Upper CI] Third trimester: <1 mile: 1.10 (0.98-1.23) 1-2 miles: 1.05 (0.99-1.13) 2-4 miles: 1.06 (1.02-1.10) ZIP code level: 1.12 (1.05-1.19) **Notes:** All results above did not persist in multipollutant model (CO, NO_2, O_3, PM_{10}) See paper for results based on exposure category groupings.
Author: Woodruff et al. (2008, 098386) **Period of Study:** 1999-2002 **Location:** U.S. counties with >250,000 residents	**Health Outcome:** Postneonatal deaths all causes; respiratory; SIDS; ill-defined + SIDS; other causes. **Study Design:** Retrospective cohort **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** 24 h **Mean (SD) unit:** All causes: 0.70 ppm **Range (Min, Max):** Percentiles: 25th: 0.48; 75th: 0.87 **Copollutant correlation:** PM_{10}: r = 0.18 SO_2: r = 0.27 O_3: r = -0.46	**Increment:** 0.39 ppm **OR for Post-neonatal mortality [Lower CI, Upper CI]** Avg exposure over the first 2 mo of life: All causes: 1.01 (0.95-1.07) Respiratory: 1.14 (0.93-1.40) SIDS: 0.88 (0.76-1.03) Ill-defined + SIDS: 0.93 (0.84-1.02) Other causes: 1.02 (0.97-1.07)
Author: Yang et al. (2004, 094376) **Period of Study:** 1994-2000 **Location:** Taipei, Taiwan	**Health Outcome:** Postneonatal mortality (27 days-1 yr old) **Study Design:** Case crossover **Statistical Analyses:** Poisson regression **Age Groups Analyzed:** NA **Sample Description:** NR	**Averaging Time:** 24-h **Mean (SD) unit:** 15.8 ppm x10 **Range (Min, Max):** 3.20, 48.4 **Copollutant:** NR	**Increment:** Interquartile range: 0.56 ppm OR for Post-neonatal mortality [Lower CI, Upper CI] **Lag examined**: 0-2 Lag 0-2: 1.038 (0.663-1.624)

Table C-4. Studies of short-term CO exposure and respiratory morbidity

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Andersen et al. (2008, 096150) **Period of Study:** Dec 1998-Dec 2004 **Location:** Copenhagen, Denmark	**Health Outcome:** Wheezing symptoms **Study Design:** Panel **Statistical Analyses**: Logistic regression (GEE) **Age Groups Analyzed:** 0-3 yrs **Sample Description:** 205 children of mothers with asthma	**Averaging Time:** 24h **Mean (SD) unit:** 0.29 (0.10) ppm **Range (percentiles):** 25th = 0.22; 75th = 0.34 **Copollutant: correlation** PM_{10}: r = 0.45 $PM_{2.5}$: r = 0.45 UFPNC: r = 0.52 NO_2: r = 0.75 NO_X: r = 0.74 O_3: r = -0.63	**Increment:** NR **OR Estimate [Lower CI, Upper CI] ;** lag: **Lags examined:** 0, 1, 2, 3, 4, 2-4 Lag 0: 0.96 (0.80, 1.15) Lag 1: 0.92 (0.77, 1.10) Lag 2: 1.08 (0.92, 1.28) Lag 3: 1.07 (0.90, 1.26) Lag 4: 1.02 (0.84, 1.23) 3d mean: 1.07 (0.87, 1.32)
Author: Bhattacharyya et al. (2009, 180154) **Period of Study:** 1997-2006 **Location:** NR (National Health Interview Survey as aggregated in the Integrated Health Interview Series served as data source)	**Health Outcome:** Respiratory morbidity **Study Design:** Cross-sectional study **Statistical Analyses:** SPSS version 14.0, univariate linear regression analysis **Age Groups Analyzed:** 18+ yr (avg: 45.2 yr) **Sample Description:** Hay fever, weak/failing kidneys, sinusitis all in past 12 mo	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** 2.209-4.157ppm (decreased with increasing yr) **Copollutant:** NR	**Increment:** NR Linear regression analysis for disease condition prevalence: Hayfever: Standardized B- 0.012, p-value- <0.001; Sinusitis: Standardized B- 0.027, p-value- <0.001; Kidney Weak/Failin: Standardized B- -0.001, p-value- <0.001 **Lags examined:** NR
Author: Chen et al. (1999, 011149) **Period of Study:** 5/1995-1/1996 **Location:** 3 Taiwan communities	**Health Outcome:** Lung function (FVC, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, PEF) **Study Design:** Cross-sectional survey **Statistical Analyses:** Multivariate linear model **Population:** 941 children (Boys: 453; Girls: 488) **Age Groups Analyzed:** 8-13 yr	**Pollutant:** CO **Averaging Time:** 1-h max; 24-h avg **Mean (SD) unit**: NR **Range (Min, Max):** 1-h max: (0.4, 3.6) **Copollutant correlation:** NO_2: r = 0.86 – 0.98 **Note:** To represent the schoolchildren's exposure the daytime avg and peak concentrations were measured from 0800 to 1800.	**Increment:** NR **β Coefficient (SE); lag:** FVC (mL) 24-h avg -66.6 (40.73); 1 -147.71 (64.48); 2 2.2 (48.13); 7 1-h max -33.25 (20.74); 1 -16.48 (19.67); 2 -5.18 (16.48); 7 FEV_1 (mL) 24-h avg 20.55 (38.24); 1 -82.42 (60.95); 2 48.23 (45.58); 7 1-h max 1.2 (19.48); 1 -1.44 (18.57); 2 20.96 (15.67); 7
Author: Chen et al. (2000, 011931) **Period of Study:** 8/1996-6/1998 **Location:** Washoe County, NV	**Health Outcome:** School absenteeism **Study Design:** Time series **Statistical Analyses:** Maximum likelihood **Population:** 1st to 6th grade children: 27,793 **Age Groups Analyzed:** 1st to 6th grade children	**Pollutant:** CO **Averaging Time:** 1-h max **Mean (SD) unit:** 2.73 (1.154) ppm **Range (Min, Max):** (0.65, 2.73) **Copollutant correlation:** PM_{10}: r = 0.721 O_3: r = -0.204	**Increment:** 1.0 ppm **% Increase (Lower CI, Upper CI);** lag: 3.79% (1.04-6.55); 0

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: de Hartog et al. (2003, 001061) **Period of Study:** 1998-1999 **Location:** Amsterdam, Netherlands; Erfurt, Germany; Helsinki, Finland	**Health Outcome:** Respiratory symptoms (shortness of breath, being awakened by breathing problems, phlegm, wheezing, tripping heart) **Study Design:** Time series **Statistical Analyses:** Logistic regression **Population:** Nonsmoking individuals with CHD: Amsterdam: 37 Erfurt: 47 Helsinki: 47 **Age Groups Analyzed:** ≥ 50 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Amsterdam: 0.6 mg/m^3 Erfurt: 0.4 mg/m^3 Helsinki: 0.4 mg/m^3 **Range (Min, Max):** Amsterdam: (0.4, 1.6) Erfurt: (0.1, 2.5) Helsinki: (0.1, 1.0) **Copollutant:** $PM_{2.5}$; NO_2	**Increment:** 0.25 mg/m^3 **Odds Ratio (Lower CI, Upper CI); lag:** Incidence of symptoms Shortness of breath 1 (0.92-1.1); 0 0.96 (0.88-1.05); 1 1 (0.92-1.09); 2 1.07 (0.98-1.16); 3 1.03 (0.9-1.18); 0-4 Being awakened by breathing problems 1.02 (0.92-1.14); 1 1.03 (0.93-1.15); 2 1.11 (1-1.22); 3 1.16 (0.98-1.37); 0-4 Phlegm 1.05 (0.93-1.19); 0 1.02 (0.91-1.14); 1 1.08 (0.96-1.22); 2 1.09 (0.97-1.22); 3 1.13 (0.94-1.35); 0-4 Prevalence of symptoms Shortness of breath 1 (0.94-1.06); 0 0.99 (0.94-1.05); 1 0.99 (0.93-1.05); 2 1.01 (0.95-1.07); 3 0.98 (0.9-1.07); 0-4 Being awakened by breathing problems 1.01 (0.93-1.1); 1 0.99 (0.91-1.08); 2 1.1 (1.02-1.19); 3 1.13 (1-1.29); 0-4
Author: Delfino et al. (2003, 050460) **Period of Study:** 11/1999-1/2000 **Location:** Los Angeles, CA	**Health Outcome:** Asthma symptoms (Cough, wheeze, sputum production, shortness of breath, chest tightness) (symptom scores >1, symptoms scores >2); Lung function (PEF) **Study Design:** Panel study **Statistical Analyses:** Asthma symptoms: GEE Lung function: Generalized linear mixed model **Population:** 22 asthmatic Hispanic children **Age Groups Analyzed:** 10-15 yr	**Pollutant:** CO **Averaging Time:** 1-h max; 8-h max **Mean (SD) unit:** 1-h max: 7.7 (3.1) ppb 8-h max: 5.0 (2.0) ppb **Range (Min, Max):** 1-h max: (2, 17) 8-h max: (1, 10) **Copollutant correlation:** NO_2: r = 0.65; O_3: r = -0.17; Acetaldehyde: r = 0.51; Acetone: r = 0.28; Formaldehyde: r = 0.41; Benzene: r = 0.50; Ethylbenzene: r = 0.62; Tetrachloroethylene: r = 0.63; Toluene: r = 0.71; m,p - Xylene: r = 0.72; PM_{10}: r = 0.50; EC: r = 0.60; OC: r = 0.55; SO_2: r = 0.69	**Increment:** 5.0 ppb & 3.0 ppb **Odds Ratio (Lower CI, Upper CI); lag:** 1-max Increment: 5.0 ppb Symptom scores >1 0.95 (0.52-1.75); 0 1.11 (0.75-1.65); 1 Symptom scores >2 0.48 (0.07-3.53); 0 .28 (0.53-3.12); 1 8-h max Increment: 3.0 ppb Symptom scores >1 0.95 (0.55-1.62); 0 1.2 (0.77-1.86); 1 Symptom scores >2 0.53 (0.10-2.92); 0 1.43 (0.41-5.00); 1
Author: Estrella et al. (2005, 099124) **Period of Study:** 1/2000-4/2000 **Location:** Quito, Ecuador	**Health Outcome:** Acute respiratory infection **Study Design:** Prospective study **Statistical Analyses:** Logistic regression; Poisson **Population:** 960 children **Age Groups Analyzed:** 6-11 yr	**Pollutant:** CO **Averaging Time: NR** **Mean (SD) unit**: NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR **Odds Ratio (Lower CI, Upper CI); lag:** Acute respiratory infection ARI in children COHb >2.5% vs. COHb <2.5%: Adjusted Logistic Regression Model 3.25 (1.65-6.38) ARI in children COHb >2.5% vs. COHb <2.5%: Crude Logistic Regression Model 2.06 (1.30-3.20) Log-Linear Model (Each Percent Increase in COHb above 2.5%) 1.15 (1.03-1.28)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Fischer et al. (2002, 025731) **Period of Study:** NR **Location:** Utrecht, Netherlands	**Health Outcome:** Lung function (FVC, FEV_1, PEF, MMEF) **Study Design:** Panel study **Statistical Analyses:** Restricted max likelihood linear model **Population:** 68 children **Age Groups Analyzed:** 10-11	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 921 $\mu g/m^3$ **Range (Min, Max):** (319, 1540) **Copollutant:** PM_{10}; BS; NO_2; NO	**Increment:** 100 $\mu g/m^3$ mL (SE); lag: FVC: 0.5 (0.4); 1; 0.1 (0.2); 2 FEV1: -0.4 (0.5); 1; -0.2 (0.2); 2 m/s (SE); lag: PEF: -1.1 (2.8); 1; -0.6 (1.1); 2 MMEF: -0.5 (1.4); 1; -0.3 (0.6); 2
Author: Ho et al. (2007, 093265) **Period of Study:** Oct 1995-Mar 1996 **Location:** Taipei, Taiwan	**Health Outcome:** Asthma **Study Design:** Panel **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** 10-17 yr **Sample Description:** A stratified cluster random sample of students (n=69,367) from 1,139,452 students sampled nationwide	**Averaging Time:** 8 h **Mean (SD) unit:** NR **Range (min, max):** NR **Copollutant:** NO, NO_2, NO_X, O_3, SO_2, PM_{10}, PSI	**Increment:** very high, high, med, low, very low OR Estimate [Lower CI, Upper CI] ; lag: **Lags examined:** NR Females: 1.984 (1.536, 2.561) Males: 1.780 (1.377, 2.302) Monthly attack rate vs single air pollutant concentrations Estimate (p-value): 0.0750 (0.3336)
Author: Lagorio et al. (2006, 089800) Period of Study: 5/1999-6/1999; 11/1999-12/1999 **Location:** Rome, Italy	**Health Outcome:** Lung function (FVC, $FEV_{1)}$ **Study Design:** Time-series panel study **Statistical Analyses:** Generalized estimating equations (GEE) **Population:** COPD panel: 11 Asthma panel: 11 IHD panel: 7 **Age Groups Analyzed:** COPD panel: 50-80 yr Asthma panel: 18-64 yr IHD panel: 40-64 yr **Notes:** Asthma panel was restricted to never smokers, while COPD and IHD panels include former smokers if smoking cessation occurred at least 1 yr prior to enrollment.	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Overall: 7.4 (6.2) mg/m^3 Spring: 2.1 (0.3) mg/m^3 Winter: 12.3 (4.9) mg/m^3 **Range (Min, Max):** Overall: (1.6, 28.9) **Copollutant correlation:** $PM_{2.5}$: r = 0.67 $PM_{10-2.5}$: r = -0.09 PM_{10}: r = 0.55 NO_2: r = 0.05 O_3: r = -0.87 SO_2: r = 0.65	**Increment:** 1 mg/m^3 **β Coefficient (SE); lag:** COPD panel FVC (% of predicted) -0.14 (0.15);0 -0.13 (0.18); 0-1 0.15 (0.23); 0-2 FEV1 (% of predicted) -0.05 (0.13); 0 -0.12 (0.16); 0-1 -0.03 (0.2); 0-2 Asthma panel FVC (% predicted) 0.02 (0.12); 0 -0.001 (0.13); 0-1 -0.06 (0.16); 0-2 FEV1 (% predicted) -0.05 (0.14); 0 -0.16 (0.15); 0-1 -0.28 (0.18); 0-2 IHD panel FVC (% of predicted) 0.176 (0.101); 0 0.132 (0.120); 0-1/ 0.132 (0.165); 0-2 FEV1 (% of predicted) 0.204 (0.120); 0 0.114 (0.142); 0-1 0.159 (0.194); 0-2
Author: Moon et al. (2009, 190297) **Period of Study:** Apr 2003-May 2003 **Location:** Seoul, Incheon, Busan, & Jeju, Korea	**Health Outcome:** Respiratory symptoms **Study Design:** Panel **Statistical Analyses:** Logistic regression (GEE) **Age Groups Analyzed:** < 13 yr **Sample Description:** 696 children	**Averaging Time:** 24h **Mean (SD) unit:** NR **IQ Range:** 0.12ppm **Copollutant:** PM_{10}, SO_2, NO_2, O_3	**Increment:** 0.12 ppm (IQR) **OR Estimate [Lower CI, Upper CI] ; lag:** **Lags examined:** lag days 0-3 Lower resp. symptoms: 1.005 (1.003, 1.008), lag 0 Upper resp. symptoms: 1.006 (1.003, 1.008), lag 0-2 Irritation symptoms: 1.004 (1.001, 1.006), lag 1-3

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Mortimer et al. (2008, 187280) **Period of Study:** Nov 2000-Apr 2005 **Location:** Fresno, California	**Health Outcome:** Allergic sensitization **Study Design:** Panel **Statistical Analyses:** Multistep modeling **Age Groups Analyzed:** 6-11 yr **Sample Description:** 170 children with physician diagnosed asthma	**Averaging Time:** 24-h avg, 24-h max, 8-h max **Mean (SD) unit:** NR **IQ Range (24-h avg, 24-h max, 8-h max):** 0.28, 0.79, 0.52 **Copollutant:** entire prenatal correlation NO_2: r = 0.74 O_3: r = -0.40 PM_{10}: r = 0.32	**Increment:** IQR **OR Estimate [Lower CI, Upper CI] ; lag:** **Lags examined:** NR Entire Pregnancy: CO 24-h avg: 1.45 (1.02, 2.07) CO 24-h max: 1.53 (1.01, 2.33) CO 24-h avg: 1.55 (1.01, 2.37)
Author: Nkwocha et al. (2008, 190304) **Period of Study:** Feb 2005-Jul 2006 **Location:** Port Harcourt, Nigeria	**Health Outcome:** Respiratory symptoms **Study Design:** Panel **Statistical Analyses:** Mixed Effects models **Age Groups Analyzed:** 0-5 yr **Sample Description:** 250 children	**Averaging Time:** 8 h **Mean (SD) unit:** NR **Range (min, max):** 1.3 µg/m^3, 1.83 µg/m^3 **Copollutant:** NO_2, SO_2, PM_{10}	**Increment:** NR **Lags examined:** NR **R Estimate:** Dry season: 0.13 Wet season: 0.25
Author: O'Connor et al. (2008, 156818) **Period of Study:** Aug 1998-Jul 2001 **Location:** Boston, MA; the Bronx, NY; Chicago, IL; Dallas, TX; New York, NY; Seattle, WA; Tuscon, AZ	**Health Outcome:** respiratory symptoms **Study Design:** panel **Statistical Analyses:** Mixed Effects Models **Age Groups Analyzed:** 5-12 yr **Sample Description:** 861 children with persistent asthma and atopy living in low-income census tracts	**Averaging Time:** 8 h **Mean (SD) unit:** NR **Range (10th-90th):** 872.1 ppb **Copollutant:** PM_{10}, SO_2, NO_2, O_3	**Increment:** 872.1 ppb **Lags examined:** NR **Change Estimate [Lower CI, Upper CI]:** FEV_1: -0.56 (-1.31, 0.20) PEFR: -0.49 (-1.24, 0.27) Pollution Impact*[Lower CI, Upper CI]: Wheeze-cough: 1.26 (1.03, 1.55) Nighttime asthma: 1.35 (1.07, 1.71) Slow play: 1.28 (1.04, 1.59) OR [Lower CI, Upper CI]: Missed School: 1.08 (0.76, 1.53) *Coefficients from the negative binomial model and indicate the multiplicative effect per unit change
Author: Park et al. (2002, 093798) **Period of Study:** 3/1996-12/1999 **Location:** Seoul, Korea	**Health Outcome:** School absenteeism **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Population:** ~1,264 children (671 Boys, 593 girls) **Age Groups Analyzed:** 1st through 6th grade students	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.11 (0.40) ppm **Range (Min, Max):** (0.39, 2.97) **Copollutant correlation:** PM_{10}: r = 0.56; NO_2: r = 0.70; SO_2: r = 0.67; O_3: r = -0.46	**Increment:** 0.52 ppm **Relative Risk (Lower CI, Upper CI); lag:** Total Absences: 0.95 (0.94-0.97); 0 Non-Illness Related Absences: 0.99 (0.96-1.02); 0 Illness-Related Absences: 0.96 (0.94-0.98); 0
Author: Park et al. (2005, 088673) **Period of Study:** 3/2002-6/2002 **Location:** Incheon, Korea	**Health Outcome:** Lung function (PEF variability (>20%), Mean PEF); Respiratory symptoms (night respiratory symptoms, cough, inhaler use) **Study Design:** Panel study **Statistical Analyses:** GEE; Poisson GAM **Population:** 64 bronchial asthmatics **Age Groups Analyzed:** 16-75 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Control days: 0.6368 (0.1522) ppm Dust days: 0.6462 (0.0945) ppm **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR **Relative Risk (Lower CI, Upper CI); lag:** PEF variability (>20%): 1.43 (0.54-3.75) Night respiratory symptoms: 0.98 (0.51-1.86) β Coefficient (SE); lag: PEF variability (>20%): 0.9737 (0.3187) Mean PEF (L/min): -10.103 (2.7146) Night respiratory symptoms: -0.018 (0.3654) Cough: 0.0855 (0.1826) Inhaler Use: 0.0796 (0.1733)

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Penttinen et al. (2001, 030335) **Period of Study:** 11/1996-4/1997 **Location:** Helsinki, Finland	**Health Outcome:** Lung function (PEF) **Study Design:** Panel study **Statistical Analyses:** First order autoregressive linear model **Population:** 57 nonsmoking adult asthmatics **Age Groups Analyzed:** NR	**Pollutant:** CO **Averaging Time:** 24-h avg **Median unit:** 0.4 mg/m^3 **Range (Min, Max):** (0.1, 1.1) mg/m^3 **Copollutant correlation:** PM_{10}: r = -0.03 $PM_{10-2.5}$: r = -0.30 $PM_{2.5}$: r = 0.32 PM_1: r = 0.39 PNC: r = 0.44 NC0.01-0.1: r = 0.43 NC0.1-1: r = 0.47 NO: r = 0.60 NO_2: r = 0.44	**Increment:** 0.2 mg/m^3 β Coefficient (SE); lag: PEF Deviations (L/min) Morning 0.27 (0.38); 0 -1.08 (0.36); 1 0.23 (0.38); 2 -1.11 (1.19); 5-day avg Afternoon -0.4 (0.43); 0 -0.13 (0.41); 1 -0.71 (0.41); 2 -3.03 (1.06); 5-day avg Evening -0.7 (0.45); 0; -0.31 (0.44); 1 0.3 (0.44); 2 -3.62 (1.19); 5-day avg Co-pollutant models with PNC Morning: -0.67 (0.64); 1 Afternoon: -0.46 (0.69); 0 Evening: -0.46 (0.73); 0
Author: Rabinovitch et al. (2004, 096753) **Period of Study:** 11/1999-3/2000; 11/2000-3/2001; 11/2001-3/2002 **Location:** Denver, CO	**Health Outcome:** Lung function (FEV_1); asthma exacerbation; bronchodilator use **Study Design:** Panel study **Statistical Analyses:** Pulmonary function: Mixed effects model; Asthma exacerbation and medication use: GLM **Population:** Urban poor asthmatic children: 1999-2000: 41 2000-2001: 63 2001-2002: 43 **Age Groups Analyzed:** 6-12 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.0 (0.4) ppm **Range (Min, Max):** (0.3, 3.5) **Copollutant:** $PM_{2.5}$; PM_{10}; NO_2; SO_2; O_3	**Increment:** 0.4 ppm β Coefficient (SE); lag: FEV1 AM: -0.001 (0.008); 3-day ma PM: 0.015 (0.01); 3-day ma Odds Ratio (Lower CI, Upper CI); lag: Asthma exacerbation: 1.012 (0.913-1.123); 3-day ma Bronchodilator use: 1.065 (1.001-1.133); 3-day ma
Author: Ranzi et al. (2004, 089500) **Period of Study:** 2/1999-5/1999 **Location:** Emilia-Romagna, Italy	**Health Outcome:** Lung function; respiratory symptoms, medication use **Study Design:** Panel study **Statistical Analyses:** GLM **Population:** 120 "asthma-like" school children **Age Groups Analyzed:** 6-11 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Urban area: 1.54 mg Rural area: 1.22 mg **Range (Min, Max):** NR **Copollutant: NO2;** TSP; $PM_{2.5}$	The study did not present quantitative results for CO.
Author: Rodriguez et al. (2007, 092842) **Period of Study:** 1996-2003 **Location:** Perth, Australia	**Health Outcome:** Respiratory symptoms (body temperature, cough, wheeze/rattle chest, runny/blocked nose) **Study Design:** Panel study **Statistical Analyses:** Logistic regression, GEE **Population:** 263 children at high risk of developing asthma **Age Groups Analyzed:** 0-5 yr	**Pollutant:** CO **Averaging Time:** 8-h avg **Mean (SD) unit:** 1.408 ppm **Range (Min, Max):** (0.012, 8.031) **Copollutant:** NR	**Increment:** NR **Odds Ratio (Lower CI, Upper CI); lag:** Body Temperature 1.024 (0.911-1.151); 0 1.056 (0.943-1.184); 5 0.991 (0.962-1.021); 0-5 Cough 1.001 (0.996-1.005); 0 1.064 (0.941-1.02); 5 1.028 (0.996-1.061); 0-5 Wheeze/Rattle Chest 1.089 (0.968-1.226); 0 1.136 (1.016-1.26); 5 1.035 (1.005-1.066); 0-5 Runny/Blocked Nose 1.094 (0.824-1.453); 0 1.38 (1.028-1.853); 5 1.101 (1.025-1.183); 0-5

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Schildcrout et al. (2006, 089812) **Period of Study:** 11/1993-9/1995 **Location:** 8 North American cities: Albuquerque, NM Baltimore, MD Boston, MA Denver, CO San Diego, CA Seattle, WA St. Louis, MO Toronto, ON, Canada	**Health Outcome:** Asthma symptoms; rescue inhaler use **Study Design:** Panel study **Statistical Analyses:** Asthma symptoms: Logistic regression; Rescue Inhaler Use: Poisson regression **Population:** 990 asthmatic children **Age Groups Analyzed:** 5-12 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NO_2; O_3; PM_{10}; SO_2	**Increment:** 1.0 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Asthma Symptoms 1.08 (1.01-1.14); 0 1.07 (0.99-1.16); 1 1.08 (1.02-1.15); 2 1.05 (1.01-1.09); 0-2 Asthma Symptoms + 20 ppb increase in NO_2 1.07 (1-1.14); 0 1.04 (0.96-1.11); 1 1.09 (1.02-1.16); 2 1.04 (1-1.08); 0-2 + 25 µg/m^3 increase in PM_{10} 1.08 (1.01-1.15); 0 1.06 (0.99-1.14); 1 1.08 (1.02-1.14); 2 1.05 (1.01-1.08); 0-2 + 10 ppb increase in SO_2 1.07 (0.99-1.16); 0 1.06 (0.96-1.19); 1 1.1 (1.02-1.18); 2 1.05 (1-1.09); 0-2 Rescue Inhaler Use 1.07 (1.01-1.13); 0 1.05 (0.99-1.1); 1 1.06 (1.01-1.1); 2 1.04 (1.01-1.07); 0-2 Rescue Inhaler Use + 20 ppb increase in NO_2 1.05 (0.99-1.12); 0 1.04 (0.98-1.11); 1 1.07 (1.02-1.12); 2 1.04 (1-1.07); 0-2 + 25 µg/m^3 increase in PM_{10} 1.06 (0.99-1.13); 0 1.05 (0.99-1.11); 1 1.05 (1.01-1.09); 2 1.03 (1-1.07); 0-2 + 10 ppb increase in SO_2 1.04 (0.96-1.12); 0 1.04 (0.97-1.1); 1 1.08 (1.03-1.13); 2 1.04 (1-1.08); 0-2
Author: Silkoff et al. (2005, 087471) **Period of Study:** 11/11/1999-3/31/2000; 11/1/2000-3/16/2001 **Location:** Denver, CO	**Health Outcome:** Lung function (FEV1, PEF); recorded symptoms; rescue medication use **Study Design:** Panel study **Statistical Analyses:** Rescue medication use and total symptom score: GEE; Lung function: Mixed effects model **Population:** 1st winter: 16 with a history of more than 10 pack yr of tobacco use, airflow limitation with FEV1 of less than 70% of predicted value, and FEV1/ FVC ratio of less than 60% 2nd winter: 18 with a history of more than 10 pack yr of tobacco use, airflow limitation with FEV1 of less than 70% of predicted value, and FEV1/ FVC ratio of less than 60% **Age Groups Analyzed**: ≥ 40 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1999-2000: 1.2 (0.555) ppm 2000-2001: 1.1 (0.5) ppm **Range (Min, Max):** 1999-2000: (0.340, 3.790) 2000-2001: (0.360, 2.810) **Copollutant:** NR	The study did not present quantitative results for CO.

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: Slaughter et al. (2003, 086294) **Period of Study:** 12/1994-8/1995 **Location:** Seattle, WA	**Health Outcome:** Asthma severity; medication use **Study Design:** Panel study **Statistical Analyses:** Asthma severity: Ordinal logistic regression; Medication use: Poisson **Population:** 133 mild-to-moderate asthmatic children **Age Groups Analyzed:** 5-13 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Median unit:** 1.47 ppm IQR (25th, 75th): (0.23, 1.87) **Copollutant:** NR	**Increment:** Increased asthma attack severity: 0.67 ppm Increased rescue inhaler use: 1.0 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Increased asthma attack severity: Without transition: 1.21; 1 With transition: 1.17; 1 Increased rescue inhaler use: Without transition: 1.09 (1.03-1.16); 1 With transition: 1.06 (1.01-1.1); 1
Author: Steerenberg et al. (2001, 017157) **Period of Study:** NR **Location:** Bilthoven and Utrecht, the Netherlands	**Health Outcome:** Lung function (PEF); exhaled nitric oxide; inflammatory nasal markers **Study Design:** Panel study **Statistical Analyses:** Restricted max likelihood linear model **Population:** 126 children **Age Groups Analyzed:** 8-13 yr **Notes:** The study was only conducted for a two mo period: February and March.	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Utrecht: 0.8 mg/m^3 Bilthoven: 0.5 mg/m^3 **Range (Min, Max):** Utrecht: (0.3, 2.3) Bilthoven: (0.3, 0.9) **Copollutant:** NR	The study did not present quantitative results for CO.
Author: Timonen et al. (2002, 025653) **Period of Study:** 2/1994-4/1994 **Location:** Kuopio, Finland	**Health Outcome:** Exercise induced bronchial responsiveness; Lung function (FVC, FEV1, MMEF, AEFV) **Study Design:** Panel study **Statistical Analyses:** Linear regression **Population:** 33 children with chronic respiratory symptoms **Age Groups Analyzed:** 7-12 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.6 mg/m^3 **Range (Min, Max):** (0.1, 2.8) **Copollutant correlation:** PM_{10}: r = 0.52 BS: r = 0.80 PNC0.01-0.03: r = 0.81 PNC0.03-0.1: r = 0.87 PNC0.1-0.3: r = 0.71 PNC0.3-1.0: r = 0.60 PNC1.0-3.2: r = 0.84 PNC3.2-10: r = 0.79 NO_2: r = 0.85	**Increment:** 0.32 mg/m^3 **β Coefficient (SE); lag:** Exercise induced responsiveness ΔFEV_1 (%) -0.081 (0.647); 0 0.03 (0.262); 1 0.087 (0.26); 2 -0.091 (0.275); 3 0.19 (0.599); 0-3 ΔMMEF (%) 0.442 (1.79); 0 0.52 (0.723); 1 0.313 (0.719); 2 -0.616 (0.75); 3 0.096 (1.64); 0-3 ΔAEFV (%) 0.287 (1.19); 0 0.281 (0.482); 1 0.904 (0.474); 2 0.15 (0.483); 3 1.6 (1.05); 0-3 FVC (mL) 0.064 (10.9); 0 -4.79 (4.51); 1 -9.78 (4.24); 2 -13.9 (4.7); 3 -29.4 (10.1); 0-3 FEV_1 (mL) 19.2 (13.2); 0 -9.04 (5.45); 1 -9.15 (5.21); 2 -11.7 (5.77); 3 -17.5 (12.5); 0-3 MMEF (mL/s) 22.2 (36.9); 0 -23 (15.2); 1 -4.63 (14.7); 2 -30.9 (16); 3 -24.9 (34.8); 0-3 AEFV (L2/s) -0.093 (0.088); 0 -0.068 (0.036); 1 -0.06 (0.035); 2 -0.05 (0.039); 3 -0.076 (0.083); 0-3

Study	Design	Concentrations	CO Effect Estimates (95% CI)
Author: von Klot et al. (2002, 034706) **Period of Study:** 9/1996-3/1997 **Location:** Erfurt, Germany	**Health Outcome:** Asthma symptoms; medication use **Study Design:** Panel study **Statistical Analyses:** Logistic regression **Population:** 53 adults with asthma or asthma symptoms **Age Groups Analyzed:** 37-77 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.9 mg/m^3 **Range (Min, Max):** (0.3, 3.0) **Copollutant correlation:** NC0.01-0.1: r = 0.66 NC0.1-0.5: r = 0.79 NC0.5-2.5: r = 0.46 MC0.1-0.5: r = 0.66 MC0.01-2.5: r = 0.65 $PM_{2.5-10}$: r = 0.42 PM_{10}: r = 0.69 NO_2: r = 0.82 SO_2: r = 0.32	**Increment:** 0 and 5-day avg lag: 0.6 mg/m^3 14-day avg lag: 0.54 mg/m^3 **Odds Ratio (Lower CI, Upper CI); lag:** Prevalence: Inhaled β2-agonist use 0.98 (0.93-1.03); 0 1.04 (0.97-1.12); 0-4 0.93 (0.86-1.01); 0-13 Prevalence: Inhaled corticosteroid use 1.05 (1-1.11); 0 1.25 (1.17-1.34); 0-4 1.06 (0.97-1.15); 0-13 Prevalence: Wheezing 1.03 (0.97-1.08); 0 1.13 (1.05-1.22); 0-4 1.14 (1.05-1.25); 0-13 Co-pollutant models Inhaled β2-agonist use CO+MC0.01-2.5: 1 (0.91-1.11); 0-4 CO+NC00.01-0.1: 1.01 (0.91-1.11); 0-4 Inhaled corticosteroid use CO+MC0.01-2.5: 0.89 (0.81-0.98); 0-13 CO+NC: 0.01-0. 1: 0.81 (0.72-0.91); 0-13 Wheezing CO+MC0.01-2.5: 1.15 (1.04-1.27); 0-4 CO+NC0.01-0.1: 1.09 (0.98-1.22); 0-4
Author: Yu et al. (2000, 013254) **Period of Study:** 11/1993-8/1995 **Location:** Seattle, Washington	**Health Outcome:** Asthma symptoms (Wheezing, coughing, chest tightness, shortness of breath) **Study Design:** Panel study **Statistical Analyses:** Repeated measures logistic regression models (GEE) **Population:** 133 mild-to-moderate asthmatics **Age Groups Analyzed**: 5-13 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.6 ppm **Range (Min, Max)**: (0.65, 4.18) **Copollutant correlation:** $PM_{1.0}$: r = 0.82 PM_{10}: r = 0.86 SO_2: r = 0.31	**Increment**: 1.0 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Marginal GEE 1.22 (1.03-1.45); 0 1.3 (1.11-1.52); 1 1.26 (1.09-1.46); 2 Transition GEE 1.18 (1.02-1.37); 0 1.25 (1.1-1.42); 1 1.18 (1.04-1.33); 2

Table C-5. Studies of short-term CO exposure and respiratory hospital admissions and ED visits.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Abe et al. (2009, 190536) **Period of Study:** January 1-December 31, 2005 **Location:** Tokyo, Japan	ED Visits **Health Outcome:** Asthma **Study Design:** Time-series **Statistical Analyses:** Bivariate Pearson correlation coefficitnes, ARIMA model **Age Groups Analyzed:** Children: ≤14 yr, Adults: ≤ 15 yr **Sample Description:** Data from daily number of ambulance transports to ED for asthma	**Averaging Time:** NR **Mean (SD) unit:** 11.5ppm **Range (Min, Max):** 3-44ppm **Copollutant:** NR	**Increment:** 0.1ppm ARIMA model for ambulance transports to ED for asthma exacerbation among adults: β coefficient: 0.151, SE: 0.098, t statistic: 1.537, P value: .125 ARIMA model for ambulance transports to ED for asthma exacerbation among children: β coefficient: 0.019, SE: 0.034, t statistic: 0.549, P value: 0.583 Lags examined: 0 On the day with the highest CO the number of transports was 25. The number of transports for adults and CO had significant bivariate correlations. The fitted ARIMA model had no significant associations.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Anderson et al. (2001, 017033) **Period of Study:** 10/1994-12/1996 **Location:** West Midlands; U.K.	Hospital Admission **Health Outcome (ICD9):** Respiratory diseases asthma (493) COPD (490-492, 494-496) **Study Design:** Time series **Statistical Analyses:** Regression with quasi-likelihood approach and GAM **Age Groups Analyzed:** All ages 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** 0.8 (0.7) ppm **Range (Min, Max):** (0.2, 10) **Copollutant:** correlation PM_{10}: r = 0.55; $PM_{2.5}$: r = 0.54; $PM_{2.5-10}$: r = 0.10; BS: r = 0.77; SO_4^{2-}: r = 0.17; NO_2: r = 0.73; O_3: r = -0.29; SO_2: r = 0.49	**Increment:** 1.0 ppm **% Increase (Lower CI, Upper CI); lag:** Respiratory Diseases Age Group All ages: 0.3% (-1.10 to 1.70); 0-1 0-14: 1.50% (-0.60 to 3.60); 0-1 15-64: -0.70% (-3.60 to 2.30); 0-1 ≥ 65: 0.00% (-2.10 to 2.10); 0-1 Asthma Age Group 0-14: 3.90% (-0.50 to 8.50); 0-1 15-64: -4.90% (-10.60 to 1.10); 0-1 COPD Age Group ≥ 65: 1.00% (-2.50 to 4.60); 0-1
Author: Andersen et al. (2007, 093201) **Period of Study:** 1/1999-12/2004 **Location:** Copenhagen, Denmark	Hospital Admission **Health Outcome (ICD10):** Respiratory diseases: chronic bronchitis (J41-42), emphysema (J43), COPD (J44), asthma (j45), status asthmaticus (j46), pediatric asthma (j45), pediatric asthmaticus (j46) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** 5-18 yr; ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.3 (0.1) ppm IQR (25th, 75th): (0.22, 0.34) **Copollutant; correlation:** PM_{10}: r = 0.45	**Increment:** 0.12 ppm **Relative Risk (Lower CI, Upper CI); lag:** Respiratory Disease Age Group: ≥ 65 CO: 1.024 (0.997-1.053); 0-4 CO, PM_{10}: 1.001 (0.961-1.042); 0-4 Asthma Age Group: 5-18 CO: 1.104 (1.018-1.198); 0-5 CO, PM_{10}: 1.023 (0.911-1.149); 0-5
Author: Atkinson et al. (1999, 007882) **Period of Study:** 1/1992-12/1994 **Location:** London, U.K.	ED Visits **Health Outcome (ICD9):** Respiratory complaints: wheezing, inhaler request, chest infection, chronic obstructive lung disease (COLD), difficulty breathing, cough, other respiratory complaints. e.g., croup, pleurisy, noisy breathing; Asthma (493) **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups Analyzed:** All ages 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.8 (0.4) ppm **Range (Min, Max):** (0.2, 5.6) **Copollutant; correlation:** NO_2 O_3 SO_2 PM_{10} BS	**Increment:** 0.8 ppm **% Increase (Lower CI, Upper CI); lag**: Respiratory complaints Age Group All ages: 0.76% (-0.83, 2.38); 1 0-14: 2.92% (0.60, 5.30); 1 15-64: 2.15% (-0.27, 4.63); 1 ≥ 65: 4.29% (1.15, 7.54); 0 Asthma visits: Single-pollutant model Age Group: All ages: 3.32% (0.56, 6.16); 1 0-14: 4.13% (-0.11, 8.54); 0 15-64: 4.41% (0.46, 8.52); 1 Multi-pollutant model Age Group: 0-14 CO, NO_2: 2.05% (-2.25, 6.54); 0 CO, O_3: 4.48% (0, 9.16); 0 CO, SO_2: 2.34% (-1.94, 6.81); 0 CO, PM_{10}: 2.93% (-1.53, 7.58); 0 CO, BS: 4.19% (-0.04, 8.60); 0

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Bedeschi et al. (2007, 090712) **Period of Study:** 1/2001-3/2002 **Location:** Reggio Emilia, Italy	ED Visits **Health Outcome (ICD9):** Asthma (493); Asthma-like disorders, i.e., asthma, bronchiolitis, dyspnea/ shortness of breath; Other respiratory disorders (i.e., upper and lower respiratory illness including sinusitis, bronchitis, and pneumonia) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, penalized splines **Age Groups Analyzed:** <5 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.4 (0.7) mg/m^3 **Range (Min, Max):** (0.4, 4.6) **Copollutant; correlation:** PM_{10}: r = 0.61 TSP: r = 0.61 SO_2: r = 0.71 NO_2: r = 0.77	The study did not provide quantitative results for CO.
Author: Bell et al. (2008, 091268) **Period of Study:** 1/1995-12/2002 **Location:** Taipei, Taiwan	Hospital Admissions **Health Outcome (ICD9):** Pneumonia (486); asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SE) unit:** 0.9 ppm **Range (Min, Max):** (0.3, 3.6) **Copollutant:** NR	**Increment:** 0.5 ppm **% Increase (Lower CI, Upper CI); lag** Asthma (avg correlation between monitor pairs = 0.75 (13 monitors)) 3.29% (-0.74 to 7.49); 0 .49% (-4.25 to 3.41); 1 -0.84% (-4.43 to 2.88); 2 0.48% (-4.02 to 3.18); 3 0.74% (-4.62 to 6.4); 0-3 Pneumonia (avg correlation between monitor pairs = 0.75 (13 monitors)) 1.91% (-1.97 to 5.95); 0 0.03% (-3.65 to 3.85); 1 0.36% (-3.2 to 4.04); 2 -1.29% (-4.77 to 2.32); 3 0.21% (-5.03 to 5.73); 0-3 Asthma (avg correlation between monitor pairs = 0.88 (5 monitors)) 1.68% (-1.68 to 5.15); 0 -1.19% (-4.29 to 2.01); 1 -0.83% (-3.83 to 2.26); 2 -0.35% (-3.32 to 2.71); 3 -0.31% (-4.9 to 4.5); 0-3 Pneumonia (avg correlation between monitor pairs = 0.88 (5 monitors)) 1.24% (-2.02 to 4.6); 0 -0.01% (-3.06 to 3.13); 1 0.57% (-2.4 to 3.62); 2 -0.85% (-3.78 to 2.16); 3 0.31% (-4.23 to 5.06); 0-3 Asthma (monitors with ≥ 0.75 between monitor correlations (11 monitors), avg correlation between monitor pairs = 0.81) 2.87% (-0.91 to 6.79); 0 -0.71% (-4.2 to 2.91); 1 -0.73% (-4.08 to 2.73); 2 -0.41% (-3.72 to 3.01); 3 0.51% (-4.6 to 5.89); 0-3 Pneumonia (monitors with ≥ 0.75 between monitor correlations (11 monitors) to avg correlation between monitor pairs = 0.81) 0.98% (-1.68 to 5.76); 0 -0.12% (-3.54 to 3.42); 1 0.37% (-2.95 to 3.8); 2 -1.08% (-4.34 to 2.3); 3 0.3% (-4.71 to 5.57); 0-3

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Bellini et al. (2007, 097787) **Period of Study:** 1996-2002 **Location:** 15 Italian cities	Hospital Admissions **Health Outcome:** Respiratory conditions **Study Design:** Time-series; Meta-analysis **Statistical Analyses:** 1. GLM for city-specific estimates 2. Bayesian random-effects for meta analysis **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant: correlation** NR	**Increment:** 1 mg/m^3 **% Increase (Lower CI, Upper CI); Lag** Respiratory conditions All ages: Season: Winter: 0.58%; 0-1 Summer: 3.47%; 0-1 All Season: 1.25%; 0-3 **Note:** Estimates from Biggeri et al. (2004)
Author: Braga et al. (2001, 016275) **Period of Study:** 1/1993-11/1997 **Location:** Sao Paulo, Brazil	Hospital Admissions **Health Outcome (ICD9):** Respiratory (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** ≤ 2 yr 3-5 yr 6-13 yr 14-19 yr 0-19 yr	**Pollutant:** CO **Averaging Time:** Maximum 8-h avg **Mean (SD) unit:** 4.8 (2.3) ppm **Range (Min, Max):** (0.6, 19.1) **Copollutant:** correlation PM_{10}: r = 0.60 O_3: r = -0.07 SO_2: r = 0.47	**Increment:** 3 ppm **% Increase (Lower CI, Upper CI); lag:** Respiratory Age Group: ≤ 2: 5.00% (3.30-6.80); 0-6 3-5: 4.90% (1.40-8.50); 0-6 6-13: 1.00% (-2.50 to4.60); 0-6 14-19: 11.30% (5.90-16.80); 0-6 0-19: 4.90% (3.50-6.40); 0-6
Author: Burnett et al. (1999, 017269) Period of Study: 1/1980-12/1994 **Location:** Toronto, ON, Canada	Hospital Admissions **Health Outcome (ICD9):** Asthma (493); COPD (490-492, 496); respiratory infection (464, 466, 480-487, 494) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.18 ppm **IQR (25th, 75th):** (0.9, 1.4) **Copollutant:** correlation $PM_{2.5}$: r = 0.49 $PM_{10-2.5}$: r = 0.20 PM_{10}: r = 0.43 NO_2: r = 0.55 SO_2: r = 0.37 O_3: r = -0.23	**Increment:** 1.18 ppm **% Increase (t-value); lag:** Asthma: 5.35% (3.92); 0 COPD: 2.93% (1.48); 0 Respiratory Infection: 5.00% (4.25); 0 Asthma: Multipollutant model CO, SO_2, O_3: 5.15% CO, $PM_{2.5}$, SO_2, O_3: 4.63% CO, $PM_{10-2.5}$, SO_2, O_3: 5.25% CO, PM_{10}, SO_2, O_3: 4.80% CO, $PM_{10-2.5}$, O_3: 4.00% COPD: Multipollutant model CO, SO_2, O_3: 3.02% CO, $PM_{2.5}$, SO_2, O_3: 2.46% CO, $PM_{10-2.5}$, SO_2, O_3: 3.00% CO, PM_{10}, SO_2, O_3: 2.75% CO, $PM_{10-2.5}$, O_3: 3.00%
Author: Burnett et al. (2001, 093439) **Period of Study:** 1/1980-12/1994 **Location:** Toronto, ON, Canada	Hospital Admissions **Health Outcome (ICD9):** Asthma (493); Acute bronchitis/ bronchiolitis (466); croup (464.4) ; pneumonia (480-486) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** <2 yr	**Pollutant:** CO **Averaging Time:** 1-h avg **Mean (SD) unit:** 1.9 ppm **IQR (25th, 75th):** (1.3, 2.3) **Copollutant:** correlation O_3: r = 0.24	**Increment:** 1.9 ppm **% Increase (Lower CI, Upper CI); lag** Respiratory problems CO: 19.20%; 0-1 CO, O_3: 14.30%; 0-1

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Cakmak et al. (2006, 093272) **Period of Study:** 4/1993-3/2000 **Location:** 10 Canadian cities	Hospital Admissions **Health Outcome (ICD9):** Actue bronchitis/bronchiolitis (466); pneumonia (480-486); chronic/ unspecified bronchitis (490, 491); emphysema (492); asthma (493); bronchiectasis (494); chronic airway obstruction (496) **Study Design:** Time series **Statistical Analyses:** 1. Poisson 2. Restricted Maximum Likelihood Method **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.8 ppm **Range (Min, Max):** (0.0, 6.5) **Copollutant:** correlation SO_2 NO_2 O_3	**Increment:** 0.8 ppm **% Increase (Lower CI, Upper CI); lag:** Respiratory disease CO: 0.60% (0.20, 1); 2.8 CO, SO_2, NO_2, O_3: -0.20% (-0.70- 0.30); 2.8
Author: Cheng et al. (2007, 093034) **Period of Study:** 1996-2004 **Location:** Kaohsiung, Taiwan	Hospital Admissions **Health Outcome (ICD9):** Pneumonia (480-486) **Study Design:** Bidirectional case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.76 ppm **Range (Min, Max):** (0.14, 1.72) **Copollutant:** correlation PM_{10} SO_2 NO_2 O_3	**Increment:** 0.31 ppm **Odds Ratio (Lower CI, Upper CI); lag:** OR for pneumonia and exposure to various pollutants for all ages in areas ≥ 25°C or <25°C Pollutant and Temperature CO, ≥ 25 ºC: 1.18 (1.14-1.23); 0-2 CO, <25 ºC: 1.47 (1.41-1.53); 0-2 CO, PM_{10}, ≥ 25 ºC: 1.15 (1.11-1.2); 0-2 CO, PM_{10}, <25 ºC: 1.28 (1.21-1.35); 0-2 CO, SO_2, ≥ 25 ºC: 1.22 (1.17-1.27); 0-2 CO, SO_2, <25 ºC: 1.49 (1.42-1.56); 0-2 CO, NO_2, ≥ 25 ºC: 1.2 (1.15-1.27); 0-2 CO, NO_2, <25 ºC: 1.01 (0.95-1.08); 0-2 CO, O_3, ≥ 25 ºC: 1.16 (1.12-1.2); 0-2 CO, O_3, <25 ºC: 1.44 (1.38-1.5); 0-2
Author: Chiu et al. (2009, 190249) **Period of Study:** 1996-2004 **Location:** Taipei, Taiwan	Hospital Admissions **Health Outcome:** pneumonia HA **Study Design:** case-crossover **Statistical Analyses:** Conditional Logistic regression **Age Groups Analyzed:** All ages **Sample Description:** 152,594 HA for 47 hospitals in Taipei city	**Averaging Time:** 24h **Mean (SD) unit:** 1.26 ppm **Range (min, max)**: 0.12, 3.66 **Copollutant:** correlation PM_{10}: r = 0.34 SO_2: r = 0.57 NO_2: r = 0.69 O_3: r = -0.31	Increment: 0.57 ppm (IQR) **OR Estimate [Lower CI, Upper CI] ; lag:** Lags examined: one wk before to one wk after CO: ≥23°C: 1.25 (1.21, 1.29) <23°C: 1.12 (1.09, 1.15) CO + PM_{10}: ≥23°C: 1.23 (1.19, 1.27) <23°C: 1.05 (1.02, 1.09) CO + SO_2: ≥23°C: 1.25 (1.21, 1.30) <23°C: 1.27 (1.22,1.31) CO + NO_2: ≥23°C: 0.97 (0.93, 1.02) <23°C: 1.14 (1.09, 1.20) CO + O_3: ≥23°C: 1.24 (1.20, 1.28) <23°C: 1.21 (1.17, 1.24)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Cho et al. (2000, 099051) Period of Study: 1/1996-12/1996 **Location:** 3 South Korea cities:	Hospital Admissions **Health Outcome (ICD9):** Bronchial asthma; COPD; bronchitis **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All Ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Daejeon: 1.424 (0.611) ppm Ulsan: 0.950 (0.211) ppm Suwon: 1.270 (0.549) ppm **Range (Min, Max):** Daejeon: (.364, 3.504) Ulsan: (.380, 1.675) Suwon: (.250, 3.616) **Copollutant:** correlation Daejeon SO_2: r = 0.280; NO_2: r = 0.041; TSP: r = 0.193; O_3: r = -0.101; O_3 Max: r = -0.069 Ulsan SO_2: r = 0.108; NO_2: r = 0.446; TSP: r = 0.286; O_3: r = -0.195; O_3 Max: r = -0.107 Suwon SO_2: r = 0.556; NO_2: r = 0.291; TSP: r = 0.496; O_3: r = -0.371; O_3 Max: r = -0.365	**Increment:** 1,000 ppm **Relative Risk (Lower CI, Upper CI); lag:** Estimates obtained using dummy variables to apply environmental indicators to the model Daejeon CO: 1.26 (1.08-1.47) TSP, SO_2, NO_2, O_3: 1.21 (1.02-1.44) Ulsan CO: 3.55 (1.65-7.63) TSP, SO_2, NO_2, O_3: 2.51 (1.06-5.93) Suwon CO: 1.24 (0.97-1.59) TSP, SO_2, NO_2, O_3: 1.19 (0.88-1.61) Estimates obtained using actual measured integrated environmental pollution indicator values Daejeon CO: 1.34 (1.14-1.58) Ulsan CO: 1.27 (0.94-1.71) Suwon CO: 3.55 (1.27-9.93)
Author: Delfino et al. (2008, 156390) **Period of Study:** January 1, 2000-December 31, 2003 **Location:** Orange County, California	ED Visits **Health Outcome:** Asthma **Study Design:** Longitudinal, Cohort **Statistical Analyses:** Proportional hazards models in SAS version 9.2 **Age Groups Analyzed:** 0-18 yr **Sample Description:** Various gender, race, insurance status, income, poverty level, residence distance to treating hospital	**Averaging Time:** NR **Mean (SD) unit: Cool season:** 0.114 (0.052), Warm season: 0.103 (0.048) **Range (Min, Max):** Cool season: 0.014 -0.378, Warm season: 0.013-0.482 **Copollutant:** NO_X	**Increment:** 0.056 ppm HR (95% CI): Unadjusted: 1.072 (1.016 – 1.131), Adjusted: 1.073 (1.013 – 1.137), Male: 1.054 (0.978 – 1.137), Female: 1.100 (1.011 – 1.197), 0 yr: 1.158 (1.041 – 1.289), 1-5 yr: 1.021 (0.933 – 1.117), 6-18 yr: 1.076 (0.972 – 1.191), Median or less poverty: 1.054 (0.979 – 1.134), Greater than the median poverty: 1.094 (1.006 – 1.190), Greater than the median income: 1.120 (1.034 – 1.213), Median or less income: 1.041 (0.959 – 1.129), Private insurance: 1.102 (1.006 – 1.206), Government sponsored or self-pay insurance: 1.061 (0.989 – 1.138), Unknown insurance: 0.913 (0.591 – 1.412), White: 1.113 (1.027 – 1.205), Hispanic: 1.081 (0.996 – 1.173), Non-Hispanic nonwhite: 0.804 (0.601 – 1.074) Lags examined: NR The point estimates for CO are stronger in girls than in boy and in infants than in older children. There is little difference in coefficients between adjusted and unadjusted CO models. There were significant increased risks of repeated hospital encounters of 7% to 10% per IQR increase in traffic-related CO exposure.
Author: Farhat et al. (2005, 089461) Period of Study: 8/1996-8/1997 **Location:** Sao Paulo, Brazil	Hospital Visits & ED Visits **Health Outcome (ICD9):** Pneumonia/bronchopneumonia (480-486); asthma (493); bronchiolitis (466) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** 3.8 (1.6) ppm **Range (Min, Max):** (1.1, 11.4) **Copollutant:** correlation PM_{10}: r = 0.72; SO_2: r = 0.49; NO_2: r = 0.59; O_3: r = -0.8	**Increment:** 1.8 ppm **% Increase (Lower CI, Upper CI); lag:** Lower Respiratory Tract Disease ED Visits CO, PM_{10}: -0.10% (-5.60 to 5.30); 0-2 CO, NO_2: -1.20% (-6.70 to 4.20); 0-2 CO, SO_2: 3.70% (-1.00 to 8.40); 0-2 CO, O_3: 4.80% (0.50-9.10); 0-2 CO, PM_{10}, NO_2, SO_2, O_3:- 0.64% (-6.90 to 5.60); 0-2 Pneumonia/ Bronchopneumonia Hospital Admissions CO, PM_{10}: 4.40% (-7.90 to 16.70); 0-2 CO, NO_2: 4.40% (-88.70 to 17.50); 0-2 CO, SO_2: 7.80% (-2.50 to 18.20); 0-2 CO, O_3: 9.60% (-0.50 to 19.70); 0-2 CO, PM_{10} to NO_2, SO_2, O_3:5.10% (-9.60 to 19.70); 0-2 Asthma/ Bronchiolitis Hospital Admissions CO, PM_{10}: 6.10% (-14.90 to 27.10); 0-2 CO, NO_2: 2.40% (-16.90 to 21.70); 0-2 CO, SO_2: 10.60% (-6.60 to 27.80); 0-2 CO, O_3: 12.40% (-3.60 to 28.40); 0-2 CO, PM_{10} to NO_2, SO_2, O_3: 8.80% (-15.60 to 33.30); 0-2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Fung et al. (2006, 089789) Period of Study: 6/1995-3/1999 **Location:** Vancouver, Canada	Hospital Admissions **Health Outcome (ICD9):** Respiratory Illness **Study Design:** 1. Dewanji and Moolgavkar 2. Time-series 3. Bidirectional case-crossover **Statistical Analyses:** 1. Dewanji and Moolgavkar 2. Poisson 3. Conditional logistic regression **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.69 0.25) ppm **Range (Min, Max):** (0.28, 2.03) **Copollutant:** correlation CoH: r = 0.85; O_3: r = -0.53; NO_2: r = 0.74; SO_2: r = 0.61; PM_{10}: r = 0.46; $PM_{2.5}$: r = 0.23; $PM_{10-2.5}$: r = 0.51	**Increment:** 0.24 ppm **Relative Risk (Lower CI, Upper CI); lag** Dewanji and Moolgavkar 1.008 (0.997-1.02); 0 1.012 (0.999-1.025); 0-2 1.010 (0.995-1.025); 0-4 1.009 (0.991-1.026); 0-6 Time-series 1.012 (1.000-1.023); 0 1.017 (1.003-1.032); 0-2 1.017 (1.001-1.035); 0-4 1.016 (0.996-1.036); 0-6 Bidirectional case-crossover 1.010 (0.006-1.023); 0 1.012 (0.996-1.027); 0-2 1.012 (0.995-1.03); 0-4 1.010 (0.991 1.031; 0-6
Author: Fusco et al. (2001, 020631) **Period of Study:** 1/1995 10/1997 **Location:** Rome, Italy	Hospital Admissions **Health Outcome (ICD9):** Respiratory conditions (460-519, excluding 470-478); acute respiratory infections plus pneumonia (460-466, 480-486); COPD (490-492, 494-496) asthma (493) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages 0-14 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 3.6 (1.2) mg/m^3 **IQR (25th, 75th):** (2.8, 4.3) **Copollutant:** correlation All Year SO_2: r = 0.56 NO_2: r = 0.31 O_3: r = -0.57 Cold Season SO_2: r = 0.37 NO_2: r = 0.41 O_3: r = -0.44 Warm Season SO_2: r = 0.44 NO_2: r = 0.59 O_3: r = -0.38	**Increment:** 1.5 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** Age Group: All Ages Respiratory conditions 2.80% (1.30-4.30); 0 1.80% (0.20-3.30); 1 0.20% (-1.30 to 1.80); 2 0.50% (-2.00 to 1.10); 3 0.70% (-0.80 to 2.20); 4 CO, NO_2: 2.30% (0.60-4.00); 0 Acute Respiratory Infections plus pneumonia 2.20% (0.00-4.40); 0 2.10% (-0.10 to 4.40); 0 1.70% (-0.50 to 4.00); 2 -0.90% (-3.00 to 1.30); 3 1.50% (-0.70 to 3.70); 4 CO, NO_2: 0.00% (-2.30 to 2.40); 0 Asthma 5.50% (0.90-10.40); 0 0.80% (-3.80 to 5.70); 1 -1.30% (-5.90 to 3.50); 2 -3.00% (-7.40 to 1.60); 3 0.60% (-4.00 to 5.30); 4 CO, NO_2: 4.80% (0.30-9.50); 0 COPD 4.30% (1.60-7.10); 0 -0.20% (-2.90 to 2.50); 1 -0.20% (-2.90 to 2.60); 2 -0.30% (-3.00 to 2.40); 3 -0.10% (-2.80 to 2.60); 4 CO, NO_2: 4.80% (0.90-7.90); 0 Warm Season Respiratory Conditions: 10.80% (6.70-14.80); 0 Acute respiratory infections plus pneumonia: 8.60% (2.90-14.60); 0 COPD: 13.90% (6.80-21.50); 0 Age Group: 0-14 Respiratory conditions 2.50 (-0.30 to 5.50); 0 0.80 (-2.10 to 3.80); 1; 0.20 (-2.70 to 3.10); 2 -1.00 (-3.70 to 1.90); 3 3.20 (0.40- 6.20); 4 CO, NO_2: 4.10 (-1.20 to 9.80); 1 Acute Respiratory Infections plus Pneumonia 2.50 (-0.80 to 5.80); 0 -0.10 (-3.40 to 3.20); 1 0.90 (-2.30 to 4.30); 2 -2.00 (-5.10 to 1.20); 3 3.20 (0.00-6.60); 4 CO, NO_2: 6.90 (0.80-13.40); 1 Asthma 6.30 (-0.50 to 13.50); 0 8.20 (1.10-15.70); 1; -0.70 (-7.30 to 6.30); 2

Study	Design	Concentrations	Effect Estimates (95% CI)
			3.50 (-3.20 to 10.60); 3; 4.80 (-1.90 to 12.00); 4 CO, NO_2: 3.30 (-4.20 to 11.30); 1
Author: Gouveia and Fletcher (2000, 010436) **Period of Study:** 11/1992-9/1994 **Location:** Sao Paulo, Brazil	Hospital Admissions **Health Outcome (ICD9):** All respiratory diseases Pneumonia (480-486); asthma (493); bronchitis (466, 490, 491) **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups Analyzed:** <1 yr; <5 yr	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** 5.8 (2.4) ppm **Range (Min, Max):** (1.3, 22.8) **Copollutant:** correlation PM_{10}: r = 0.63 SO_2: r = 0.65 NO_2: r = 0.35	**Increment:** 6.9 ppm **Relative Risk (Lower CI, Upper CI); lag:** All respiratory diseases Age Group: <5: 1.017 (0.971-1.065); 0 Pneumonia Age Group: <5: 1.015 (0.961-1.071); 0; <1: 1.035 (0.975-1.099); 2 Asthma Age Group: <5: 1.081 (0.98-1.192); 0
Author: Hajat et al. (1999, 000924) **Period of Study:** 1/1992-12/1994 **Location:** London, U.K.	General Practitioner Visits **Health Outcome (ICD9):** Asthma (493); lower respiratory diseases (464, 466, 476, 480-483, 485-487, 490-492, 494-496, 500, 501, 503-505, 510-515, 518, 519, 786) **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups Analyzed:** All ages 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** All yr: 0.8 (0.4) ppm Warm Season (April-September): 0.7 (0.3) ppm Cool Season (October-March): 1.0 (0.5) ppm **Range (10th, 90th):** All Year: (0.5, 1.3) Warm Season: (0.4, 1.0) Cool Season: (0.5, 1.6) **Copollutant:** correlation All Year NO_2: r = 0.72; SO_2: r = 0.51; BS: r = 0.85; O_3: r = -0.40; PM_{10}: r = 0.56 Warm Season NO_2: r = 0.70; SO_2: r = 0.32; BS: r = 0.65; O_3: r = -0.12; PM_{10}: r = 0.58 Cool Season NO_2: r = 0.84; SO_2: r = 0.58; BS: r = 0.87	**Increment:** 0.8 & 0.7 ppm **% Increase (Lower CI, Upper CI); Lag** All Year: Asthma – Single Day Lags Increment: 0.8 ppm Age Group 0-14: 4.10% (-0.10 to 8.40); 2 15-64: 0.90% (-2.10 to 4.10); 0 ≥ 65: 7.50% (0.50-14.90); 2 All ages: 1.60% (-1.20 to 4.60); 2 Asthma – Cumulative exposure Increment: 0.7 ppm Age Group 0-14: 6.90% (1.30-12.90); 0-3 15-64: 1.00% (-3.20 to 5.40); 0-2 ≥ 65: 8.20% (0.40-16.60); 0-2 All ages: 1.80% (-1.50 to 5.20); 0-2 Lower Respiratory Diseases – Single Day Lags Increment: 0.8 ppm Age Group 0-14: 4.40 (1.70-7.10); 2 15-64: 1.10 (-0.70 to 3.00); 2 ≥ 65: -2.60 (-4.80 to -0.30); 3 All ages: 2.00 (0.50-3.40); 2 Lower Respiratory Diseases – Cumulative exposure Increment: 0.7 ppm for 0-2 and 0-3; 0.8 for 0-1 Age Group 0-14: 3.00% (-1.00 to 7.20); 0-3 15-64: -0.70% (-2.90 to 1.50); 0-1 ≥ 65: -1.60% (-5.10 to 2.00); 0-3 All ages: 1.80% (0.10-3.60); 0-2 Warm or Cold Seasons: Asthma, Increment: 0.8 ppm Age Group & Season 0-14 & Warm Season: 11.40% (3.30-20.00); 2 0-14 & Cold Season: 2.90% (-3.20 to 9.40); 2 15-64 & Warm Season: 4.80% (-0.60 to 10.60); 0 15-64 & Cold Season: -0.30% (-4.80 to 4.50); 0 ≥ 65 & Warm Season: 15.60% (3.10-29.60); 2 ≥ 65 & Cold Season: 4.20% (-6.00 to 15.60); 2 Lower Respiratory Diseases, Increment: 0.8 ppm Age Group & Season 0-14 & Warm Season: 2.70% (-2.90 to 8.60); 2 0-14 & Cold Season: 6.20% (2.30-10.20); 2 15-64 & Warm Season: 6.20% (2.30-10.20); 2 15-64 & Cold Season: 2.40% (-1.20 to 6.10); 2 ≥ 65 & Warm Season: 1.00% (-1.60 to 3.80); 2 ≥ 65 & Cold Season: -2.20% (-6.50 to 2.40); 3

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Hajat et al. (2002, 030358) **Period of Study:** 1/1992-12/1994 **Location:** London, U.K.	General Practitioner Visits **Health Outcome (ICD9):** Upper respiratory diseases (URD) **Study Design:** Time-series **Statistical Analyses:** Poisson, GAM, LOESS **Age Groups Analyzed:** 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** All yr: 0.8 (0.4) ppm Warm Season (April-September): 0.7 (0.3) ppm Cool Season (October-March): 1.0 (0.5) ppm **Range (10th, 90th):** All Year: (0.5, 1.3) Warm Season: (0.4, 1.0) Cool Season: (0.5, 1.6) **Copollutant:** NR	**Increment:** 0.6 ppm, 0.8 ppm, & 1.1 ppm **% Increase (Lower CI, Upper CI); lag:** Warm Season, Increment: 0.6 ppm Age Group 0-14: 2.90% (-0.60 to 6.40); 1 14-64: 7.90% (4.80-11.10); 1 ≥ 65: 4.90% (-1.80 to 12.10); 3 Cold Season, Increment: 1.1 ppm Age Group 0-14: -2.50% (-4.90 to 0.10); 1 14-64: 0.60% (-1.60 to 2.90); 1 ≥ 65: 5.60% (0.90-10.60); 3 All Year, Increment: 0.8 ppm Age Group 0-14: -2.20% (-4.00 to -0.30); 1 14-64: 2.70% (0.10-5.50); 1 ≥ 65: 5.80% (2.40 to 9.30); 3
Author: Hapcioglu et al. (2006, 093263) Period of Study: 1/1997-12/2001 **Location:** Istanbul, Turkey	Hospital Admissions **Health Outcome (ICD9):** COPD (490-492, 494-496) **Study Design:** Cross sectional **Statistical Analyses:** Pearson Correlation Coefficient **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Monthly **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	Correlation Coefficient: Between CO exposure and COPD: 0.57 Between CO exposure and COPD when controlling for temperature: 0.25
Author: Hinwood et al. (2006, 088976) **Period of Study:** 1/1992-12/1998 **Location:** Perth, Australia	Hospital Admissions **Health Outcome (ICD9):** COPD (490.00-496.99 excluding asthma); pneumonia/ influenza (480.00-489.99); Asthma (493) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** All Year: 2.3 (1.3) ppm; November-April: 2.2 (1.3) ppm; May-October: 2.4 (1.2) ppm **Range (10th, 90th):** All Year: (0.9, 4.2) November-April: (0.8, 4.2) May-October: (1.1, 4.2) **Copollutant:** correlation All Year: NO_2: r = 0.57 O_3: r = 0.00 November-April: NO_2: r = 0.55 O_3: r = 0.00 May-October: NO_2: r = 0.57 O_3: r = 0.16	**Increment:** 2.3 ppm **Odds Ratio (Lower CI, Upper CI); Lag** Pneumonia 0.99999 (0.9737-1.0268); 0 1.00650 (0.9806-1.0331); 1 1.00351 (0.9779-1.0298); 2 1.00424 (0.9790-1.0301); 3 1.00581 (0.9752-1.0374); 0-1 1.01005 (0.9755-1.0458); 0-2 1.00805 (0.9701-1.0474); 0-3 COPD 0.99915 (0.9693-1.0297); 0 1.00205 (0.9727-1.0323); 1 0.98630 (0.9577-1.0158); 2 0.98970 (0.9619-1.0182); 3 0.99960 (0.9647-1.0357); 0-1 0.99260 (0.9538-1.0329); 0-2 0.99160 (0.9493-1.0357); 0-3
Author: Hwang and Chan (2002, 023222) **Period of Study:** 1998 **Location:** 50 communities in Taiwan	Clinic Visits **Health Outcome (ICD9):** Lower respiratory tract infections (466, 480-486) **Study Design:** Time series **Statistical Analyses:** 1. General linear regression 2. Bayesian hierarchical modeling **Age Groups Analyzed:** All Ages 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** 1.00 (0.30) ppm **Range (Min, Max):** (0.51, 1.71) **Copollutant:** NR	**Increment:** 0.1 ppm **% Increase (Lower CI, Upper CI); Lag** Age Group: All Ages 0.80% (0.60-1.00); 0 0.10% (-0.10 to 0.30); 1 0.10% (-0.10 to 0.30); 2 Age Group: 0-14 0.70% (0.50-1.00); 0 0.10% (-0.20 to 0.30); 1 0.20% (-0.10 to 0.40); 2 Age Group: 15-64 0.90% (0.60-1.10); 0 0.20% (0.00-0.50); 1 0.20% (-0.10 to 0.40); 2 Age Group: ≥ 65 1.10% (0.80-1.50); 0 0.60% (0.30-1.00); 1 0.40% (0.10-0.80); 2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Ito et al. (2007, 091262) **Period of Study:** 1999-2002 **Location:** New York City, NY	ED Visits **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** All Season: 1.31 (0.43) ppm Warm Months (April-September): 1.22 (0.32) ppm Cold Months (October-March): 1.41 (0.5) ppm **Range (5th, 95th):** All season: (0.77, 2.11) Warm months (April-September): (0.75, 1.82) Cold months (October-March): (0.78, 2.33) **Copollutant:** NR	**Increment:** 1.3 ppm **Relative Risk (Lower CI, Upper CI); Lag** Warm months: 1.15 (1.07-1.25); 0-1
Author: Jayaraman et al. (2008, 180352) **Period of Study:** 2004-2005 **Location:** New Delhi, India	Hospital Admissions **Health Outcome:** respiratory **Study Design:** time series **Statistical Analyses:** Poisson regression (GAM) **Age Groups Analyzed:** All ages Sample Description: daily HA for respiratory unit of Safdarjung hospital	**Averaging Time:** 24-h **Mean (SD) unit:** 2,379.14 (1,289.18) µg/m^3 **Range (min, max):** 588, 8458 **Copollutant:** SO_2: r = 0.217* NO_2: r = 0.204* SPM: r = 0.071 RSPM: r = 0.120 O_3: r = 0.063 *p < 0.05	**Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] ; lag:** Lags examined: lag days 0-3 Single Pollutant: 0.9989 (0.985, 2.715), 2 Multi-pollutant: 0.998 (0.993, 1.004), 2 Winter, all ages: 1.027 (1.004, 1.051), 2 Winter, males 50-69: 2.625 (1.048, 1.158)
Author: Karr et al. (2007, 090719) Period of Study: 1995-2000 **Location:** South Coast Air Basin, CA	Hospital Admissions **Health Outcome (ICD9):** Acute bronchiolitis (466.1) **Study Design:** Matched case control **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** Infants: 3 wk to 1 yr	**Pollutant:**CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Chronic: 1,770 ppb Subchronic: 1,720 ppb **Range (Min, Max):** Chronic: (120, 8300) Subchronic: (130, 5070) **Copollutant:** NR	**Increment:** 910 ppb, 960 ppb **Odds Ratio (Lower CI, Upper CI); lag:** Increment: 910 ppb Subchronic broncholitis: 1 (0.97-1.03) Increment: 960 ppb Chronic broncholitis: 1 (0.97-1.03)
Author: Karr et al. (2006, 088751) **Period of Study:** 1995-2000 **Location:** South Coast Air Basin, CA	Hospital Admissions **Health Outcome (ICD9):** Acute bronchiolitis (466.1) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** Infants: 3 wk to1 yr	**Pollutant:**CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1-day lag: Index*: 1,730 ppb Referent*: 1,750 ppb 4-day lag: Index*: 1,760 ppb Referent*: 1,790 ppb **Range (Min, Max):** Lag 1: Index*: (4, 9600) Referent*: (4, 9600) Lag 4: Index* (4, 8710) Referent* (4, 9600) **Copollutant:** NR * Index days: days lagged in reference to date of hospitalization of a case. Referent days: are for each case and includes all days that are the same day of wk and in the same mo as the index day for that case for CO.	**Increment:** 1361, 1400 ppb **Odds Ratio (Lower CI, Upper CI); Lag** Increment: 1361 ppb Age Group: Overall: 0.99 (0.96-1.02); 1 25-29 wk: 0.86 (0.68-1.1); 1 29 1/7 – 34 wk: 1 (0.86-1.15); 1 34 1/7 – 37 wk: 0.95 (0.87-1.04); 1 37 1/7 – 44 wk: 1 (0.97-1.03); 1 Increment: 1400 ppb Age Group: Overall: 0.97 (0.94-1); 4 25-29 wk: 0.93 (0.72-1.2); 4 29 1/7 – 34 wk: 0.89 (0.77-1.03); 4 34 1/7 – 37 wk: 0.98 (0.90-1.08); 4 37 1/7 – 44 wk: 0.97 (0.94-1); 4

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Kim et al. (2007, 092837) **Period of Study:** 2002 **Location:** Seoul, Korea	Hospital Admissions **Health Outcome (ICD10):** Asthma (J45 and J46) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All Ages	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** Daily Concentration: 8.6 (4.6) ppm Relevant Concentration: 2.8 (2.8) ppm **Range (Min, Max):** Daily Concentration: (0.8, 44.0) Relevant Concentration: (0.0, 30.4) **Copollutant:** NR	**Relative Risk (Lower CI, Upper CI); lag:** Individual Level SEP Quintile 1: 1.06 (1.02-1.09); 1-3 ma Quintile 2: 1.05 (1.02-1.09); 1-3 ma Quintile 3: 1.05 (1.01-1.08); 1-3 ma Quintile 4: 1.07 (1.03-1.11); 1-3 ma Quintile 5: 1.05 (1.00-1.09); 1-3 ma Regional Level SEP Quintile 1: 0.99 (0.92-1.07); 1-3 ma Quintile 2: 1.06 (1.02-1.11); 1-3 ma Quintile 3: 1.04 (1.02-1.07); 1-3 ma Quintile 4: 1.10 (1.06-1.15); 1-3 ma Quintile 5: 1.06 (1.03-1.09); 1-3 ma Overall: 1.06 (1.04-1.07); 1-3 ma Relative Effect Modification for SES Individual Level SEP Quintile 1: 1 Quintile 2: 1 (0.95.1.04); 1-3 ma Quintile 3: 0.99 (0.94-1.03); 1-3 ma Quintile 4: 1.02 (0.97-1.06); 1-3 ma Quintile 5: 0.99 (0.94-1.04); 1-3 ma Regional Level SEP Quintile 1: 1 Quintile 2: 1.05 (0.97-1.14); 1-3 ma Quintile 3: 1.03 (0.96-1.11); 1-3 ma Quintile 4: 1.08 (1-1.16); 1-3 ma Quintile 5: 1.05 (0.97-1.13); 1-3 ma
Author: Kontos et al. (1999, 011326) Period of Study: 1/1987-12/1992 **Location:** Piraeus, Greece	Hospital Admissions **Health Outcome (ICD9):** Respiratory conditions (laryngitis, bronchiolitis, tonsillitis, acute rhinopharyngitis, otitis, bronchopneumonia, pneumonia, asthma) **Study Design:** Time series **Statistical Analyses:** Stochastic dynamical system approach **Age Groups Analyzed:** 0-14 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean Range (SD) unit:** 1987: 4.2 mg/m^3 1992: 3.6 mg/m^3 **Range (Min, Max):** NR **Copollutant:** correlation 1987-1989 Smoke: r = 0.2979; SO_2: r = 0.2166; NO_2: r = 0.1913 1990-1992 Smoke: r = 0.5383; SO_2: r = 0.43283; NO_2: 0.5223	This study did not present quantitative results for CO.
Author: Lee et al. (2002, 034826) **Period of Study:** 12/1997-12/1999 **Location:** Seoul, Korea	Hospital Admissions **Health Outcome (ICD10):** Asthma (J45, J46) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** <5 yr	**Pollutant:** CO **Averaging Time:** 1-h max **Mean Range (SD) unit:** 1.8 (0.7) ppm IQR (25th, 75th): (1.2, 2.2) **Copollutant:** correlation PM_{10}: r = 0.598 SO_2: r = 0.812 NO_2: r = 0.785 O_3: r = -0.388	**Increment:** 1.0 ppm **Relative Risk (Lower CI, Upper CI); lag:** RR for asthma and exposure to various pollutants for children under 15 yr old Pollutant: CO: 1.16 (1.10-1.22); 2-3 avg CO, PM_{10}: 1.13 (1.07-1.20); 2-3 avg CO, SO_2: 1.17 (1.08-1.27); 2-3 avg CO, NO_2: 1.04 (0.95-1.14); 2-3 avg CO, O_3: 1.16 (1.11-1.22); 2-3 avg CO, O_3, PM_{10}: 1.148 (1.084-1.217); 2-3 avg CO, O_3, PM_{10}, SO_2: 1.168 (1.075-1.269); 2-3 avg CO, O_3, PM_{10}, SO_2, NO_2: 1.098 (0.994-1.214); 2-3 avg

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Lee et al. (2006, 098248) **Period of Study:** 1/2002-12/2002 **Location:** Seoul, Korea	Hospital Admissions **Health Outcome (ICD10):** Asthma (J45-46) **Study Design:** Time series **Statistical Analyses:** GAM with stringent parameters **Age Groups Analyzed:** <15 yr	**Pollutant:** CO **Averaging Time:** Maximum 2-h avg **Mean (SD) unit:** High SES: 6.08 (2.10) ppb Moderate SES: 6.35 (2.44) ppb Low SES: 6.67 (2.59) ppb **Range (Min, Max):** NR **Copollutant:** correlation NO_2: r = 0.55 SO_2: r = 0.72 PM_{10}: r = 0.28 O_3: r = -0.36	**Increment:** 3.01 ppb, 0.26 ppb, 4.52 ppb, 3.68 ppb **Relative Risk (Lower CI, Upper CI); lag:** Increment: 3.01 ppb Overall: 1.07 (0.96-1.20); 0 Increment: 0.26 ppb High SES: 1.06 (0.96-1.17); 0 Increment: 4.52 ppb Moderate SES: 0.96 (0.84-1.10); 0 Increment: 3.68 ppb Low SES: 1.02 (0.85-1.24); 0
Author: Lee et al. (2007, 090707) **Period of Study:** 1996-2003 **Location:** Kaohsiung, Taiwan	Hospital Admissions **Health Outcome (ICD9):** COPD (490-492, 494, 496) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.77 ppm **Range (Min, Max):** (0.23, 1.72) **Copollutant:** PM_{10} SO_2 NO_2 O_3	**Increment:** 0.29 ppm **Odds Ratio (Lower CI, Upper CI); lag:** CO <25°C: 1.398 (1.306-1.496); 0-2 ≥ 25°C: 1.189 (1.123-1.259); 0-2 CO. PM_{10} <25°C: 1.257 (1.152-1.371); 0-2 ≥ 25°C: 1.149 (1.079-1.224); 0-2 CO, SO_2 <25°C: 1.396 (1.295-1.504); 0-2 ≥ 25°C: 1.241 (1.161-1.326); 0-2 CO, NO_2 <25°C: 0.973 (0.877-1.080); 0-2 ≥ 25°C: 1.196 (1.104-1.297); 0-2 CO, O_3 <25°C: 1.378 (1.286-1.477); 0-2 ≥ 25°C: 1.170 (1.105-1.239); 0-2
Author: Lin et al. (1999, 040437) **Period of Study:** 5/1991-4/1993 **Location:** Sao Paulo, Brazil	ED Visits **Health Outcome (ICD9):** Respiratory illness (lower respiratory illness, upper respiratory illness, wheezing) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** <3 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 5 ppm **Range (Min, Max):** (1, 12) **Copollutant:** correlation PM_{10}: r = 0.50 NO_2: r = 0.35 SO_2: r = 0.56 O_3: r = 0.04	Increment: NR **Relative Risk (Lower CI, Upper CI); lag:** Overall Respiratory Illnesses CO: 1.206 (1.066-1.364); 0-5 CO, PM_{10}, O_3, SO_2, NO_2: 0.945 (0.808-1.105); 0-5 Lower Respiratory Illness CO: 1.203 (0.867-1.669); 0-5 CO, PM_{10}, O_3, SO_2, NO_2: 0.971 (0.641-1.472); 0-5 Upper Respiratory Illness CO: 1.237 (1.072-1.428); 0-5 CO, PM_{10}, O_3, SO_2, NO_2: 0.944 (0.785-1.135); 0-5 Wheezing CO: 0.813 (0.606-1.091); 0-5 CO, PM_{10}, NO_2, SO_2, O_3: 0.74 (0.505-1.085); 0-5

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Lin et al. (2003, 042549) **Period of Study:** 1/1981-12/1993 **Location:** Toronto, ON, Canada	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 6-12 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.18 (0.50) ppm **Range (Min, Max):** (0, 6.10) **Copollutant:** correlation SO_2: r = 0.37 NO_2: r = 0.55 O_3: r = -0.16 $PM_{2.5}$: r = 0.45 $PM_{10-2.5}$: r = 0.17 PM_{10}: r = 0.38	**Increment:** 0.5 ppm Odds Ratio (Lower CI, Upper CI); lag: Boys: Adjusting for Daily Weather Variables 1.05 (1-1.11); 1 / 1.07 (1.01-1.14); 2 1.08 (1.01-1.16); 3 / 1.08 (1-1.17); 4 1.07 (0.99-1.16); 5 / 1.07 (0.98-1.17); 6 1.07 (0.98-1.17); 7 Adjusting for PM and Daily Weather Variables 1.05 (0.99-1.11); 1 / 1.08 (1.01-1.16); 2 1.09 (1.01-1.18); 3 / 1.10 (1.02-1.20); 4 1.09 (1.00-1.18); 5 / 1.09 (0.99-1.19); 6 1.09 (0.99-1.20); 7 Girls: Adjusting for Daily Weather Variables 1.00 (0.93-1.06); 1 / 1.01 (0.94-1.10); 2 1.00 (0.91-1.09); 3 / 0.98 (0.89-1.09); 4 1.01 (0.91-1.13); 5 / 1.03 (0.92-1.16); 6 1.04 (0.93-1.17); 7 Adjusting for PM and Daily Weather Variables 1.00 (0.93-1.07); 1 / 1.01 (0.92-1.10); 2 0.99 (0.90-1.09); 3 / 0.97 (0.87-1.08); 4 0.99 (0.89-1.11); 5 / 1.02 (0.90-1.15); 6 1.05 (0.93-1.20); 7
Author: Lin et al. (2004, 055600) **Period of Study:** 1/1987-12/1998 **Location:** Vancouver, BC Canada	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** GAM, LOESS **Age Groups Analyzed:** 6-12 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.96 (0.52) ppm **Range (Min, Max):** (0.23, 4.90) **Copollutant:** correlation SO_2: r = 0.67 NO_2: r = 0.73 O_3: r = -0.35	Increment: 0.5 ppm **Relative Risk (Lower CI, Upper CI); lag:** Boys High SES: 1.06 (0.98-1.14); 1 / 1.06 (0.97-1.15); 2 1.07 (0.97-1.17); 3 / 1.03 (0.93-1.14); 4 1.01 (0.91-1.12); 5 / 1.01 (0.91-1.13); 6 1.06 (0.94-1.18); 7 Low SES: 1.06 (0.99-1.14); 1 / 1.03 (0.95-1.12); 2 1.01 (0.93-1.11); 3 / 0.99 (0.90-1.09); 4 0.96 (0.87-1.06); 5 / 0.98 (0.88-1.08); 6 0.98 (0.88-1.09); 7 Girls High SES: 1.05 (0.94-1.16); 1 / 1.02 (0.90-1.15); 2 0.97 (0.85-1.11); 3 / 0.95 (0.83-1.10); 4 0.93 (0.80-1.08); 5 / 0.95 (0.82-1.11); 6 1.01 (0.87-1.19); 7 Low SES: 1.01 (0.92-1.11); 1 / 0.98 (0.89-1.10); 2 0.99 (0.88-1.11); 3 / 1.05 (0.93-1.19); 4 1.07 (0.94-1.21); 5 / 1.07 (0.94-1.23); 6 1.04 (0.91-1.20); 7
Author: Lin et al. (2005, 087828) **Period of Study:** 1998-2001 **Location:** Toronto, Canada	Hospital Admissions **Health Outcome (ICD9):** Respiratory infections (464, 466, and 480-487) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** <5 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.16 (0.38) ppm **Range (Min, Max):** (0.38, 2.45) **Copollutant:** correlation $PM_{2.5}$: r = 0.10 $PM_{10-2.5}$: r = 0.06 PM_{10}: r = 0.10 SO_2: r = 0.12 NO_2: r = 0.20 O_3: r = -0.11	**Increment:** 0.44 ppm Odds Ratio (Lower CI, Upper CI); Lag Boys No adjustment: 1.11 (1.01-1.22); 0-3 / 1.10 (1.00-1.22); 0-5 Adjustment for weather variables: 1.13 (1.03-1.24); 0-3 / 1.13 (1.02-1.25); 0-5 Adjustment for weather variables and PM: 1.08 (0.98-1.20); 0-3 / 1.08 (0.97-1.20); 0-5 Girls No adjustment: 0.99 (0.89-1.10); 0-3 / 1.00 (0.89-1.13); 0-5 Adjustment for weather variables: 1.02 (0.92-1.14); 0-3: / 1.05 (0.93-1.18); 0-5 Adjustment for weather variables and PM: 1.01 (0.90-1.13); 0-3 / 1.02 (0.90-1.15); 0-5 Total No adjustment: 1.06 (0.98-1.14); 0-3 / 1.06 (0.98-1.15); 0-5 Adjustment for weather variables: 1.09 (1.01-1.17); 0-3 / 1.10 (1.01-1.19); 0-5 Adjustment for weather variables and PM: 1.05 (0.97-1.14); 0-3 / 1.06 (0.97-1.15); 0-5

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Linn et al. (2000, 002839) **Period of Study:** 1992-1995 **Location:** Los Angeles, CA	Hospital Admissions **Health Outcome (ICD9):** APR-DRG Codes: Pulmonary (75-101); COPD (88) ICD9 Codes: Asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** 0-29 yr; ≥ 30 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Winter 1.7 (0.8) ppm Spring 1.0 (0.3) ppm Summer 1.2 (0.4) ppm Fall 2.1 (0.8) ppm **Range (Min, Max):** Winter: (0.5, 5.3) Spring: (0.4, 2.2) Summer: (0.3,2.7) Fall: (0.6, 4.3) **Copollutant:** correlation Winter NO_2: r = 0.89; PM_{10}: r = 0.78; O_3: r = -0.43 Spring NO_2: r = 0.92; PM_{10}: r = 0.54; O_3: r = 0.29 Summer NO_2: r = 0.94; PM_{10}: r = 0.72; O_3: r = 0.03 Fall NO_2: r = 0.84; PM_{10}: r = 0.58; O_3: r = -0.36	**Increment:** 1.0 ppm **β (SE); lag:** Pulmonary Age Group: ≥ 30 All Year: 0.007 Winter: 0.016 Spring: 0.014 Summer: 0.020 Fall: 0.020 Asthma Age Group 0-29 All Year: 0.036 Asthma Age Group: ≥ 30; All Year: 0.028 Winter: 0.045 Fall: 0.039 COPD Age Group: ≥ 30 All Year: 0.019 Winter: 0.035 Fall: 0.029

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Luginaah et al. (2005, 057327) **Period of Study:** 4/1995-12/2000 **Location:** Windsor, ON, Canada	Hospital Admissions **Health Outcome (ICD9):** Respiratory illness (460-519) **Study Design:** Time series and case crossover **Statistical Analyses:** 1. Time-series: Poisson 2. Case-crossover: conditional logistic regression **Age Groups Analyzed:** All ages 0-14 yr 15-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 1-h max **Mean (SD) unit:** 1.3 (1.0) ppm **Range (Min, Max):** (0, 11.82) **Copollutant:** correlation NO_2: r = 0.38 SO_2: r = 0.16 O_3: r = 0.10 CoH: r = 0.31 PM_{10}: r = 0.21	Increment: 1.17 ppm **Relative Risk (Lower CI, Upper CI); Lag** Females and Case-crossover study design Age Group: All ages: 1.037 (0.968-1.111); 1 1.063 (0.976-1.158); 2 1.087 (0.982-1.203); 3 Age Group: 0-14: 1.147 (1.006-1.307); 1 1.186 (1.020-1.379); 2 1.221 (1.022-1.459); 3 Age Group: 15-64: 1.005 (0.884-1.141); 1 1.007 (0.859-1.181); 2 1.032 (0.858-1.240); 3 Age Group: ≥ 65: 1.014 (0.922-1.116); 1 1.024 (0.907-1.156); 2 1.035 (0.893-1.200); 3 Males and Case-crossover study design Age Group: All Ages: 0.950 (0.884-1.020); 1 0.945 (0.862-1.036); 2 0.965 (0.866-1.075); 3 Age Group: 0-14: 1.003 (0.904-1.113); 1 0.997 (0.871-1.141); 2 0.970 (0.824-1.141); 3 Age Group: 15-64: 1.036 (0.870-1.233); 1 1.033 (0.821-1.299); 2 0.991 (0.760-1.293); 3 Age Group: ≥ 65: 0.867 (0.775-0.970); 1 0.865 (0.752-0.994); 2 0.946 (0.807-1.109); 3 Female and Time-series study design Age Group: All Ages: 1.049 (0.993-1.108); 1 1.032 (0.993-1.188); 2 1.051 (0.993-1.112); 3 Age Group: 0-14: 1.077 (0.979-1.184); 1 1.068 (1.001-1.139); 2 1.100 (0.997-1.213); 3 Age Group: 15-64: 1.072 (0.962-1.195); 1 1.025 (0.944-1.112); 2 1.081 (0.963-1.213); 3 Age Group: ≥ 65: 1.029 (0.957-1.118); 1 1.030 (0.928-1.144); 2 1.013 (0.899-1.142); 3 Male and Time-series study design Age Group: All Ages: 0.989 (0.932-1.049); 1 0.986 (0.946-1.029); 2 0.987 (0.929-1.048); 3 Age Group: 0-14: 1.034 (0.949-1.126); 1 0.996 (0.933-1.062); 2 0.968 (0.881-1.064); 3 Age Group: 15-64: 0.994 (0.854-1.157); 1 0.988 (0.884-1.104); 2 0.951 (0.806-1.121); 3 Age Group: ≥ 65: 0.901 (0.817-0.994); 1 0.904 (0.803-1.019); 2 0.963 (0.845-1.098); 3

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Martins et al. (2002, 035059) Period of Study: 5/1996-9/1998 **Location:** Sao Paulo, Brazil	ED Visits **Health Outcome (ICD10):** Chronic lower respiratory disease (CLRD: J40-47) for chronic bronchitis, emphysema, other COPD, asthma, and bronchiectasia **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** >64 yr	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Mean (SD) unit:** 3.7 (1.7) ppm **Range (Min, Max):** (1.0, 12.6) **Copollutant: correlation** NO_2: r = 0.62; SO_2: r = 0.51; PM_{10}: r = 0.73; O_3: r = 0.07	**Increment:** 1.63 ppm **β (SE); lag:** Chronic Lower Respiratory Diseases Age Group >64: 0.0489 (0.0274); 2
Author: Masjedi et al. (2003, 052100) Period of Study: 9/1997-2/1998 **Location:** Tehran, Iran	ED Visits **Health Outcome (ICD9):** Total acute respiratory conditions; asthma (493); COPD (490-492, 494, 496) **Study Design:** Time series **Statistical Analyses:** Multiple step-wise regression **Age Groups Analyzed:** Adults	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 8.85 ppm **Range (Min, Max):** (2.15, 23.8) **Copollutant:** NR	**Increment:** NR **β (p-value); lag;** Asthma: -0.779 (0.12) COPD: 0.012 (0.71) Acute Respiratory conditions: -0.086 (0.400) Correlation coefficients: Mean 3-day CO levels and asthma: -0.300 (0.149) Mean weekly CO level and asthma: -0.14 (0.2) Mean 10-day CO levels and asthma: -0.05 (0.43)
Author: McGowan et al. (2002, 030325) **Period of Study:** 6/1988- 12/1998 **Location:** Christchurch, New Zealand	Hospital Admissions **Health Outcome (ICD9):** Pneumonia (480-487); acute respiratory infections (460-466); chronic lung diseases (491-492, 494-496); asthma (493) **Study Design:** Time series **Statistical Analyses:** Generalized Additive Model **Age Groups Analyzed:** <15 yr; >64 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.16 (1.51) mg/m^3 **Range (Min, Max):** (0, 15.7) **Copollutant:** NR	This study did not provide quantitative results for CO.
Author: Migliaretti et al. (2007, 193772) **Period of Study:** 1/1997-12/1999 **Location:** Turin, Italy	Hospital Admissions **Health Outcome (ICD9):** Respiratory illness (chronic bronchitis, emphysema, and other COPD) (490-496) **Study Design:** Case control **Statistical Analyses:** Multiple logistic regression **Age Groups Analyzed:** ≥ 15 yr 15-64 yr >64 yr	**Pollutant:** CO **Averaging Time:** 8-h median **Median (SD) unit:** 3.36 (1.57) mg/m^3 **Range (Min, Max):** NR **Copollutant:** correlation TSP	**Increment:** 1 mg/m3 **Odds Ratio (Lower CI, Upper CI); lag:** CO Age Group ≥ 15: 1.053 (1.030-1.070) 15-64: 1.040 (0.987-1.085) >64: 1.054 (1.027-1.083) CO , TSP Age Group ≥ 15: 1.058 (1.024-1.096) 15-64: 1.062 (0.993-1.135) >64: 1.054 (1.011-1.099)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Moolgavkar (2000, 010274) **Period of Study:** 1987-1995 **Location:** 3 U.S. counties: Los Angeles County,CA Cook County, IL Maricopa County, AZ	Hospital Admissions **Health Outcome (ICD9):** COPD plus asthma (490-496) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All Ages 0-19 yr 20-64 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h median **Median unit:** Cook: 993 ppb LA: 1347 ppb Maricopa: 1240 ppb **Range (Min, Max):** Cook: (224, 3912) LA:(237,5955) Maricopa: (269, 4777) **Copollutant:** correlation Cook County: NO_2: r = 0.63; SO_2: r = 0.35; O_3: r = -0.28 LA County: NO_2: r = 0.80; SO_2: r = 0.78; O_3: r = -0.52 Maricopa County: NO_2: r = 0.66; SO_2: r = 0.53; O_3: r = -0.61	**Increment:** 1.0 ppm **% Increase (t-statistic); lag:** Age Group: ≥ 65 Cook County CO: 2.60 (1.9); 0; / 3.00 (2.2); 1; / 1.30 (1.0); 2; 1.40 (1.1); 3; / 1.10 (0.8); 4; / 2.30 (1.8); 5 Los Angeles County CO: 5.40 (11.3); 0; / 4.90 (10.1); 1; / 5.00 (10.2); 2; 4.90 (10.1); 3; / 4.00 (8.3); 4; / 4.30 (8.6); 5; CO, PM_{10}: 4.30 (3.3); 0; / 5.30 (4.2); 1; / 5.10 (4.0); 2; 6.80 (5.6); 3; / 6.90 (5.4); 4; / 6.30 (4.7); 5; CO, $PM_{2.5}$: 3.00 (1.9); 0; / 3.90 (2.5); 1; / 4.20 (2.6); 2; 6.50 (4.4); 3; / 5.80 (3.8); 4; / 5.10 (3.1); 5 Maricopa County CO: 1.40 (1.0); 0; / 0.80 (0.6); 1; / 1.20 (0.9); 2; 1.20 (0.9); 3; / 1.50 (1.1); 4; / 4.90 (3.8); 5 Age Group: 0-19 Los Angeles County CO: 8.20 (14.4); 0; / 9.00 (15.9); 1; / 9.20 (16.4); 2; 8.50 (15.0); 3; / 7.00 (12.1); 4; / 4.80 (8.1); 5; CO, PM_{10}: 7.50 (14.4); 0; /: 7.40 (5.2); 1; / 6.40 (4.3); 2; 8.00 (5.5); 3; / 6.30 (4.0); 4; / 5.30 (3.5); 5; CO, $PM_{10-2.5}$: 5.70 (3.4); 0; / 7.50 (4.9); 1; / 5.60 (3.3); 2; 5.40 (3.5); 3; / 4.40 (2.7); 4; / 1.80 (1.1); 5 Age Group: 20-64 Los Angeles County CO: 3.70 (8.6); 0; / 3.90 (9.1); 1; / 4.50 (10.6); 2; 3.50 (8.3); 3; / 3.40 (7.9); 4; / 3.50 (7.9); 5; CO, PM_{10}: 5.00 (4.6); 0; / 3.00 (2.7); 1; / 3.10 (2.8); 2; 5.20 (4.7); 3; / 5.90 (5.1); 4; / 4.90 (4.4); 5; CO, $PM_{2.5}$: 3.50 (2.5); 0; / 0.60 (0.4); 1; / 1.10 (0.8); 2; 5.70 (4.1); 3; / 4.70 (3.3); 4; / 3.90 (2.8); 5; CO, $PM_{10-2.5}$: 2.80 (2.2); 0; / 2.50 (2.0); 1;/ 0.60 (0.5); 2; 3.90 (3.2); 3; / 3.40 (2.8); 4; / 4.00 (3.4); 5
Author: Moolgavkar (2003, 042864) **Period of Study:** 1987-1995 **Location:** 2 U.S. counties: Los Angeles County, CA, and Cook County, IL	Hospital Admissions **Health Outcome (ICD9):** COPD plus asthma (490-496) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, Poisson GLM with natural splines **Age Groups Analyzed:** All Ages; ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h median **Median unit:** Cook: 993 ppb LA: 1347 ppb Maricopa: 1240 ppb **Range (Min, Max):** Cook: (224, 3912) LA: (237,5955) **Copollutant:** correlation Cook County: NO_2: r = 0.63; SO_2: r = 0.35; O_3: r = -0.28 Los Angeles County: NO_2: r = 0.80; SO_2: r = 0.78; O_3: r = -0.52	**Increment:** 1 ppm **% Increase (t-statistic); lag:** COPD–Los Angeles County CO: GAM-30 (10-8): 5.48 (17.67); 0; / 5.67 (18.22); 1; / 5.90 (19.01); 2; 5.28 (16.94); 3; / 4.59 (14.50); 4; / 4.10 (12.80); 5 GAM-100 (10-8): 2.37 (8.67); 0; / 2.41 (8.73); 1; / 2.41 (8.76); 2; 1.81 (6.58); 3; / 1.38 (4.94); 4; / 1.07 (3.82); 5 NS-100: 2.28 (5.65); 0; / 2.29 (5.50); 1; / 2.32 (5.33); 2; 1.74 (4.10); 3; / 1.30 (3.16); 4; / 1.00 (2.46); 5 COPD–Cook County CO: GAM-100 (10-8): 2.11 (1.62); 0; / 2.85 (2.16); 1; / 1.14 (0.86); 2; 1.05 (0.79); 3; / 0.43 (0.33); 4; / 0.34 (0.26); 5

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Neidell et al. (2004, 057330) **Period of Study:** 1992-1998 **Location:** California	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Linear Regression **Age Groups Analyzed:** 0-1 yr 1-3 yr 3-6 yr 6-12 yr 12-18 yr	**Pollutant:** CO **Averaging Time:** 24-h avg Mean (SD) unit: 1.777 (1.037) ppm Range (Min, Max): NR **Copollutant:** correlation O_3 PM_{10} NO_2	**Increment:** NR **β (SE); lag;** Single-pollutant model Age Group 0-1: -0.007 (0.009); 1-3: 0.027 (0.009); 3-6: 0.053 (0.010); 6-12: 0.047 (0.009); 12-18: 0.025 (0.008) Fixed effect controlling for O_3, PM_{10}, and NO_2 Age Group 0-1: -0.01 (0.01); 1-3: 0.024 (0.011); 3-6: 0.049 (0.011); 6-12: 0.023 (0.011); 12-18: 0.021 (0.009) Fixed effect controlling for O_3, PM_{10}, NO_2 and avoidance behavior Age Group 0-1: -0.010 (0.010); 1-3: 0.027 (0.011); 3-6: 0.051 (0.011); 6-12: 0.025 (0.011); 12-18: 0.021 (0.009)
Author: Norris et al. (1999, 040774) **Period of Study:** 9/1995- 12/1996 **Location:** Seattle, WA	ED Visits **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Semiparametric Poisson GAM **Age Groups Analyzed:** <8 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.6 (0.5) ppm **Range (Min, Max):** (0.6, 4.1) **Copollutant: correlation** PM_{10}: r = 0.74 NO_2 (1-h max): r = 0.47 NO_2 (24-h avg.): r = 0.66 SO_2 (1-h max): r = 0.15 SO_2 (24-h avg.): r = 0.32	**Increment:** 0.6 ppm **Relative Risk (Lower CI, Upper CI); Lag** High Utilization: 1.04 (0.93-1.16); 1 Low Utilization: 1.15 (1.05-1.28); 1 All: 1.10 (1.02-1.19); 1
Author: Peel et al. (2005, 056305) **Period of Study:** 1/1993- 8/2000 **Location:** Atlanta, GA	ED Visits **Health Outcome (ICD9):** Asthma (493, 786.09); COPD (491, 492, 496); URI (460-466, 477); pneumonia (480-486) **Study Design:** Time series **Statistical Analyses:** 1. Poisson GEE or asthma, URI, all respiratory 2. Poisson GLM for pneumonia and COPD **Age Groups Analyzed:** Primary Analysis: All Ages Secondary Analysis: 2-18 yr	**Pollutant:** CO **Averaging Time:** 1-h max **Mean (SD) unit:** 1.8 (1.2) ppm **Range (10th, 90th):** (0.5, 3.4) **Copollutant:** NR	**Increment:** 1.0 ppm **Relative Risk (Lower CI, Upper CI); Lag** Health Condition All respiratory illnesses: 1.011 (1.004-1.019); 0-2 URI: 1.012 (1.003-1.021); 0-2 / 1.066 (1.045-1.087); 0-13 Asthma: 1.010 (0.999-1.022); 0-2 1.076 (1.047-1.105); 0-13 Pneumonia: 1.009 (0.996-1.021); 0-2 1.045 (1.011-1.080); 0-13 COPD: 1.026 (1.004-1.048); 0-2 1.032 (0.975-1.092); 0-13 RR for asthma and exposure to CO for children age 2-18: 1.019 (1.004-1.035); 0-2 RR for all respiratory illnesses and CO exposure for all ages AQS (1/1/93- 8/31/00): 1.011 (1.004-1.019); 0-2 AQS (8/1/98- 8/31/00): 1.010 (1.000-1.021); 0-2 ARIES (8/1/98- 8/31/00): 1.018 (1.003-1.033); 0-2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Sauerzapf et al. (2009, 180082) **Period of Study:** Jan 2006-Feb 2007 **Location:** Norfolk county, England	Hospital Admissions **Health Outcome:** COPD **Study Design:** Case crossover **Statistical Analyses:** Logistic Regression **Age Groups Analyzed:** 18+ yr (90% of patients 60+ yr) **Sample Description:** 1,050 COPD admissions	**Averaging Time:** 24 h **Mean (SD) unit:** Control days: 194.46 (80.93) Case days: 204.73 (119.97) **Range (min, max):** Control days: 105.20, 408.10 Case days: 108.70, 432.20 **Copollutant:** NO, NO_2, NO_X, O_3 * Control days = 7 days prior to admission; Case days = day of admission	**Increment:** 10 µg/m^3 **Lags examined:** 0-8 OR Estimate [Lower CI, Upper CI]; lag: Unadjusted: 1.010 (1.001, 1.019); lag 0-7 Adjusted: 1.015 (1.005, 1.025); lag 0-7 Unadjusted: 1.013 (1.001, 1.025); lag 1-8 Adjusted: 1.018 (1.005, 1.031); lag 1-8
Author: Sheppard et al. (1999, 086921) **Period of Study:** 1987-1994 **Location:** Seattle, WA	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** <65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1831 ppb **IQR (25th, 75th):** (1277, 2201) **Copollutant:** correlation PM_{10}: r = 0.83; $PM_{2.5}$: r = 0.78; $PM_{10-2.5}$: r = 0.56; O_3: r = -0.18; SO_2: r = 0.24	**Increment:** 924 ppb % **Increase (Lower CI, Upper CI); Lag** CO: 6% (3, 9); 3 CO, $PM_{2.5}$: 5% (1, 8); 3
Author: Slaughter et al. (2005, 073854) **Period of Study:** 1/1995-6/2001 **Location:** Spokane, WA	Hospital Admissions & ED Visits **Health Outcome (ICD9):** Respiratory causes (460-519) Asthma (493); COPD (491, 492, 494, 496) acute respiratory tract infections not including colds and sinusitis (464-466, 490) **Study Design:** Time series **Statistical Analyses:** Poisson GLM, Natural Splines **Age Groups Analyzed:** All ages, Adults	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (5th, 95th):** (1.25, 3.05) **Copollutant:** correlation PM_1: r = 0.63 $PM_{2.5}$: r = 0.62 PM_{10}: r = 0.32 $PM_{10-2.5}$: r = 0.32	**Increment:** 1.0 ppm **Relative Risk (Lower CI, Upper CI); lag:** ED Visits All Respiratory Illnesses Age Group: All Ages: 0.99 (0.96-1.02); 1 / 1.01 (0.98-1.04); 2 1.03 (1.00-1.06); 3 Asthma Age Group: All Ages: 1.00 (0.95-1.06); 1 / 1.01 (0.96-1.07); 2 1.06 (1.00-1.11); 3 COPD Age Group: Adults: 0.92 (0.85-1.00); 1 / 0.99 (0.91-1.08); 2 1.01 (0.93-1.10); 3 Hospital Admissions: All Respiratory Illnesses Age Group: All Ages: 0.99 (0.95-1.02); 1 / 1.00 (0.96-1.04); 2 0.99 (0.96-1.03); 3 Asthma Age Group: All Ages: 1.02 (0.92-1.13); 1 / 1.06 (0.96-1.17); 2 1.00 (0.91-1.11); 3 COPD Age Group: Adults: 0.94 (0.86-1.03); 1 / 1.04 (0.95-1.13); 2 0.97 (0.88-1.06); 3

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Stieb et al. (2000, 011675) **Period of Study:** 7/1992- 3/1996 **Location:** Saint John, Canada	ED Visits **Health Outcome (ICD9):** Asthma; COPD; respiratory infections; all respiratory illnesses **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg 1-h max **Mean (SD) unit:** All yr: 0.5 (0.3) ppm May-September: 0.6 (0.3) ppm All yr: 1.6 (1.1) ppm, May-September: 1.7 (0.9) ppm **Range (Min, Max): NR** **Copollutant: correlation** H_2S: r = -0.10; NO_2: r = 0.68; O_3: r = -0.05; SO_2: r = 0.31; TRS: r = 0.07; PM_{10}: r = 0.28; $PM_{2.5}$: r = 0.27; H+: r = 0.23; SO_4^{2-}: r = 0.27; CoH: r = 0.55	**Increment:** 0.5 & 1.7 ppm **AI% Increase (Lower CI, Upper CI); lag:** Respiratory Illnesses Increment: 0.5 ppm All Year: -3.40; 7 Increment: 1.7 ppm May- September: -5.70
Author: Sun et al. (2006, 090768) **Period of Study:** 1/2004- 12/2004 **Location:** Taiwan	ED Visits **Health Outcome (ICD9):** Asthma (493) **Study Design:** Cross sectional **Statistical Analyses:** Pearson correlation analysis **Age Groups Analyzed:** <16 yr; 16-55 yr	**Pollutant:** CO **Averaging Time:** Monthly **Mean (SD) unit**: NR **Range (Min, Max):** NR **Copollutant:** NR	Incre**ment: NR** **Correlation Coefficient:** Asthma Age Group: <16: 0.653 16-55: 0.425
Author: Tenias et al. (2002, 026077) **Period of Study:** 1/1994- 12/1995 **Location:** Valencia, Spain	ED Visits **Health Outcome (ICD9):** COPD (491, 492, 494, 496) **Study Design:** Time series **Statistical Analyses:** 1. Poisson autoregressive 2. Sensitivity: GAM, LOESS **Age Groups Analyzed:** >14 yr	**Pollutant:** CO **Averaging Time:** 24-h avg 1-h max **Mean (SD) unit:** 24-h avg All yr: 3.1 mg/m^3 Warm Months: 2.5 mg/m^3 Cold Months: 3.7 mg/m^3 1-h avg All yr: 6.7 mg/m^3 Warm Months: 5.4 mg/m^3 Cold Months: 8.0 mg/m^3 **Range (Min, Max):** 24-h avg: (0.9, 7.1) 1-h max: (1.6, 17.2) **Copollutant:** correlation SO_2: r = 0.734; NO_2: r = 0.180; O_3: r = -0.517	Increment: 1 mg/m^3 **Relative Risk (Lower CI, Upper CI); Lag** 24-h avg All Year: 1.074 (0.998- 1156); 1 Cold Months: 1.070 (0.991-1.156); 1 Warm Months: 1.129 (0.960-1.329); 1 1-h max All Year: 1.039 (1.014-1.066); 1 Cold Months: 1.037 (1.010-1.064); 1 Warm Months: 1.058 (0.994-1.127); 1 All Year: sinusoidal terms: 1.039 (1.010-1.066); 1 All Year: humidity and temperature variables: 1.040 (1.014-1.067); 1 All Year: GAM, LOESS: 1.042 (1.019-1.066); 1
Author: Thompson et al. (2001, 073513) **Period of Study:** 1/1993- 12/1995 **Location:** Belfast, Northern Ireland	ED Visits **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** Children	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Warm Season: 0.57 (0.41) ppm Cold Season: 0.74 (0.73) ppm **IQR (25th, 75th):** Warm Season: (0.3, 0.7) Cold Season: (0.4, 0.8) **Copollutant:** correlation SO_2 (log): r = 0.64; PM_{10} (log): r = 0.57; O_3: r = -0.52; NO_X (log): r = 0.74; NO (log): r = 0.71; NO_2: r = 0.69	**Increment:** NR **Relative Risk (Lower CI, Upper CI); lag:** Temperature included in the model: 1.04 (1.00-1.09); 0 / 1.07 (1.02-1.12); 0-1 1.06 (1.00-1.12); 0-2 / 1.07 (1.00-1.14); 0-3 Warm Season: 1.06 (0.98-1.16); NR Cold Season: 1.07 (1.01-1.14); NR Adjusted for benzene level: 0.92 (0.83-.02); 0-1 avg. **Note:** The increment the study uses to calculate effect estimates is a doubling in CO levels, but The study did not provide this value.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Tolbert et al. (2007, 090316) **Period of Study:** 1/1993- 12/2004 **Location:** Atlanta, GA	ED Visits **Health Outcome (ICD9):** Respiratory disease: asthma (493, 786.07, 786.09); COPD (491, 492, 496); URI (460-465, 460.0, 477); pneumonia (480-496); bronchiolitis (466.1, 466.11, 466.19)) **Study Design:** Time series **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 1-h max **Mean (SD) unit:** 1.6 ppm **Range (Min, Max):** (0.1, 7.7) **Copollutant: correlation** PM_{10}: r = 0.51; O_3: r = 0.27; NO_2: r = 0.70; SO_2: r = 0.28; Coarse PM: r = 0.38; $PM_{2.5}$: r = 0.47; SO_4: r = 0.14;EC: r = 0.66; OC: r = 0.59; TC: r = 0.63; OHC: r = 0.29	**Increment:** 1.22 ppm **Relative Risk (Lower CI, Upper CI); lag:** **Respiratory Diseases:** 1.016 (1.009-1.022); 3 **Note:** The study only provides results of the multi-pollutant models in figures, not quantitatively.
Author: Trapasso and Keith (1999, 180127) **Period of Study:** 1/1994- 12/1994 **Location:** Bowling Green, KY	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Time series **Statistical Analyses:** Spearman Rank Correlation Coefficient **Age Groups Analyzed:** All ages	**Pollutant: CO** **Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR **Correlation Coefficient (lag)** CO Mean: r = 0.19;0 CO Mean: r = 0.27; 1 CO Mean: r = 0.21; 2 CO Max: r = 0.26; 0 CO Max: r = 0.36; 1 CO Max: r = 0.24; 2
Author: Tsai et al. (2006, 089768) **Period of Study:** 1996-2003 **Location:** Kaohsiung, Taiwan	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.77 ppm **Range (Min, Max):** (0.23, 1.72) **Copollutant:** PM_{10} SO_2 NO_2 O_3	**Increment:** 0.29 ppm **Odds Ratio (Lower CI, Upper CI); lag** OR for getting asthma and exposure to various pollutants for all ages at either <25°C or ≥ 25°C CO <25°C: 1.414 (1.300-1.537); 0-2 ≥ 25°C: 1.222 (1.138-1.312); 0-2 CO, PM_{10} <25°C: 1.251 (1.125-1.393); 0-2 ≥ 25°C: 1.178 (1.088-1.274); 0-2 CO, SO_2 <25°C: 1.207 (1.076-1.354); 0-2 ≥ 25°C: 1.290 (1.188-1.400); 0-2 CO, NO_2 <25°C: 0.916 (0.807-1.039); 0-2 ≥ 25°C: 1.249 (1.127-1.384); 0-2 CO, O_3 <25°C: 1.396 (1.282-1.520); 0-2 ≥ 25°C: 1.195 (1.113-1.284); 0-2
Author: Vigotti et al. (2007, 090711) **Period of Study:** 1/2000- 12/2000 **Location:** Pisa, Italy	ED Visits **Health Outcome (ICD9):** Respiratory disease: asthma (493); dry cough (468); acute bronchitis (466) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** <10 yr; >65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.5 (0.7) ug/m^3 **Range (Min, Max):** (0.3, 3.5) **Copollutant:** correlation NO_2: r = 0.62 PM_{10}: r = 0.70	**Increment:** 1mg/m^3 **% Increase (Lower CI, Upper CI); lag** Age Group <10: 18.60% (-6.90 to 51.10); 1 >65: 26.50% (3.40-54.80); 4

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Villeneuve et al. (2006, 091179) **Period of Study:** 1995-2000 **Location:** Toronto, ON, Canada	Physician Visits **Health Outcome (ICD9):** Allergic rhinitis (177) **Study Design:** Time series **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** >65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.1 (0.4) ppm **Range (Min, Max):** (0.0, 2.2) **Copollutant:** $PM_{2.5}$ PM_{10} $PM_{10-2.5}$ SO_2 NO_2 O_3	Increment: 0.4 ppm **Odds Ratio (Lower CI, Upper CI); Lag** The study did not present quantitative results for CO.
Author: Xirasagar et al. (2006, 093267) **Period of Study:** 1998- 2001 **Location:** Taiwan	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Cross sectional **Statistical Analyses:** Spearman Rank Correlations **Age Groups Analyzed:** 0-14 yr; <2 yr; 2-5 yr; >5 yr	**Pollutant:** CO **Averaging Time:** Monthly **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR **Correlation Coefficient (Lag)** Age Group: <2: r = -0.208 2-5: r = -0.281 >5: r = -0.134
Author: Yang et al. (2007, 092848) **Period of Study:** 1996-2003 **Location:** Taipei, Taiwan	Hospital Admissions **Health Outcome (ICD9):** Asthma (493) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.33 ppm **Range (Min, Max):** (0.32, 3.62) **Copollutant:** PM_{10} SO_2 NO_2 O_3	**Increment:** 0.53 ppm **Odds Ratio (Lower CI, Upper CI); Lag** CO <25°C: 1.076 (1.019-1.136); 0-2 ≥ 25°C: 1.277 (1.179-1.383); 0-2 CO, PM_{10} <25°C: 1.050 (0.983-1.122); 0-2 ≥ 25°C: 1.332 (1.216-1.459); 0-2 CO, SO_2 <25°C: 1.131 (1.059-1.207); 0-2 ≥ 25°C: 1.278 (1.174-1.392); 0-2 CO, NO_2 <25°C: 0.915 (0.839-0.997); 0-2 ≥ 25°C: 1.177 (1.049-1.320); 0-2 CO, O_3 <25°C: 1.169 (1.102-1.240); 0-2 ≥ 25°C: 1.275 (1.177-1.382); 0-2
Author: Yang et al. (2007, 092847) **Period of Study:** 1996-2003 **Location:** Taipei, Taiwan	Hospital Admissions **Health Outcome (ICD9):** COPD: (490-492, 494, 496) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.33 ppm **Range (Min, Max):** (0.32, 3.66) ppm **Copollutant:** PM_{10} SO_2 NO_2 O_3	**Increment:** 0.53 ppm **Odds Ratio (Lower CI, Upper CI); Lag** CO <20°C: 0.975 (0.921,1.033); 0-2 ≥ 20°C: 1.227 (1.178-1.277); 0-2 CO, PM_{10} <20°C: 0.925 (0.863-0.992); 0-2 ≥ 20°C: 1.177 (1.123-1.235); 0-2 CO, SO_2 <20°C: 0.895 (0.832-0.962); 0-2 ≥ 20°C: 1.274 (1.219-1.331); 0-2 CO, NO_2 <20°C: 1.000 (0.910-1.099); 0-2 ≥ 20°C: 1.061 (0.998-1.129); 0-2 CO, O_3 <20°C: 0.935 (0.875-0.999); 0-2 ≥ 20°C: 1.234 (1.185-1.285); 0-2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Yang et al. (2005, 090184) **Period of Study:** 1/1994- 12/1998 **Location:** Vancouver, Canada	Hospital Admissions **Health Outcome (ICD9):** COPD (490-492, 494, 496) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** .71 (0.28) ppm **Range (Min, Max):** (0.30, 2.48) **Copollutant:** correlation O_3: r = -0.56 NO_2: r = 0.73 SO_2: r = 0.67 PM_{10}: r = 0.50	**Increment:** 0.3 ppm **Relative Risk (Lower CI, Upper CI); lag** CO 1.03 (1.00-1.06); 0 / 1.04 (1.01-1.08); 0-1 1.05 (1.01-1.09); 0-2 / 1.05 (1.00-1.10); 0-3 1.06 (1.01-1.11); 0-4 / 1.07 (1.02-1.12); 0-5 1.08 (1.02-1.13); 0-6 MultiPollutant: CO, O_3: 1.11 (1.04-1.18); 0-6 CO, NO_2: 1.04 (0.95-1.14); 0-6 CO, SO_2: 1.11 (1.01-1.22); 0-6 CO, PM_{10}: 1.02 (0.93-1.12); 0-6 CO, PM_{10}, O_3, NO_2, SO_2: 1.08 (0.96-1.22); 0-6 CO, O_3, NO_2, SO_2: 1.10 (0.98-1.23); 0-6
Author: Yang et al. (2003, 055621) **Period of Study:** 1/1986- 12/1998 **Location:** Vancouver, BC, Canada	Hospital Admissions **Health Outcome (ICD9):** Respiratory diseases (460-519) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** <3 yr; ≥ 65 yr	**Pollutant**: CO **Averaging Time:** 24-h avg **Mean (SD) unit**: 0.98 (0.54) ppm **IQR (25th, 75th):** (0.62, 1.16) **Copollutant: correlation** O_3: r = -0.52 CoH NO_2 SO_2	**Increment:** 0.54 ppm **Odds Ratio (Lower CI, Upper CI); lag** OR for respiratory diseases and exposure to various pollutants for people <3 and ≥ 65 Age Group: <3 CO alone: 1.04 (1.01-1.07); 1 CO, O_3: 1.04 (1.01-1.07); 1 CO, O_3, CoH, NO_2, SO_2: 1.02 (0.96-1.08); 1 Age Group: ≥ 65 CO alone: 1.02 (1.00-1.04); 1 CO, O_3: 1.02 (1.00-1.04); 1 CO, O_3, CoH, NO_2, SO_2: 0.96 (0.93-1.00); 1
Author: Yang et al. (2004, 087488) **Period of Study:** 6/1/1995-3/31/1999 **Location:** Vancouver, Canada	Hospital Admissions **Health Outcome (ICD9):** Respiratory diseases (460-519); pneumonia (480-486); asthma (493) **Study Design:** Case control **Statistical Analyses:** Pearson's correlation coefficient **Age Groups Analyzed:** <3 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.70 (0.30) ppm **IQR (25th, 75th):** (0.50, 0.80) **Copollutant:** correlation PM_{10}: r = 0.46; $PM_{2.5}$: r = 0.24; $PM_{10-2.5}$: r = 0.33; O_3: r = -0.53; NO_2: r = 0.74; SO_2: r = 0.61	This study did not present quantitative results for CO.
Author: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston, MA	Hospital Admissions **Health Outcome (ICD9):** Pneumonia (480-487) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **IQR (25th, 75th):** (0.39, 0.60) **Copollutant:** correlation $PM_{2.5}$: r = 0.52; BC: r = 0.82; NO_2: r = 0.67; O_3: r = -0.30	**Increment:** 0.475 ppm **% Increase (Lower CI, Upper CI); lag:** 5.45 (1.10, 9.51); 0 5.12 (0.83, 9.16); 0-1

Table C-6. Studies of long-term CO exposure and respiratory morbidity.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Goss et al. (2004, 055624) **Period of Study:** 1999-2000 **Location:** U.S.	**Health Outcome:** Lung function (FEV_1, cystic fibrosis pulmonary exacerbation) **Study Design:** Cohort **Statistical Analyses:** Logistic regression **Population:** 11,484 cystic fibrosis patients **Age Groups Analyzed:** >6 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 0.692 (0.295) ppm **IQR (25th, 75th):** (0.48, 0.83) **Copollutant:** NR	**Increment:** 1.0 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Two or more pulmonary exacerbations during 2000 1.02 (0.85-1.22)
Author: Guo et al. (1999, 010937) **Period of Study:** 10/1995-5/1996 **Location:** Taiwan	**Health Outcome:** Asthma **Study Design:** Cohort **Statistical Analyses:** Logistic regression **Population:** 331,686 nonsmoking children **Age Groups Analyzed:** Middle-school children (mean age = 13.8 yr)	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 853 (277) ppb **Range (Min, Max):** (381, 1610) **Copollutant:** NR	**Increment:** 326 ppb **% Increase (Lower CI, Upper CI); lag:** Boys Physician-diagnosed asthma: 1.17% (0.63-1.72) Questionnaire-diagnosed asthma: 1.10% (0.45-1.75) Girls Physician-diagnosed asthma: 0.84% (0.45-1.22) Questionnaire-diagnosed asthma: 1% (0.44-1.56)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Hirsch et al. (1999, 003537) **Period of Study:** Population: 9/1995-6/1996 Air: 4/1994-4/1995 **Location:** Dresden, Germany	**Health Outcome:** Asthma symptoms in the past 12 mo (wheeze, morning cough); Doctor's diagnosis (asthma, bronchitis); Lung function (bronchial hyperresponsiveness (BHR), FEV_1 <85% pred., $FEF_{25-75\%}$ <70% pred.) **Study Design:** Cross sectional **Statistical Analyses:** Multiple logistic regression **Population:** 5-7: 2,796; 9-11: 2,625 **Age Groups Analyzed:** 5-7 and 9-11 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 0.69 mg/m^3 **Range (Min, Max):** (0.32, 1.54) **Copollutant:** NR	**Increment:** 0.2 $\mu g/m^3$ **Prevalence Odds Ratio (Lower CI, Upper CI); lag:** Symptoms in the past 12 mo: Wheeze Home Exposure Age Groups: 5-7; 9-11: 1.05 (0.93-1.18) Home/School Exposure Age Groups: 9-11: 1.02 (0.85-1.22) Morning Cough Home Exposure Age Groups: 5-7; 9-11: 1.12 (1.01-1.23) Age Group: 9-11: 1.13 (0.98-1.3) Doctor's diagnosis: Asthma Home Exposure Age Groups: 5-7; 9-11: 1.07 (0.94-1.21) Age Groups: 9-11: 1.16 (0.97-1.38) Doctor's diagnosis: Bronchitis Age Groups: 5-7; 9-11: 1.19 (1.11-1.27) Age Group: 9-11: 1.24 (1.12-1.38) Lung function: BHR Age Groups: 5-7; 9-11: 0.79 (0.63-0.99) Age Group: 9-11: 0.77 (0.6-0.99) Lung function: FEV1 <85% pred. Age Groups: 5-7; 9-11: 1.09 (0.81-1.47) Age Group: 9-11: 1.01 (0.73-1.41) Lung function: FEV25-75% <70% pred. Age Groups: 5-7; 9-11: 1.15 (0.94-1.39) Age Group: 9-11: 1.07 (0.86-1.34) Symptoms in the past 12 mo: Wheeze Age Groups: 5-7; 9-11 Atopic children: 1 (0.81-1.24) Nonatopic children: 1.05 (0.83-1.31) Morning cough Age Groups: 5-7; 9-11 Atopic children: 1.03 (0.82-1.29) Nonatopic children: 1.22 (1.05-1.41) Doctor's diagnosis: Asthma Atopic children: 1.05 (0.83-1.32) Nonatopic children: 1.29 (1.05-1.59) Doctor's diagnosis: Bronchitis Age Groups: 5-7; 9-11 Atopic children: 1 (0.86-1.16) Nonatopic children: 1.21 (1.1-1.33) Notes: Atopic Children were defined as those children with specific IgE to aeroallergens >0.7 kU-L-1; Nonatopic Children were defined as those children with specific IgE to aeroallergens ≤ 0.7 kU-L-1.
Author: Hwang et al. (2006, 088971) **Period of Study:** 2001 **Location:** Taiwan	**Health Outcome:** Allergic rhinitis **Study Design:** Cross sectional **Statistical Analyses:** Two-stage hierarchical model (logistic and linear regression) **Population:** 32,143 Taiwanese school children **Age Groups Analyzed:** 6-15 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit**: 664 (153) ppb **Range (Min, Max):** (416, 964) **Copollutant:** correlation NO_X: r = 0.88 O_3: r = -0.37 PM_{10}: r = 0.27 SO_2: r = 0.40	Increment: 100 ppb **Adjusted Odds Ratio (Lower CI, Upper CI); lag:** Physician-diagnosed allergic rhinitis 1.05 (1.04-1.07) CO, SO_2: 1.04 (1.02-1.06) CO, PM_{10}: 1.05 (1.03-1.07) CO, O_3: 1.07 (1.05-1.09) Male: 1.06 (1.03-1.08); Female: 1.05 (1.02-1.08) Parental atopy: Yes: 1.05 (1.02-1.08) Parental atopy: No: 1.06 (1.03-1.08) Parental Education: <6: 1 (0.91-1.09) Parental Education: 6-8: 1.07 (1.02-.12) Parental Education: 9-11: 1.05 (1.02-1.08) Parental Education: ≥ 12: 1.06 (1.03-1.09) ETS: Yes: 1.06 (1.03-1.08); ETS: No: 1.05 (1.02-1.08) Visible Mold: Yes: 1.07 (1.03-1.11) Visible Mold: No: 1.05 (1.03-1.07)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Hwang et al. (2005, 089454) **Period of Study:** 2001 **Location:** Taiwan	**Health Outcome:** Asthma **Study Design:** Cross sectional **Statistical Analyses:** Two-stage hierarchical model (logistic and linear regression) **Population:** 32,672 Taiwanese school children **Age Groups Analyzed:** 6-15 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 664 (153) ppb **Range (Min, Max):** (416, 964) **Copollutant:** correlation NO_X: r = 0.88 O_3: r = -0.37 PM_{10}: r = 0.27 SO_2: r = 0.40	**Increment:** 100 ppb **Adjusted Odds Ratio (Lower CI, Upper CI); lag:** Physician-diagnosed asthma: 1.045 (1.017-1.074) CO, SO_2: 1.066 (1.034-1.099) CO, PM_{10}: 1.079 (1.047-1.112) CO, O_3: 1.063 (1.1-1.474) CO, SO_2, O_3: 1.111 (1.074-1.15) CO, PM_{10}, O_3: 1.119 (1.084-1.155) Male: 1.49 (1.37-1.63); Female: 1 Parental atopy: Yes: 1 Parental atopy: No: 2.72 (2.5-2.97) Parental Education: <6: 1 Parental Education: 6-8: 1.17 (0.9-1.52) Parental Education: 9-11: 1.61 (1.26-2.05) Parental Education: ≥ 12: 2.43 (1.9-3.09) ETS: Yes: 0.85 (0.78-0.92); ETS: No: 1 Visible Mold: Yes: 1.27 (1.16-1.4); Visible Mold: No: 1 Maternal smoking during pregnancy: Yes: 1.18 (0.89-1.56) Maternal smoking during pregnancy: No: 1 Cockroaches noted monthly: Yes: 1.15 (1.03-1.29) Cockroaches noted monthly: No: 1 Water damage: Yes: 0.96 (0.81-1.12) Water damage: No: 1
Author: Lee et al. (2003, 049201) **Period of Study:** 10/1995-5/1996 **Location:** Taiwan	**Health Outcome:** Allergic rhinitis **Study Design:** Cohort **Statistical Analyses:** Multiple logistic regression **Population:** 331,686 nonsmoking children **Age Groups Analyzed:** 12-14 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 853 (277) ppb **Range (Min, Max):** (381, 1610) **Copollutant:** NR	The study did not present quantitative results for CO.
Author: Meng et al. (2007, 093275) **Period of Study:** 11/2000-9/2001 **Location:** Los Angeles County and San Diego County, California	**Health Outcome:** Asthma **Study Design:** Cohort **Statistical Analyses:** Logistic regression **Population:** 1,609 physician-diagnosed asthmatics **Age Groups Analyzed:** ≥ 18 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** correlation Traffic: r = -0.04; O_3: r = -0.55; PM_{10}: r = 0.42; $PM_{2.5}$: r = 0.52; NO_2: r = 0.55	The study did not present quantitative results for CO.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Mortimer et al. (2008, 122163) **Period of Study:** 1989-2000 **Location:** San Joaquin Valley, CA	**Health Outcome:** Lung function (FVC, FEV_1, PEF, FEF25-75, FEV_1/FVC, FEF25-75/FVC, FEF25, FEF75) **Study Design:** Cohort **Statistical Analyses:** 1. DSA algorithm 2. GEE **Population:** 232 asthmatic children **Age Groups Analyzed:** 6-11 yr	**Pollutant:** CO **Averaging Time:** 8-h max monthly mean **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant;** correlation: Lifetime NO_2 (24-h avg): r = 0.68 O_3 (8-h max): r = -0.40 PM_{10} (24-h avg): r = 0.05 Prenatal CO (8-h max): r = 0.52 NO_2 (24-h avg): r = 0.37 O_3 (8-h max): r = -0.16 PM_{10} (24-h avg): r = -0.05	**Increment:** NR Effect Size per IQR Increase in Pollutant (SE): FEF25-75: 24-h avg CO exposure during 1st trimester 0.90% (0.0113) FEV_1/FVC Daily max CO exposure during ages 0 to 3 -2.50% (0.0016) FEF25-75/FVC 24-h avg CO exposure during ages 0 to 6 and diagnosed with asthma <2 yr old -4.80% (0.0446) FEF25 24-h avg CO exposure during ages 0 to 6 and diagnosed with asthma <2 yr old plus 24-h avg PM_{10} exposure during 2nd trimester and mother smoked when pregnant -6.70% (0.015) Coefficient (SE): FVC 24-h avg CO exposure during 2nd trimester -0.0878 (0.0415) FEF25-75 Lifetime 24-h avg CO exposure -0.94454 (0.3975) FEF25-75/FVC -0.1090 (0.0303) FEV_1/FVC Prenatal 8-h max CO exposure: 0.1711 (0.0653) Lifetime 1-h max CO exposure: -0.3242 (0.0919) 24-h avg CO exposure during ages 0-3 and diagnosed with asthma <2 yr old: -0.1814 (0.0599) FEF25 24-h avg CO exposure during ages 0-6 and diagnosed with asthma <2 yr old: -1.0460 (0.1953) FEF75 Lifetime 8-h max CO exposure: -0.4214 (0.1423)
Author: Singh et al. (2003, 052686) **Period of Study:** NR **Location:** Jaipur, India	**Health Outcome:** Lung function **Study Design:** Panel study **Statistical Analyses:** Parametric statistical methods **Population:** Campus panel: 142 Commuter panel: 158 **Age Groups Analyzed:** ~20 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit**: Roadside: 3,175 $\mu g/m^3$ Campus: 2,150 $\mu g/m^3$ **Range (Min, Max):** NR **Copollutant:** NR	The study did not present quantitative results for CO.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Sole et al. (2007, 090706) **Period of Study:** **Location:** Sao Paulo West, Sao Paulo South, Santo Andre, Curitba, & Porto Alegre, Brazil	**Health Outcome:** Symptoms of asthma, rhinitis, and eczema **Study Design:** Panel **Statistical Analyses:** Logistic Regression **Age Groups Analyzed:** 13-14 yr	**Averaging Time:** Annual **Mean (SD) unit:** Sao Paulo West: 7.70 ppm Sao Paulo South: 7.50 ppm Santo Andre: 9.80 ppm Curitba: 7.90 ppm Porto Alegre: 1.51 ppm **Range (min, max):** NR **Copollutant:** NO_2, SO_2, O_3	**Increment:** Risk in relation to center w/ lowest annual mean (Porto Alegre = ref) **OR Estimate [Lower CI, Upper CI]:** **Lags examined:** NR **Current Wheezing:** Sao Paulo West: 1.26 (1.11, 1.42) Sao Paulo South: 1.03 (0.91, 1.18) Santo Andre: 1.36 (1.20, 1.56) Curitba: 1.05 (0.93, 1.19) **Severe Asthma:** Sao Paulo West: 1.20 (0.95, 1.50) Sao Paulo South: 0.59 (0.45, 0.78) Santo Andre: 0.62 (0.48, 0.81) Curitba: 0.64 (0.50, 0.82) **Nighttime Coughing:** Sao Paulo West: 1.06 (0.95, 1.17) Sao Paulo South: 0.93 (0.84, 1.03) Santo Andre: 0.91 (0.82, 1.02) Curitba: 0.99 (0.89, 1.10) **Rhinoconjunctivitis:** Sao Paulo West: 1.31 (1.15, 1.15) Sao Paulo South: 0.73 (0.64, 0.85) Santo Andre: 0.85 (0.74, 0.97) Curitba: 1.10 (0.96, 1.25) **Severe Rhinits:** Sao Paulo West: 1.01 (0.91, 1.49) Sao Paulo South: 0.68 (0.59, 0.77) Santo Andre: 0.73 (0.64, 0.83) Curitba: 1.03 (0.91, 1.16) **Eczema:** Sao Paulo West: 1.45 (1.20, 1.74) Sao Paulo South: 1.03 (0.85, 1.25) Santo Andre: 1.03 (0.85, 1.25) Curitba: 0.90 (0.75, 1.10) **Flexural Eczema:** Sao Paulo West: 1.42 (1.15, 1.76) Sao Paulo South: 0.71 (0.56, 0.91) Santo Andre: 0.68 (0.53, 0.87) Curitba: 0.73 (0.57, 0.92) **Severe Eczema:** Sao Paulo West: 1.08 (0.86, 1.35) Sao Paulo South: 0.42 (0.31, 0.56) Santo Andre: 0.38 (0.28, 0.51) Curitba: 0.30 (0.22, 0.41)
Author: Wang et al. (1999, 008105) **Period of Study:** 10/1995-6/1996 **Location:** Kaohsiung and Pintong, Taiwan	**Health Outcome:** Asthma **Study Design:** Cross sectional **Statistical Analyses:** Multiple logistic regression **Population:** 165,173 high school students **Age Groups Analyzed:** 11-16 yr	**Pollutant:** CO **Averaging Time:** Annual median **Median (SD) unit:** 0.80 ppm **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR **Adjusted Odds Ratio (Lower CI, Upper CI); lag:** CO Concentrations: <0.80 ppm: 1.0 CO Concentrations ≥ 0.80 ppm: 1.23 (1.19-1.28) Multivariate analysis with variables for exercise, smoking, alcohol, incense use, ETS: 1.15 (1.1-1.2)
Author: Wilhelm et al. (2008, 191912) **Period of Study:** 2000-2001 **Location:** Los Angeles County or San Diego County, California	**Health Outcome:** Asthma symptoms/ED visit/HA **Study Design:** Panel **Statistical Analyses:** Logistic regression **Age Groups Analyzed:** 0-17 yr **Sample Description:** 612 children who reported a physician diagnosis of asthma at some point in their lives	**Averaging Time:** annual **Mean (SD) unit:** 1.0 ppm **Range (min, max):** 0.34, 1.8 **Copollutant:** correlation O_3: r= -0.67 PM_{10}: r= 0.41 $PM_{2.5}$: r= 0.60 NO_2: r= 0.57 traffic density: r= 0.02	**Increment:** NR **OR Estimate [Lower CI, Upper CI] ; lag:** **Lags examined:** NR No associations observed between asthma symptom outcome measures (no results shown)

Table C-7. Studies of short-term CO exposure and mortality.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Anderson et al. (2001, 017033) **Period of Study:** 10/1994-12/1996 **Location:** West Midlands, United Kingdom	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800); cardiovascular (390-459); respiratory (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h ma **Mean (SD) unit:** 0.8 (0.7) ppm **Range (Min, Max):** (0.2, 10.0) **Copollutant** correlation: PM_{10}: r = 0.55; $PM_{2.5}$: r = 0.54; $PM_{10-2.5}$: r = 0.10; BS: r = 0.77; SO_4^{2-}: r = 0.17; NO_2: r = 0.73; O_3: r = -0.29; SO_2: r = 0.49	**Increment:** 1.0 ppm **% Increase (Lower CI, Upper CI); lag:** All-cause 0.8% (-0.6 to 2.2); 0-1 Cardiovascular 2.5% (0.4-4.6); 0-1 Respiratory 1.2% (-2.1 to 4.6); 0-1
Author: Bellini et al. (2007, 097787) **Period of Study:** 1996-2002 **Location:** 15 Italian cities	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800); cardiovascular (390-459); respiratory (460-519) **Study Design:** Meta-analysis Statistical Analyses: Poisson GLM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** SO_2 NO_2 O_3 PM_{10}	**Increment:** 1 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** All-cause 1.19% (0.61-1.72); 0-1 Respiratory 0.66% (-1.46 to 2.88); 0-1 Cardiovascular 0.93% (-0.10 to 1.77); 0-1
Author: Berglind et al. (2009, 190068) **Period of Study:** 1992-2002 **Location:** Augsburg, Germany; Barcelona, Spain; Helsinki, Finland; Rome, Italy; Stockholm, Sweden	**Health Outcome:** Mortality **Study Design:** Cohort **Statistical Analyses:** Poisson regression analysis **Age Groups Analyzed:** ≥ 35 yr **Sample Description:** First-time MI patients	**Averaging Time:** 24 h **Mean (SD) unit:** Median calculated from daily 24-h means: Augsburg: 0.85 Barcelona: 0.75 Helsinki: 0.36 Rome: 1.66 Stockholm: 0.38 Range (IQR): Augsburg: 0.43 Barcelona: 0.75 Helsinki: 0.36 Rome: 1.11 Stockholm: 0.38 **Copollutant:** NR	**Increment:** 0.2 mg/m^3 % Change in Daily Nontrauma Deaths [Lower CI, Upper CI]: Mean of Lag 0 and 1: 2.61 (-0.26-5.56) Mean of Lag 0-4: 3.82 (1.00-6.72) Mean of Lag 0-14: 4.92 (2.11-7.81) Lags examined: 0, 1, 4, 14 CO had a trend towards or positive associations with all cities for 2-day mean effects on daily mortality. CO was associated with risk for the 5-day avg. The strongest association was observed for the 15-day avg.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Biggeri et al. (2005, 087395) **Period of Study:** 1990-1999 **Location:** 8 Italian Cities (Turin, Milan, Verona, Bologna, Ravenna, Florence, Rome, and Palermo)	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800); cardiovascular (390-459); respiratory (460-519); cardio-respiratory **Study Design:** Meta-analysis **Statistical Analyses:** Poisson GLM, cubic splines **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h ma **Mean (SD) unit:** Turin, 1991-1994: 5.8 mg/m^3 Turin, 1995-1998: 4.0 mg/m^3 Milan, 1990-1994: 5.9 mg/m^3 Milan, 1995-1997: 4.0 mg/m^3 Verona, 1995-1999: 2.5 mg/m^3 Ravenna, 1991-1995: 1.8 mg/m^3 Bologna, 1996-1998: 2.4 mg/m^3 Florence, 1996-1998: 2.7 mg/m^3 Rome, 1992-1994: 6.5 mg/m^3 Rome, 1995-1997: 5.4 mg/m^3 Palermo, 1997- 1999: 2.1 mg/m^3 **Range (Min, Max):** Turin, 1991-1994: (NR, 24.7) Turin, 1995-1998: (NR, 19.8) Milan, 1990-1994: (NR, 26.5) Milan, 1995-1997: (NR, 12.3) Verona, 1995-1999: (NR, 10.2) Ravenna, 1991-1995: (NR, 7.0) Bologna, 1996-1998: (NR, 11.1) Florence, 1996-1998: (NR, 8.7) Rome, 1992-1994: (NR, 22.3) Rome, 1995-1997: (NR, 18.5) Palermo, 1997- 1999: (NR, 8.0) **Copollutant:** NR	**Increment:** 1.0 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** Non-accidental Fixed: 0.93 (0.50-1.36); 0-1 Random: 0.93 (0.50-1.36); 0-1 Cardiovascular Fixed: 1.29 (0.62-1.96); 0-1 Random: 1.29 (0.62-1.96); 0-1 Respiratory Fixed: 2.44 (0.74-4.17); 0-1 Random: 2.47 (0.14-4.85); 0-1
Author: Botter et al. (2002, 011922) **Period of Study:** 1991-1993 **Location:** São Paulo, Brazil	**Health Outcome (ICD9):** Mortality **Study Design:** Longitudinal study Statistical Analyses: State space model **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** TSP; NO_2; O_3; SO_2	**Increment:** NR **β (SE):** Model 1: 0.0053 (0.0036) Model 2: 0.0046 (0.0028) Model 3: 0.0040 (0.0028) Model 4: 0.0032 (0.0028)
Author: Bremner et al. (1999, 007601) **Period of Study:** 1/1992–12/1994 **Location:** London, U.K.	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800); cardiovascular (390-459); respiratory (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson, cubic splines **Age Groups Analyzed:** All ages 0-64 yr ≥ 65 yr 65-74 yr ≥ 75 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit**: 0.8 (0.4) ppm **Range (Min, Max):** (0.2, 5.6) **Copollutant:** NO_2; O_3; SO_2; PM_{10}; BS	**Increment:** 0.8 ppm **% Increase (Lower CI, Upper CI); lag:** All-cause Age Group: All ages: 0.9% (-0.2 to 2.0); 1 0-64: 1.2% (-1.0 to 3.5); 1 ≥ 65: 0.8% (-0.4 to 1.9); 2 65-74: 0.8% (-1.2 to 2.8); 3 ≥ 75: 0.9% (-0.4 to 2.2); 2 Respiratory Age Group: All ages: 2.0% (-0.3 to 4.5); 3 0-64: 7.8% (0.2-15.9); 3 ≥ 65: 0.7% (-1.7 to 3.2); 3 65-74: 7.5% (2.1-13.2); 3 ≥ 75: 2.3% (-0.5 to 5.3); 0 Multipollutant: CO, SO_2: 1.90% (0.18-3.64); 3 CO, PM_{10}: 1.25% (0.04-2.47); 3 CO, BS: 2.41% (-0.65 to 5.57); 3 Cardiovascular Age Group: All ages: 1.4% (-0.1 to 3.0); 1 0-64: 2.1% (-1.7 to 6.0); 2 ≥ 65: 1.1% (-0.4 to 2.8); 2 65-74: 2.4% (-0.6 to 5.5); 2 ≥ 75: 1.9% (0.0-3.9); 2 Multipollutant: CO, NO_2: 2.55% (0.40-4.75); 1 CO, O_3: 3.98% (0.85-7.21); 1 CO, PM_{10}: 0.62% (-0.59 to 1.85); 1 CO, BS: 1.29% (-1.53 to 4.19); 1

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Burnett et al. (2000, 010273) **Period of Study:** 1986-1996 **Location:** 8 Canadian cities	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800) **Study Design:** Time series **Statistical Analyses:** 1. Single-pollutant models: Poisson GAM, LOESS 2. Multi-pollutant models: Principal component regression analysis **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.9 ppm **Range (Max):** 7.2 ppm **Copollutant:** correlation O_3: r = -0.05 SO_2: r = 0.42 $PM_{2.5}$: r = 0.44 $PM_{10-2.5}$: r = 0.29 PM_{10}: r = 0.45	**Increment:** 0.9 ppm **% Increase (t-value); lag:** Temporally filtered daily nonaccidental mortality (days in which PM_{10} data available) CO: 0.4 (0.4); 0; 2.0 (2.3); 1 CO, $PM_{2.5}$: -0.7 (-0.7); 0; 1.1 (1.1); 1 CO, $PM_{10-2.5}$: 0.1 (0.2); 0; 1.8 (2.1); 1 CO, PM_{10}: -0.5 (-0.6); 0; 1.2 (1.3); 1 Daily filtered non-accidental mortality Single-pollutant model: 2.1 (2.1) Multi-pollutant models: Model 1: CO, $PM_{2.5}$, $PM_{10-2.5}$, O_3, NO_2, SO_2: 0.7 (1.9) Model 2: CO, SO_4, Ni, Fe, Zn, O_3, NO_2: 0.7 (1.7)
Author: Burnett et al. (2004, 086247) **Period of Study:** 1981-1999 **Location:** 12 Canadian cities	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800) **Study Design:** Time series **Statistical Analyses:** 1. Poisson, natural splines 2. Random effects regression model **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.02 ppm **Range (Min, Max):** NR **Copollutant:** NO_2; O_3; SO_2; $PM_{2.5}$; $PM_{10-2.5}$	**Increment:** 1.02 ppm **% Increase (t-value); lag:** 0.68% (3.12); 1 CO, NO_2: 0.07% (0.30); 1
Author: Cakmak et al. (2007, 091170) **Period of Study:** 1/1997-12/2003 **Location:** Chile-7 cities	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental) (<800); CVDs (390-459); respiratory diseases (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson; Random effects regression model **Age Groups Analyzed:** All ages ≤ 64 yr 65-74 yr 75-84 yr ≥ 85 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.29 ppm **Range (Min, Max):** NR **Copollutant** correlation: O_3: r = -0.55 to -0.01 SO_2: r = 0.31 to 0.67 PM_{10}: r = 0.49 to 0.82 **Note:** Correlations are between pollutants for seven monitoring stations.	**Increment:** 1.29 ppm **% Increase (t-value); lag:** Nonaccidental: 5.88% (6.42); 1; 9.39% (6.89); 0-5 CO+PM_{10}+O_3+SO_2: 6.13% (4.34); 1 Age Group: ≤ 64 4.10% (2.52); 1; / 4.76% (2.19); 0-5 Age Group: 65-74 6.24% (3.17); 1; / 8.12% (3.88); 0-5 Age Group: 75-84 8.64% (4.82); 1; / 13.12% (5.12); 0-5 Age Group: ≥ 85 8.58% (4.45); 1; / 13.20% (4.82); 0-5 April-September 7.09% (4.02); 1; / 9.65% (4.50); 0-5 October-March 5.45% (1.14); 1; / 7.80% (1.89); 0-5 Cardiac 7.79% (4.56); 1; / 11.22% (4.8); 0-5 Respiratory 12.93% (5.78); 1; / 21.31% (6.34); 0-5
Author: Chock et al. (2000, 010407) **Period of Study:** 1989-1991 **Location:** Pittsburgh, PA	**Health Outcome (ICD9):** Mortality: Respiratory (480-486, 490-496, 507); cardiovascular (390-448); influenza (487) **Study Design:** Time series **Statistical Analyses:** Poisson GAM; Cubic B-spline basis functions **Age Groups Analyzed:** All ages <75 yr >75 yr	**Pollutant:** CO **Averaging Time:** 1-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** PM_{10}; $PM_{2.5}$; O_3; SO_2; NO_2	**Increment:** NR **β (SE); lag:** Age Group: <75 CO alone: 0.0080 (1.56); 0 PM_{10}, CO: 0.0030 (0.48); 0 PM_{10}, NO_2, CO: 0.0079 (1.14); 0 PM_{10}, O_3, SO_2, NO_2, CO: 0.072 (1.02); 0 CO -0.00738 (-1.42); -3; / 0.00133 (0.23); -2; -0.00219 (-0.38); -1; / 0.00809 (1.48); 0; -0.00129 (-0.22); 1; / 0.00512 (0.90); 2; -0.00974 (-1.87); 3 CO, PM_{10}, O_3, SO_2, NO_2 -0.01103 (-1.48); -3; / -0.00097 (-0.13); -2; 0.00514 (0.67); -1; / 0.00853 (1.15); 0; -0.00404 (-0.52); 1; / -0.00296 (-0.39); 2; -0.00346 (-0.46); 3 Season CO Winter: 0.00539 (0.78); 0 Spring: 0.01655 (1.90); 0 Summer: 0.00155 (0.14); 0 Fall: 0.00797 (1.14); 0

Study	Design	Concentrations	Effect Estimates (95% CI)
			CO, PM_{10} Winter: -0.00563 (-0.50); 0 Spring: 0.01233 (0.99); 0 Summer: -0.00712 (-0.48); 0 Fall: 0.00661 (0.73); 0 CO, PM_{10}, O_3, SO_2, NO_2 Winter: -0.01326 (-0.95); 0 Spring: 0.02501 (1.54); 0 Summer: 0.01874 (0.92); 0 Fall: 0.01011 (0.88); 0 Age Group:>75 CO Alone: -0.0035 (-0.67); 0 CO, PM_{10}: -0.0104 (-1.67); 0 CO, PM_{10}, NO_2: -0.0128 (-1.80); 0 CO, PM_{10}, O_3, SO_2, NO_2: -0.0144 (-1.99); 0 CO -0.00025 (-0.05); -3; / -0.00242 (-0.42); -2; -0.00238 (-0.41); -1; / -0.00302 (-0.54); 0; -0.00116 (-0.20); 1; / -0.00508 (-0.88); 2; -0.00251 (-0.48); 3 CO, PM_{10}, O_3, SO_2, NO_2 -0.00123 (-0.17); -3; / -0.00876 (-1.13); -2; -0.00682 (-0.88); -1; / -0.01248 (-1.66); 0; -0.00672 (-0.86); 1; / -0.00181 (-0.23); 2; -0.00515 (-0.69); 3 Season CO Winter: -0.00304 (-0.43); 0 Spring: 0.00482 (0.54); 0 Summer: 0.01178 (1.07); 0 Fall: -0.01011 (-1.43); 0 CO, PM_{10} Winter: -0.02303 (-2.03); 0 Spring: -0.00517 (-0.40); 0 Summer: 0.00735 (0.50); 0 Fall: -0.01042 (-1.14); 0 CO, PM_{10}, O_3, SO_2, NO_2 Winter: -0.03370 (-2.41); 0 Spring: -0.00652 (-0.39); 0 Summer: 0.01258 (0.61); 0 Fall: -0.01250 (-1.07); 0

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Cifuentes et al. (2000, 010351) **Period of Study:** 1988-1996 **Location:** Santiago, Chile	**Health Outcome (ICD9):** Mortality: All causes (nonaccidental) (<800) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, GAM with filtered variables & GLM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 1-h avg **Mean (SD) unit:** 2.5 ppb **Range (5th, 95th):** (0.6, 6.2) **Copollutant** correlation: $PM_{2.5}$: r = 0.80 $PM_{10-2.5}$: r = 0.47 SO_2: r = 0.62 NO_2: r = 0.65 O_3: r = -0.01	**Increment:** All yr: 2.5 ppm Winter: 3.6 ppm Summer: 1.3 ppm **Relative Risk (t-ratio); Lag** All Year CO: 1.041 (7.2); 0-1 CO, $PM_{2.5}$: 1.025 (3.5); 0-1 CO, $PM_{10-2.5}$: 1.035 (4.9); 0-1 CO, SO_2: 1.038 (6.0); 0-1 CO, NO_2: 1.026 (3.9); 0-1 CO, O_3: 1.036 (4.8); 0-1 Winter CO: 1.052 (5.9); 0-1 CO, $PM_{2.5}$: 1.025 (2.1); 0-1 CO, $PM_{10-2.5}$: 1.049 (4.3); 0-1 CO, SO_2: 1.049 (5.0); 0-1 CO, NO_2: 1.027 (2.6); 0-1 CO, O_3: 1.051 (4.4); 0-1 Summer CO: 1.053 (6.0); 0-1 CO, $PM_{2.5}$: 1.053 (5.3); 0-1 CO, $PM_{10-2.5}$: 1.053 (5.3); 0-1 CO, SO_2: 1.050 (5.2); 0-1 CO, NO_2: 1.047 (5.2); 0-1 CO, O_3: 1.042 (3.6); 0-1 All Year GAM model CO: 1.041 (7.2); 0-1 CO, $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2, O_3: 1.032 (4.6); 0-1 GAM Filtered Variables CO: 1.030 (4.3); 0-1 CO, $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2, O_3: 1.022 (2.4); 0-1 GLM CO: 1.023 (2.4); 0-1 CO, $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2, O_3: 1.013 (1.1); 0-1
Author: Conceicao et al. (2001, 016628) **Period of Study:** 1994-1997 **Location:** Sao Paulo, Brazil	**Health Outcome (ICD9):** Mortality: Respiratory diseases (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** <5 yr	**Pollutant:** CO **Averaging Time:** Max 8-h ma **Mean (SD) unit:** Total: 4.4 (2.2) ppm 1994: 5.1 (2.4) ppm 1995: 5.1 (2.4) ppm 1996: 3.9 (2.0) ppm 1997: 3.7 (1.6) ppm **Range (Min, Max):** NR **Copollutant:** PM_{10}; SO_2; O_3	**Increment:** NR **β (SE); lag:** CO: 0.0306 (0.0076); 2 CO, SO_2, PM_{10}, O_3: 0.0259 (0.0116); 2 Model 1: Pollutant concentration: 0.0827 (0.0077); 2 Model 2: 1+loess(time): 0.0285 (0.0074); 2 Model 3: 2+loess(temperature)+humidity: 0.0309 (0.0076); 2 Model 4: 3+nonrespiratory counts: 0.0306 (0.0076); 2 Model 5: 4+autoregressive parameters: 0.0292 (0.0118); 2
Author: De Leon et al. (2003, 055688) **Period of Study:** 1/1985-12/1994 **Location:** New York, NY	**Health Outcome (ICD9):** Mortality: Circulatory (390-459); cancer (140-239) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages <75 yr >75 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 2.45 ppm **IQR (25th, 75th):** (1.80, 2.97) **Copollutant:** PM_{10}; O_3; SO_2; NO_2	The study did not present quantitative results for CO.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Dominici et al. (2003, 056116) **Period of Study:** 1987-1994 **Location:** 90 U.S. cities (NMMAPS)	**Health Outcome (ICD9):** Mortality: All-cause (nonaccidental); cardiovascular; respiratory **Study Design:** Time series **Statistical Analyses:** 1. GAM with S-PLUS default convergence criteria 2. GAM with more stringent convergence criteria 3. Poisson GLM with natural cubic splines **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** O_3; NO_2; SO_2; CO	**Increment:** 1 ppm **% Increase (Lower CI, Upper CI); Lag** CO 0.08% (-0.18 to 0.34); 0 0.46% (0.18-0.73); 1 0.16% (-0.12 to 0.45); 2
Author: Fairley et al. (1999, 000896) **Period of Study:** 1989-1996 **Location:** Santa Clara, CA	**Health Outcome (ICD9):** Mortality: Respiratory; cardiovascular **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg; Max 8-h avg **Median (SD) unit:** 24-h avg: 1.4 (1.0) ppm Max 8-h avg: 2.1 (1.6) ppm **Range (Min, Max):** 24-h avg: (0.0, 7.6) Max 8-h avg: (0.2, 2.5) **Copollutant:** correlation PM_{10}: r = 0.609; $PM_{2.5}$: r = 0.435; $PM_{10-2.5}$: r = 0.326; COH: r = 0.736; NO_3: r = 0.270; SO_4: r = 0.146; O_3: r = -0.215	**Increment:** 2.2 ppm **Relative Risk (Lower CI, Upper CI); lag:** 1980-1986 CO: 1.04; 0; CO: 1.05; 1; CO, COH: 1.00; 1; CO, NO_3: 1.03; CO, NO_3, O_3, COH: 1.00 1989-1996 CO: 1.02; 0; CO: 1.04; 1; CO, $PM_{2.5}$: 0.98; CO, NO_3: 1.01; CO, NO_2, O_3, NO_3: 1.06 Respiratory mortality: CO: 1.08; 1 Cardiovascular mortality: CO: 1.04; 1
Author: Fischer et al. (2003, 043739) **Period of Study:** 1986-1994 **Location:** The Netherlands	**Health Outcome (ICD9):** Mortality: Nonaccidental (<800); pneumonia (480-486); COPD (490-496); cardiovascular (390-448) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** <45 yr 45-64 yr 65-74 yr ≥ 75 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Median (SD) unit:** 406 µg/m^3 **Range (Min, Max):** (174, 2620) **Copollutant:** PM_{10}; BS; O_3; NO_2; SO_2	**Increment:** 1,200 µg/m^3 **Relative Risk (Lower CI, Upper CI); lag:** Cardiovascular Age Group: <45: 0.965 (0.750-1.240); 0-6 45-64: 1.029 (0.941-1.125); 0-6 65-74: 1.038 (0.972-1.108); 0-6 ≥ 75: 1.024 (0.984-1.065); 0-6 COPD Age Group: <45: 1.710 (0.852-3.435); 0-6 45-64: 1.181 (0.850-1.640); 0-6 65-74: 1.377 (1.147-1.654); 0-6 ≥ 75: 1.072 (0.963-1.193); 0-6 Pneumonia Age Group: <45: 0.927 (0.463-1.856); 0-6 45-64: 2.691 (1.509-4.800); 0-6 65-74: 1.118 (0.743-1.683); 0-6 ≥ 75: 1.230 (1.090-1.389); 0-6
Author: Forastiere et al. (2005, 086323) **Period of Study:** 1998-2000 **Location:** Rome, Italy	**Health Outcome (ICD9):** Mortality: IHD (410-414) **Study Design:** Time-stratified case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** >35 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 2.4 (1.0) mg/m^3 **IQR (25th, 75th):** (1.7, 2.9) **Copollutant correlation:** PNC: r = 0.89; PM_{10}: r = 0.34; NO_2: r = 0.54; SO_2: r = 0.52; O_3: r = 0.01	**Increment: 1.2 mg/m3** **% Increase (Lower CI, Upper CI); lag:** 6.5% (1.0-12.3); 0 4.7% (-0.9 to 10.7); 1 2.6% (-3.0 to 8.5); 2 -0.1% (-5.5 to 5.5); 3 7.0% (0.8-13.7); 0-1

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Forastiere et al. (2007, 090720) **Period of Study:** 1998-2001 **Location:** Rome, Italy	**Health Outcome (ICD9):** Mortality: Malignant neoplasms (140-208); diabetes mellitus (250); hypertensive (401-405); previous AMI (410, 412); IHD (410-414); conduction disorders of the heart (426); dysrhythmia (427); heart failure (428); cerebrovascular (430-438); peripherical artery disease (440-448); COPD (490-496) **Study Design:** Time-stratified case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** >35 yr	**Pollutant:** CO **Averaging Time:** 24-h avg Mean **(SD) unit:** NR **IQR (25th, 75th):** NR **Copollutant:** PM_{10}; $PM_{2.5}$; NO_X; Benzene	This study did not present quantitative results for CO.
Author: Goldberg et al. (2001, 016548) **Period of Study:** 1984-1993 **Location:** Montreal, Quebec, Canada	**Health Outcome (ICD9):** Mortality: Upper respiratory diseases (472-478); acute upper respiratory diseases (460-465); acute lower respiratory (466, 480-487, 512, 513, 518, 519) **Study Design:** Time series **Statistical Analyses:** Poisson GAM; LOESS **Age Groups Analyzed:** <65 yr; ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.8 (0.5) ppm **Range (Min, Max):** (0.1, 5.1) **Copollutant:** TSP; PM_{10}; $PM_{2.5}$; Sulfates; COH; SO_2; NO_2; NO; O_3	The study did not present quantitative results for CO.
Author: Goldberg et al. (2003, 035202) **Period of Study:** 1984-1993 **Location:** Montreal, Quebec, Canada	**Health Outcome (ICD9):** Mortality: CHF (428) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.8 (0.5) ppm **Range (Min, Max):** (0.1, 5.1) **Copollutant:** $PM_{2.5}$; Sulfate; SO_2; NO_2; O_3	**Increment:** 0.50 ppm **% Increase (Lower CI, Upper CI); lag:** Daily mortality from CHF -0.99% (-6.31 to 4.63); 0 0.12% (-5.29 to 5.84); 1 -1.38% (-8.81 to 6.66); 0-2 Daily mortality among persons classified as having CHF before death 2.10% (-0.24 to 4.49); 0 2.28% (-0.09 to 4.72); 1 2.86% (-0.46 to 6.29); 0-2
Author: Goldberg et al. (2006, 088641) **Period of Study:** 1984-1993 **Location:** Montreal, Quebec, Canada	**Health Outcome (ICD9):** Mortality: Diabetes (250) **Study Design:** Time series **Statistical Analyses:** Poisson, natural splines **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.8 (0.5) ppm **Range (Min, Max):** (0.1, 5.1) **Copollutant:** $PM_{2.5}$; Sulfate; SO_2; NO_2; O_3	**Increment:** 0.50 ppm **% Increase (Lower CI, Upper CI); lag:** Daily mortality from diabetes 2.64% (-2.56 to 8.12); 0 6.54% (1.31-12.03); 1 8.08% (1.03-15.62); 0-2 Daily mortality among persons classified as having diabetes before death 1.15% (-1.69 to 4.07) ; 0 1.30% (-1.58 to 4.27) ; 1 2.63% (-1.42 to 6.85) ; 0-2
Author: Gouveia et al. (2000, 012132) **Period of Study:** 1991-1993 **Location:** Sao Paulo, Brazil	**Health Outcome (ICD9):** Mortality: Respiratory; cardiovascular; all other causes **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** All ages >65 yr <5 yr	**Pollutant:** CO **Averaging Time:** Maximum 8-h moving avg Mean **(SD) unit:** 5.8 (2.1) ppm **Range (Min, Max):** (1.3, 16.2) **Copollutant:** PM_{10}; SO_2; NO_2; O_3	**Increment:** 5.1 ppm **Relative Risk (Lower CI, Upper CI); lag:** Age Group: All ages: All-causes 1.012 (0.994-1.031); 0 Age Group: >65 All-causes: 1.020 (0.996-1.046); 0 Respiratory: 0.981 (0.927-1.037); 2 CVD: 1.041 (1.007-1.076); 0 Age Group: <5 Respiratory: 1.086 (0.950-1.238); 0 Pneumonia: 1.141 (0.962-1.321); 2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Gwynn et al. (2000, 074109) **Period of Study:** 5/1988-10/1990 **Location:** Buffalo, NY	**Health Outcome (ICD9):** Mortality: Respiratory (466, 480-486); Circulatory (401-405, 410-414, 415-417); All non-accidental causes (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant correlation:** H+: r =0.15; SO_4^{2-}: r = 0.24; O_3: r = -0.23; SO_2: r = 0.11; NO_2: r = 0.65	**Increment:** NR β (SE); lag: Respiratory mortality: 0.032466 (0.053802); 0 Circulatory mortality: 0.039216 (0.026544); 3 Total mortality: 0.040214 (0.015205); 3
Author: Hoek et al. (2001, 016550) **Period of Study:** 1986-1994 **Location:** The Netherlands	**Health Outcome (ICD9):** Mortality: Heart failure (428); arrhythmia (427); cerebrovascular (430-436); thrombocytic (433, 434, 444, 452, 453); cardiovascular (390-448) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** O_3; BS; PM_{10}; SO_2; NO_2	**Increment:** 120 µg/m^3 **Relative Risk (Lower CI, Upper CI); Lag** Total CVD mortality: 1.026 (0.993-1.060); 0-6 MI and other IHD mortality: 1.050 (1.004-1.099); 0-6 Arrhythmia: 1.062 (0.937-1.203); 0-6 Heart failure mortality: 1.109 (1.012-1.216); 0-6 Cerebrovascular mortality: 1.066 (1.029-1.104); 0-6 Embolism, thrombosis: 1.065 (0.926-1.224); 0-6
Author: Hoek et al. (2000, 010350) **Period of Study:** 1986-1994 **Location:** The Netherlands	**Health Outcome (ICD9):** Mortality: Pneumonia (480-486); COPD (490-496); CVDs (CVD) (390-448) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Netherlands: 457 µg/m^3 Four Major Cities: 589 µg/m^3 **Range (Min, Max):** Netherlands: (174, 2620) Four Major Cities: (202, 4621) **Copollutant correlation:** PM_{10}: r = 0.64; BS: r = 0.89; O_3: r = -0.48; NO_2: r = 0.89; SO_2: r = 0.65; SO_4^{2-}: r = 0.55; NO_3-: r = 0.58	**Increment:** Single-day lag (1): 1,500 µg/m^3 Weekly avg (0-6): 1200 µg/m^3 **Relative Risk (Lower CI, Upper CI); Lag** CO Four Major Cities: 1.022 (0.995-1.050); 1 Four Major Cities: 1.044 (1.008-1.082); 0-6 Netherlands w/o Major Cities: 1.040 (1.020-1.060); 1 Netherlands w/o Major Cities: 1.051 (1.026-1.076); 0-6 avg Entire Netherlands: 1.035 (1.018-1.052); 1 Entire Netherlands: 1.046 (1.025-1.068); 0-6 CVD: 1.044 (1.012-1.077); 0-6 COPD: 1.194 (1.099-1.298); 0-6 Pneumonia: 1.276 (1.143-1.426); 0-6 Winter: 1.038 (1.013-1.063); 0-6 Summer: 1.199 (1.108-1.296); 0-6 Multi-pollutant model CO, PM_{10} Total mortality: 0.969 (0.914-1.028); 0-6 CVD: 1.005 (0.918-1.101); 0-6 BS, CO Total mortality: 0.980 (0.933-1.030); 0-6 CVD: 0.927 (0.860-0.999); 0-6 CO, SO_4^{2-} Total mortality: 0.990 (0.951-1.030); 0-6 CVD: 0.999 (0.939-1.063); 0-6
Author: Honda et al. (2003, 193774) **Period of Study:** 1976-1990 **Location:** Tokyo, Japan	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Median (SD) unit:** 1.6 ppm **Range (Min, Max):** (0, 6.8) **Copollutant correlation:** NO: r = 0.403; NO_2: r = 0.415; Oxidant: r = 0.396; SO_2: r = 0.675	**Increment:** NR **Rate Ratio (Lower CI, Upper CI); lag:** CO concentration <1.1 ppm: 1.00 (reference category) 1.1-1.6 ppm: 1.017 (1.009, 1.026) 1.6-2.2 ppm: 1.031 (1.020, 1.041) >2.2 ppm: 1.051 (1.039, 1.063)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Hong et al. (2002, 035060) **Period of Study:** 1/1991-12/1997 **Location:** Seoul, Korea	**Health Outcome (ICD9):** Mortality: Hemorrhagic and ischemic stroke (431-434) **Study Design:** Time series Statistical Analyses: Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.44 (0.70) ppm **Range (Min, Max):** (0.430, 5.14) **Copollutant:** TSP; SO_2; NO_2; O_3	**Increment:** 0.76 ppm **Relative Risk (Lower CI, Upper CI); lag:** 1.06 (1.02, 1.09); 1 Multipollutant: CO, TSP: 1.07 (1.03, 1.11); 1 CO, NO_2: 1.06 (1.00, 1.11); 1 CO, SO_2: 1.05 (1.01, 1.10); 1 CO, O_3: 1.09 (1.05, 1.13); 1
Author: Hong et al. (1999, 011195) **Period of Study:** 1/1995-12/1995 **Location:** Inchon, Korea	**Health Outcome (ICD9):** Mortality: Cardiovascular (400-440); respiratory (460-519); nonaccidental causes (<800) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.7 (0.8) ppm **Range (Min, Max):** (0.3, 5.1) **Copollutant:** SO_2; NO_2; O_3	**Increment**: 1 ppm **Relative Risk (Lower CI, Upper CI); lag:** Total mortality: 0.993 (0.950, 1.037); 0-4 Cardiovascular mortality: 0.965 (0.892, 1.044); 0-4
Author: Hong et al. (2002, 024690) **Period of Study:** 1/1995-12/1998 **Location:** Seoul, Korea	**Health Outcome (ICD9):** Mortality: Stroke (160-169) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.2 (0.5) ppm **Range (Min, Max):** (0.4, 3.4) **Copollutant: correlation** PM_{10}: r = 0.22; NO_2: r = 0.64; SO_2: r = 0.90; O_3: r = -0.35	**Increment:** 0.3 ppm **% Increase (Lower CI, Upper CI); lag:** CO: 2.2% (0.4, 4.1); 2 CO (stratified by PM_{10} concentration): <median concentration of PM_{10}: 1.1; 2 ≥ median concentration of PM_{10}: 3.6; 2
Author: Hong et al. (1999, 008087) **Period of Study:** 1/1995-8/1996 **Location:** Inchon, South Korea	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory; cardiovascular **Study Design:** Time series **Statistical Analyses:** Poisson GAM; LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 15.2 (7.1) ppb **Range (Min, Max):** (2.9, 51.2) **Copollutant:** PM_{10}; NO_2; SO_2; O_3	**Increment: 100 ppb** **β (SE); lag:** Total Mortality CO 0.0019 (0.0015); 1 0.0024 (0.0041); 0-4 CO, PM_{10}, NO_2, SO_2, O_3 -0.0009 (0.0019); 1 -0.0018 (0.0043); 0-4 Cardiovascular Mortality CO 0.0019 (0.0073); 1 -0.0008 (0.0028); 0-4 CO, PM_{10}, NO_2, SO_2, O_3 -0.0053 (0.0078); 1 -0.0037 (0.0033); 0-4 Respiratory Mortality CO 0.0148 (0.0065); 1 0.0063 (0.0171); 0-4 CO, PM_{10}, NO_2, SO_2, O_3 0.0121 (0.0079); 1 -0.0034 (0.0183); 0-4
Author: Keatinge et al. (2001, 017063) **Period of Study:** 1976-1995 **Location:** London, England	**Health Outcome (ICD9):** Mortality: Nonaccidental causes (<800) **Study Design:** Time series **Statistical Analyses:** Single- and multiple-delay regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit**: NR **Range (Min, Max):** NR **Copollutant:** SO_2; PM_{10}	The study did not present quantitative results for CO.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Kettunen et al. (2007, 091242) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Health Outcome (ICD10):** Mortality: Stroke (I60-I61, I63-I64) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, penalized thin-plate splines **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time**: Max 8-h ma **Median (SD) unit:** Cold Season: 0.5 mg/m^3 Warm Season: 0.4 mg/m^3 **Range (Min, Max):** Cold Season: (0.1, 2.4) Warm Season: (0.1, 1.1) **Copollutant: correlation** Cold Season: $PM_{2.5}$: r = 0.32; UFP: r = 0.47 Warm Season: $PM_{2.5}$: r = 0.24; UFP: r = 0.39	**Increment:** 0.2 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** Cold Season 0.47 (-3.29 to 4.39); 0; / -0.63 (-4.39 to 3.28); 1; -2.69 (-6.46 to 1.24); 2; / -0.19 (-3.93 to 3.69); 3 Warm Season 3.95 (-3.78 to 12.30); 0; / 8.33 (0.63 to 16.63); 1; 6.97 (-0.59 to 15.11); 2; / 7.54 (-0.05 to 15.71); 3
Author: Klemm et al. (2004, 056585) **Period of Study:** 8/1998-7/2000 **Location:** Fulton County and DeKalb County, GA (ARIES)	**Health Outcome (ICD9):** Mortality: Nonaccidental (<800); cardiovascular (390-459); respiratory (460-519); cancer (140-239) **Study Design:** Time series **Statistical Analyses:** Poisson GLM, natural cubic splines **Age Groups Analyzed:** <65 yr; ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 1-h max **Median (SD) unit:** 1,310 (939.13) ppb **Range (Min, Max**): (303.58, 7400) **Copollutant:** $PM_{2.5}$; $PM_{10-2.5}$; O_3; NO_2; SO_2; Acid; EC; OC; SO_4; Oxygenated HCs; NMHCs; NO_3	**Increment:** NR β (SE); lag: Quarterly Knots: 0.00002 (0.00001); 0-1 Monthly Knots: 0.00002 (0.00001); 0-1 Biweekly Knots: 0.00001 (0.00002); 0-1
Author: Knox et al. (2008, 193776) **Period of Study:** 1996-2004 **Location:** 352 English local authorities	**Health Outcome:** Mortality **Study Design:** Cross sectional **Statistical Analyses:** Linear regression **Age Groups Analyzed:** NR **Sample Description:** Data from Oxford Cancer Intelligence Unit	**Averaging Time:** NR **Meuan (SD) nit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR Significant (p<0.01) correlations (r) between CO and diseases: Lung cancer: 0.28, Stomach cancer: 0.20, Oesophagus cancer: -0.20, Prostate cancer: -0.25, Brain cancer: -0.24, Melanoma: -0.24, Hodgkin's: -0.19, Peripheral vascular disease: 0.15, Stroke: 0.16, Rheumatic heart disease: 0.27, Peptic ulcer: 0.28, Diabetes: 0.17, COPD: 0.25, Asthma: 0.14, Pneumonia: 0.44, Multiple sclerosis: -0.16, Motorneurone disease: -0.24, Parkinsons disease: -0.15 Significant (p<0.01) socially standardized correlations between diseases and exposures: Lung cancer: 0.25, Stomach cancer: 0.18, RHD: 0.19, Pneumonia: 0.37, COPD: 0.17, Peptic ulcer: 0.16 Lags examined: NR

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Kwon et al. (2001, 016699) **Period of Study:** 1994-1998 **Location:** Seoul, Korea	**Health Outcome (ICD9):** Mortality: CHF (428); cardiovascular (390-459) **Study Design:** 1. Time-series 2. Bi-directional case-crossover **Statistical Analyses:** 1. Poisson GLM, LOESS 2. Conditional logistic regression **Age Groups Analyzed:** <55 yr 55-64 yr 65-74 yr 75-84 yr ≥ 85 yr	**Pollutant:** CO **Averaging Time:** 1-h avg **Mean (SD) unit:** 12.4 ppb **Range (Min, Max):** (4.1, 38.0) **Copollutant correlation:** PM_{10}: r = 0.713; NO_2: r = 0.744; SO_2: r = 0.843; O_3: r = -0.367	**Increment:** 0.59 ppm **Odds Ratio (Lower CI, Upper CI); lag:** From GAM approach CHF patients: 1.054 (0.991-1.121); 0; 0 General Population: 1.022 (1.017- 1.029); 0 From case-crossover design CHF patients: 1.033 (0.946-1.127); 0 General Population: 1.007 (0.997- .016); 0 Modifiers and CHF patients (case-crossover design) Gender Male: 1.025 (0.890-1.180); 0 Female: 1.035 (0.925-1.157); 0 Age Group: <75: 0.948 (0.890-1.180); 0 ≥ 75: 1.116 (0.989-1.258); 0 Time from admission to death 4 or less wk: 1.088 (0.907-1.306); 0 >4 wk: 1.017 (0.920-1.124); 0 Total mortality: 1.033 (0.946-1.127); 0 Cardiovascular mortality: 1.033 (0.920-1.160); 0 Cardiac death: 1.052 (0.919-1.204); 0 Two-pollutant model in CHF patients (case-crossover design) CO alone: 1.054 (0.991-1.121); 0 CO, PM_{10}: 1.096 (0.981-1.224); 0 CO, NO_2: 1.022 (0.932-1.122); 0 CO, SO_2: 1.014 (0.909-1.131); 0 CO, O_3: 1.056 (0.992-1.124); 0
Author: Lee et al. (2007, 093042) **Period of Study:** 1/2000-12/2004 **Location:** Seoul, Korea	**Health Outcome (ICD10):** Mortality: Nonaccidental (A00-R99) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** Max 8-h ma **Mean (SD) unit:** w/ Asian dust days: 0.92 (0.42) ppm w/o Asian dust days:0.92 (0.41) ppm Asian dust days only: 1.00 (0.47) ppm **Range (Min, Max):** NR **Copollutant:** PM_{10}; NO_2; SO_2; O_3	**Increment**: 0.54 ppm **% Increase (Lower CI, Upper CI); lag:** Model with Asian Dust Days: 3.3% (2.5-4.1); 1 Model without Asian dust days: 3.3% (2.5-4.2); 1
Author: Lipfert et al. (2000, 004088) **Period of Study:** 5/1992-9/1995 **Location:** Philadelphia, PA, three nearby suburban Pennsylvania counties, and three nearby New Jersey counties	**Health Outcome (ICD9):** Mortality: Respiratory (460-519); cardiac (390-448); Cancer; other causes (<800) **Study Design:** Time series **Statistical Analyses:** Step-wise regression **Age Groups Analyzed:** <65 yr ≥ 65 yr	**Pollutant:** CO **Averaging Time**: 24-h avg; 1-h max **Mean (SD) unit:** Camden: 24-h avg: 0.75 (0.40) ppm Philadelphia: 24-h avg: 0.63 (0.40) ppm 1-h max: 1.44 (1.04) **Range (Min, Max):** Camden: (0.10, 3.8) Philadelphia: 24-h avg: (0.10, 3.3) 1-h max: (0.0, 7.8) **Copollutant:** NO; NO_2; O_3; SO_2; SO_4^{2-}; PM_{10}; $PM_{2.5}$	**Increment:** NR **Attributable Risk; lag:** Peak CO All-cause Philadelphia: 0.0054; 0-1 4 Pennsylvania Counties: 0.0081; 0-1 Pennsylvania + NJ: 0.0085; 0-1 CO All seven counties in Pennsylvania and New Jersey All ages Respirator y: -0.0067; Cardiac: 0.0131; Other: 0.0078 All-cause: <65: 0.0148; 0-1; ≥ 65: 0.0054; 0-1 Joint model with CO Philadelphia: 0.0059; 0-1 4 Pennsylvania Counties: 0.0089; 0-1 Pennsylvania + NJ: 0.0096; 0-1 Cardiac: 0.0135; 0-1; Other causes: 0.0084 <65: 0.0154; 0-1; ≥ 65: 0.0060; 0-1

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Lippmann et al. (2000, 011938) **Period of Study:** 1985-1990 1992-1994 **Location:** Detroit, MI and Windsor, ON	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); circulatory (390-459); respiratory (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson GLM **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1985-1990: 0.9 ppm 1992-1994: 0.72 ppm **Range (5th, 95th):** 1985-1990: (.46, 1.61) 1992-1994: (0.36, 1.2) **Copollutant correlation:** 1985-1990 PM_{10}: r = 0.35; TSP: r = 0.28; TSP-PM_{10}: r = 0.02; TSP-SO_4^{2-}: r = 0.18; O_3: r = -0.22; SO_2: r = 0.36; NO_2: r = 0.58 1992-1994 PM_{10}: r = 0.38; $PM_{2.5}$: r = 0.38; $PM_{10-2.5}$: r = 0.24; H+: r = 0.16; SO_4^{2-}:r = 0.32; O_3: r = 0.16; SO_2: r = 0.42; NO_2: r = 0.68	**Increment:** 1985-1990: 11.5 ppm; 1992-1994: 8.4 ppm Relative Risk (Lower CI, Upper CI); lag: 1985-1990 Total Mortality: 0.9842 (0.9667-1.002); 0 1.0103 (0.9926-1.0284); 1 1.0075 (0.9898-1.0254); 2 1.0145 (0.9967-1.0326); 3 0.9968 (0.9789-1.0151); 0-1 1.0105 (0.9925-1.0288); 1-2 1.0134 (0.9954-1.0317); 2-3 1.0003 (0.9823-1.0187); 0-2 1.0152 (0.9971-1.0336); 1-3 1.0053 (0.9873-1.0236); 0-3 Circulatory Mortality: 0.9818 (0.9574-1.0068); 0 0.9991 (0.9745-1.0243); 1 0.9980 (0.9735-1.0232); 2 1.0088 (0.9841-1.0341); 3 0.9888 (0.9640-1.0144); 0-1 0.9981 (0.9732-1.0237); 1-2 1.0042 (0.9792-1.0298); 2-3 0.9900 (0.9650-1.0157); 0-2 1.0029 (0.9777-1.0287); 1-3 0.9944 (0.9692-1.0202); 0-3 Respiratory Mortality; 0.9644 (0.9042-1.0287); 0 1.0142 (0.9518-1.0808); 1 1.0483 (0.9845-1.1164); 2 1.0468 (0.9828-1.1149); 3 0.9868 (0.9248-1.053); 0-1 1.0372 (0.9730-1.1056); 1-2 1.0554 (0.9904-1.1246); 2-3 1.0088 (0.9457-1.0762); 0-2 1.0466 (0.9817-1.1158); 1-3 1.0205 (0.9569-1.0884); 0-3 Total minus respiratory and circulatory mortality: 0.9939 (0.9668-1.0217); 0 1.0278 (1.0001-1.0562); 1 1.0178 (0.9902-1.0461); 2 1.0227 (0.9948-1.0514); 3 1.0127 (0.9860-1.0412); 0-1 1.0269 (0.9989-1.0556); 1-2 1.0249 (0.9968-1.0538); 2-3 1.0172 (0.9893-1.0458); 0-2 1.0322 (1.0041-1.0612); 1-3 1.0229 (0.9950-1.0516); 0-3 1992-1994 Total Mortality 0.9933 (0.9636-1.024); 0 1.0162 (0.9860-1.0473); 1 1.0116 (0.9816-1.0426); 2 0.9947 (0.9648-1.0254); 3 1.0056 (0.9756-1.0366); 0-1 1.0165 (0.9864-1.0476); 1-2 1.0038 (0.9739-1.0476); 2-3 1.0098 (0.9796-1.0409); 0-2 1.0104 (0.9862-1.0414); 1-3 1.0064 (0.9755-1.0382); 0-3 Circulatory Mortality 1.0076 (0.9640-1.0531); 0 1.0307 (0.9865-1.0768); 1 1.0142 (0.9705-1.0598); 2 0.9523 (0.9102-0.9964); 3 1.0229 (0.9788-1.0688); 0-1 1.0267 (0.9827-1.0727); 1-2 0.9802 (0.9375-1.0248); 2-3 1.0243 (0.9801-1.0726); 0-2 0.9987 (0.9553-1.0441); 1-3 1.0019 (0.9573-1.0487); 0-3

Study	Design	Concentrations	Effect Estimates (95% CI)
			Respiratory Mortality 0.9894 (0.8912-1.0984); 0 0.9474 (0.8521-1.0533); 1 0.9652 (0.8682-1.0732); 2 0.9931 (0.8934-1.1040); 3 0.9626 (0.8668-1.0691); 0-1 0.9485 (0.8535-1.0541); 1-2 0.9752 (0.8775-1.0838); 2-3 0.9555 (0.8802-1.0615); 0-2 0.9567 (0.8607-1.0635); 1-3 0.9584 (0.9604-1.0675); 0-3 Total minus respiratory and circulatory mortality: 0.9769 (0.9332-1.0227); 0 1.0135 (0.9682-1.0609); 1 1.0195 (0.9747-1.0664); 2 1.0429 (0.9974-1.0905); 3 0.9940 (0.9494-1.0406); 0-1 1.0197 (0.9746-1.0670); 1-2 1.0371 (0.9918-1.0845); 2-3 1.0045 (0.9596-1.0515); 0-2 1.0353 (0.9896-1.0831); 1-3 1.0215 (0.9749-1.0702); 0-3
Author: Maheswaran et al. (2005, 090769) **Period of Study:** 1994-1998 **Location:** Sheffield, United Kingdom	**Health Outcome (ICD9):** Mortality: CHD (410-414) **Study Design:** Ecological **Statistical Analyses:** Poisson **Age Groups Analyzed:** ≥ 45 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NO_X; PM_{10} **Notes:** Quintiles represent the following mean CO concentrations and category limits: 5: 482 µg/m^3 (≥ 455) 4: 443 µg/m^3 (≥ 433 to <455) 3: 426 µg/m^3 (≥ 419 to <433) 2: 405 µg/m^3 (≥ 387 to <419) 1: 360 µg/m^3 (<387)	**Increment:** NR **Rate Ratios (Lower CI, Upper CI):** CO Adjusted for sex and age Quintile: 5 (highest): 1.24 (1.14, 1.36) 4: 1.30 (1.19, 1.41) 3: 1.15 (1.05, 1.25) 2: 1.08 (0.99, 1.17) 1: (lowest): 1.00 CO Adjusted for sex, age, deprivation, and smoking Quintile: 5 (highest): 1.05 (0.95, 1.16); 4: 1.16 (1.06, 1.28); 3: 1.04 (0.95, 1.14); 2: 1.03 (0.94, 1.13); 1 (lowest): 1.00 CO Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1 km radius) Quintile: 5 (highest): 1.07 (0.96, 1.18); 4: 1.13 (1.03, 1.24); 3: 1.04 (0.95, 1.14); 2: 1.01 (0.92, 1.10); 1 (lowest): 1.00

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Maheswaran et al. (2005, 088683) **Period of Study:** 1994-1998 **Location:** Sheffield, United Kingdom	**Health Outcome (ICD9):** Mortality: Stroke deaths (430-438) **Study Design:** Ecological **Statistical Analyses:** Poisson **Age Groups Analyzed:** ≥ 45 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Quintile: 5: 482 µg/m^3; 4: 443 µg/m^3; 3: 426 µg/m^3; 2: 405 µg/m^3; 1: 360 µg/m^3 **Range (Min, Max):** NR **Copollutant correlation:** PM_{10}: r = 0.88; NO_X: r = 0.87 **Notes:** Quintiles represent the following mean CO concentrations and category limits: 5: 482 µg/m^3 (≥ 455) 4: 443 µg/m^3 (≥ 433 to <455) 3: 426 µg/m^3 (≥ 419 to <433) 2: 405 µg/m^3 (≥ 387 to <419) 1: 360 µg/m^3 (<387)	**Increment:** NR **Rate Ratios (Lower CI, Upper CI); lag:** RR for mortality and CO modeled outdoor air pollution Adjusted for sex and age Quintile: 5 (highest): 1.35 (1.19, 1.53); 4: 1.40 (1.24, 1.58); 3: 1.08 (0.95, 1.23); 2: 1.10 (0.97, 1.24); 1 (lowest): 1.00 Adjusted for sex, age, deprivation, and smoking Quintile: 5 (highest): 1.26 (1.10, 1.46); 4: 1.32 (1.15, 1.50); 3: 1.07 (0.93, 1.22); 2: 1.12 (0.99, 1.28); 1 (lowest): 1.00 Not spatially smoothed CO outdoor air pollution Quintile: 5 (highest): 1.26 (1.10, 1.46); 4: 1.32 (1.15, 1.50); 3: 1.07 (0.93, 1.22); 2: 1.12 (0.99, 1.28); 1 (lowest): 1.00 Spatially smoothed using a 1-km radius Quintile: 5 (highest): 1.16 (1.01, 1.34); 4: 1.22 (1.07, 1.39); 3: 0.95 (0.83, 1.09); 2: 0.97 (0.85, 1.11); 1 (lowest): 1.00
Author: Mar et al. (2000, 001760) **Period of Study:** 1995-1997 **Location:** Phoenix, AZ	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); cardiovascular (390-449) **Study Design:** Time series **Statistical Analyses:** Poisson **Age Groups Analyzed:** >65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.5 (0.8) ppm **Range (Min, Max):** 1995: (0.5, 4.0) ppm 1996: (0.3, 4.0) ppm 1997: (0.3, 3.7) ppm **Copollutant correlation:** $PM_{2.5}$: r = 0.85; PM_{10}: r = 0.53; $PM_{10-2.5}$: r = 0.34; NO_2: r = 0.87; O_3: r =-0.40; SO_2: r =0.53	**Increment:** 1.19 ppm **Relative Risk (Lower CI, Upper CI); lag:** Total Mortality (CO exposure): 1.06 (1.02, 1.09); 0; 1.05 (1.01, 1.09); 1 Cardiovascular Mortality (CO exposure): 1.05 (1.00, 1.11); 0; 1.10 (1.04, 1.15); 1; 1.07 (1.02, 1.12); 2; 1.07 (1.02, 1.12); 3; 1.08 (1.03, 1.13); 4

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Moolgavkar et al. (2000, 012054) **Period of Study:** 1987-1995 **Location:** Cook County, IL Los Angeles County, CA Maricopa County, AZ	**Health Outcome (ICD9):** Mortality: Circulatory (390-448); cardiovascular (390-429); cerebrovascular (430-448); COPD (490-496); asthma (493) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, spline smoother **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Median unit:** Cook county: 993 ppb Los Angeles: 1347 ppb Maricopa: 1240 ppb **Range (Min, Max):** Cook county: (224, 3912) Los Angeles: (237, 5955) Maricopa: (269, 4777) **Copollutant correlation:** PM_{10}: Cook: r = 0.30; LA: r = 0.45; Maricopa: r = 0.20 NO_2: Cook: r = 0.63; LA: r = 0.80; Maricopa: r = 0.66 SO_2: Cook: r = 0.35; LA: r = 0.78; Maricopa: r = 0.53 O_3: Cook: r = -0.28; LA: r = -0.52; Maricopa: r = -0.61	**Increment:** 1 ppm **% Change (Lower CI, Upper CI); lag:** CVD Mortality Cook County CO -1.07 (-2.67, 0.54); 0; / 1.25 (-0.36, 2.87); 1; 1.49 (-0.09, 3.07); 2; / 1.90 (0.32, 3.48); 3; 1.44 (-0.16, 3.03); 4; / 0.72 (-0.89, 2.32); 5 Los Angeles County CO 3.47 (2.94, 4.00); 0; / 3.93 (3.41, 4.46); 1; 4.08 (3.56, 4.60); 2; / 3.76 (3.24, 4.28); 3; 2.91 (2.37, 3.44); 4; / 2.63 (2.09, 3.17); 5 CO, PM_{10} 2.27 (0.88, 3.66); 0; / 4.33 (2.96, 5.69); 1; 4.72 (3.38, 6.05); 2; / 4.26 (2.90, 5.63); 3; 2.49 (1.10, 3.88); 4; / 5.93 (4.60, 7.27); 5 CO and $PM_{2.5}$ 0.43 (-1.35, 2.20); 0; / 2.88 (1.16, 4.60); 1; 4.65 (2.93, 6.37); 2; / 5.93 (4.20, 7.65); 3; 3.88 (2.13, 5.63); 4; / 5.85 (4.12, 7.58); 5 Maricopa County CO 0.81 (-0.79, 2.39); 0; / 2.20 (0.61, 3.79); 1; 3.05 (1.49, 4.61); 2; / 3.78 (2.27, 5.28); 3; 3.73 (2.27, 5.19); 4; / 2.25 (0.76, 3.72); 5 COPD Mortality Cook County CO -2.65 (-7.05, 1.75); 0; / 2.80 (-1.60, 7.19); 1; 0.98 (-3.34, 5.31); 2; / 2.20 (-2.12, 6.53); 3; 1.31 (-3.06, 5.68); 4; / 1.59 (-2.78, 5.97); 5 Los Angeles County CO 3.78 (2.31, 5.25); 0; / 5.23 (3.78, 6.69); 1; 5.71 (4.26, 7.17); 2; / 5.42 (3.95, 6.89); 3; 4.01 (2.51, 5.50); 4; / 3.82 (2.31, 5.33); 5 Maricopa County CO 1.29 (-2.19, 4.76); 0; / 4.63 (1.17, 8.09); 1; 0.07 (-3.36, 3.50); 2; / 3.00 (-0.30, 6.30); 3; 6.21 (3.02, 9.40); 4; / 3.27 (0.04, 6.50); 5 Cerebrovascular Disease Mortality Cook County -0.41 (-3.30, 2.47); 0; / 3.13 (0.23, 6.02); 1; 2.12 (-0.73, 4.97); 2; / 1.00 (-1.85, 3.86); 3; 2.50 (-0.36, 5.37); 4; / 1.88 (-1.00, 4.76); 5 Los Angeles County 3.31 (2.32, 4.31); 0; / 3.88 (2.89, 4.87); 1; 3.23 (2.25, 4.22); 2; / 2.65 (1.66, 3.65); 3; 2.11 (1.11, 3.12); 4; / 2.04 (1.02, 3.06); 5 Maricopa County 0.26 (-2.65, 3.16); 0; / 3.50 (0.60, 6.41); 1; 3.52 (0.66, 6.38); 2; / 4.61 (1.85, 7.37); 3; 4.78 (2.10, 7.46); 4; / 5.15 (2.45, 7.84); 5 **Notes:** Total Mortality effect estimates were not presented quantitatively.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Moolgavkar et al. (2003, 051316) **Period of Study:** 1987-1995 **Location:** Cook County, Illinois & Los Angeles County, California	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); circulatory (390-448) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All Ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Median unit:** Cook County: 993 ppb LA County: 1347 ppb **Range (Min, Max):** Cook County: (224, 3912) ppb LA County: (237, 5955) ppb **Copollutant correlation:** Cook County: NO_2: r = 0.63; O_3: r = -0.22; SO_2: r = 0.35; PM_{10}: r = 0.30 LA County: NO_2: r = 0.80; O_3: r = -0.52; SO_2: r = 0.78; PM_{10}: r = 0.45; $PM_{2.5}$: r = 0.58	**Increment:** 1 ppm **% Increase (t-statistic); lag** Total Mortality Cook County CO: 0.6% (1.2); 0; / 2.5% (5.4); 1; / 1.2% (2.6); 2; 1.5% (3.2); 3; / 1.1% (2.5); 4; / 0.6% (1.3); 5 CO, PM_{10}: -0.5% (-1.0); 0; / 2.2% (4.3); 1; / 1.1% (2.2); 2; 1.0% (1.9); 3; / 1.1% (2.1); 4; / 1.4% (2.7); 5 Total Mortality Los Angeles County CO: 1.3% (7.4); 0; / 1.9% (10.5); 1; / 1.6% (8.9); 2; 1.4% (8.1); 3; / 1.0% (5.9); 4; / 0.7% (4.1); 5 CO, PM_{10}: 0% (0); 0; / 2.2% (4.8); 1; / 1.4% (3.1); 2; 0.8% (1.8); 3; / 0.7% (1.6); 4; / 1.3% (3.0); 5 CO, $PM_{2.5}$: -0.1% (-1.5); 0; / 1.5% (2.5); 1; / 2.4% (3.8); 2; 0.3% (0.5); 3; / 1.6% (2.8); 4; / 1.5% (2.6); 5 Total Mortality (Season-specific) Cook County Spring (CO): 0.8% (0.9); 0; / 2.4% (2.9); 1; / 0% (0); 2; 1.2% (1.5); 3; / 0.8% (1.0); 4; / -0.1% (-0.2); 5 Summer (CO): 1.2% (1.0); 0; / 3.6% (3.0); 1; / 4.2% (3.6); 2; -0.3% (-0.2); 3; / -1.1% (-1.0); 4; /-0.7% (-0.6); 5 Fall (CO): 1.2% (1.5); 0; / 2.1% (2.7); 1; / 0% (0); 2; 0% (0); 3; /-0.5% (-0.6); 4; / -0.7% (-0.9); 5 Winter (CO): -0.7% (-1.0); 0; / 1.8% (2.3); 1; / -0.2% (-0.3); 2; 0.5% (0.6); 3; / 1.2% (1.5); 4; / 1.0% (1.3); 5 Los Angeles County Total Mortality (Season-specific) Spring (CO): 3.6% (6.3); 0; / 3.5% (6.2); 1; / 1.9% (3.4); 2; 0.6% (1.0); 3; / -0.5% (-0.8); 4; / -0.7% (-1.2); 5 Summer (CO): 3.0% (3.0); 0; / 4.7% (4.6); 1; / 5.2% (5.1); 2; 4.1% (3.8); 3; / 1.9% (1.8); 4; / 1.4% (1.3); 5 Fall (CO): 1.8% (4.6); 0; / 2.0% (5.1); 1; / 1.0% (2.6); 2; 0.6% (1.5); 3; / 0.4% (1.2); 4; / 0.2% (0.6); 5 Winter (CO): 0% (0); 0; / 0.8% (2.5); 1; / 0.9% (3.1); 2; 1.0% (3.4); 3; / 0.5% (1.7); 4; / 0.5% (1.6); 5 CVD Mortality Cook County CO: -1.1% (-1.5); 0; / 1.8% (2.5); 1; / 1.5% (2.2); 2; 1.6% (2.4); 3; / 1.4% (2.1); 4; / 0.7% (1.0); 5 CO, PM_{10}: -2.1% (-2.6); 0; / 1.5% (1.8); 1; / 1.4% (1.7); 2; 0.1% (1.1); 3; / 1.4% (1.9); 4; / 1.6% (2.1); 5 CVD Mortality Los Angeles County CO: 1.6% (6.3); 0; / 1.9% (7.6); 1; / 1.6% (6.6); 2; 1.9% (8.2); 3; / 1.6% (7.1); 4; / 1.4% (6.1); 5 CO, PM_{10}: -0.8% (-1.2); 0; / 1.9% (3.0); 1; / 2.7% (4.3); 2; 1.3% (2.2); 3; / 0.5% (0.9); 4; / 2.8% (4.7); 5 CO, $PM_{2.5}$: -2.2% (-2.7); 0; / 1.5% (1.8); 1; / 1.9% (2.0); 2; 1.9% (2.2); 3; / 2.1% (2.6); 4; / 3.7%(4.5); 5

Study	Design	Concentrations	Effect Estimates (95% CI)
			CVD Mortality (Season Specifid) Cook County Spring (CO): 0.7% (0.5); 0; / 1.4% (1.1); 1; / 0.3% (0.3); 2; 1.1% (0.9); 3; / 0.4% (3.1); 4; / 0.1% (0.6); 5 Summer (CO): -2.6% (-1.4); 0; / 2.5% (1.4); 1; / 6.5% (3.7); 2; 0.9% (0.5); 3; / -1.9% (-1.1); 4; / -1.0% (-0.6); 5 Fall (CO): 0% (0); 0; / 2.9% (2.5); / 1; 0% (0); 2; 0% (0); 3; /-0.8% (-0.7); / 4; 0% (0); 5 Winter (CO): -2.5% (-2.2); 0; / 0.7% (0.6); 1; / 0% (0); 2; 1.3% (1.1); 3; / 0.8% (0.7); 4; / 0.4% (0.4); 5 Los Angeles County CVD Mortality (Season-specific) Spring (CO): 3.0% (3.7); 0; / 3.3% (4.1); 1; / 2.3% (2.9); 2; 0.7% (0.9); 3; / -1.2% (-1.6); 4; / 0% (0); 5 Summer (CO): 4.0% (2.8); 0; / 5.2% (3.5); 1; / 6.3% (4.3); 2; 5.0% (3.3); 3; / 3.1% (2.0); 4; / 3.6% (2.3); 5 Fall (CO): 2.3% (4.2); 0; / 2.1% (3.7); 1; / 1.1% (1.9); 2; 1.2% (2.2); 3; / 1.5% (2.9); 4; / 1.0% (1.8); 5 Winter (CO): 0.3% (0.8); / 0; 0.7% (1.7); 1; / 0.8% (2.0); 2; 1.4% (3.4); 3; / 1.0% (2.3); 4; / 1.1% (2.5); 5
Author: Ostro et al. (1999, 006610) **Period of Study:** 1989-1992 **Location:** Coachella Valley, California	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory (460-519); cardiovascular (393-440) **Study Design:** Time series **Statistical Analyses:** Poisson GAM; LOESS **Age Groups Analyzed:** >50 yr	**Pollutant:** CO **Averaging Time:** 1-h max **Mean (SD) unit:** 1.35 ppm **Range (Min, Max):** (0, 6.0) **Copollutant correlation:** PM_{10}: r = -0.18; O_3: r = -0.47; NO_2: r = 0.65	**Increment:** NR **β (SE); lag:** CO: 0.0371 (0.0157); 2 CO, PM_{10}: 0.0300 (0.0194); 2
Author: Penttinen et al. (2004, 087432) **Period of Study:** 1988-1996 **Location:** Helsinki, Finland	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory (460-519); cardiovascular (393-440) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages 15-64 yr 65-74 yr ≥ 75	**Pollutant:** CO **Averaging Time:** Max 8-h avg **Median unit:** 1.2 mg/m^3 **Range (Min, Max):** (0, 12.4) **Copollutant correlation:** O_3: r = -0.46; NO_2: r = 0.59; SO_2: r = 0.55; PM_{10}: r = 0.45; TSP: r = 0.26; TSP Blackness: r = 0.26	**Increment:** 1 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** Total Mortality -1.50% (-2.78, -0.22); 0 0.15% (-1.09, 1.39); 1 -1.00% (-2.80, 0.81); 0-3 Cardiovascular Mortality -2.48% (-4.30, -0.66); 0 -0.84% (-2.61, 0.93); 1 -1.87% (-4.43, 0.69); 0- Respiratory Mortality -0.48% (-4.84, 3.87); 0 -0.14% (-4.43, 4.15); 1 -1.49% (-7.73, 4.74); 0-3
Author: Peters et al. (2000, 001756) **Period of Study:** 1982-1994 **Location:** Northern Bavaria (Rural Germany) and the Coal Basin of the Czech Republic	**Health Outcome (ICD9):** Mortality: Total (non-accidental) (<800); Cardiovascular (390-459); Respiratory (460-519); Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** (1) Poisson Regression Models by logistic regression analyses with a cubic function; (2) Poisson GAM, natural splines **Age Groups Analyzed:** All Ages	**Pollutant:** CO **Averaging Time:** 24-h avg Mean (SD) unit: Coal Basin: 0.58 (0.39) mg/m^3 Northeast Bavaria: 0.88 (0.69) mg/m^3 Range (Min, Max): Coal Basin: (-0.1, 2.88) Northeast Bavaria: (0.1, 6.2) **Copollutant correlation:** SO_2: r = 0.37; TSP: r = 0.37; NO_2: r = 0.32; O_3: r = -0.57; PM_{10}: r = 0.44; $PM_{2.5}$: r = 0.42	Increment: 1 mg/m^3 Relative Risk (Lower CI, Upper CI); lag: Coal Basin of the Czech Republic Total Mortality: 1.016 (0.998, 1.035); 0; / 1.016 (0.998, 1.034); 1; 1.013 (0.996, 1.030); 2; / 1.012 (0.995, 1.028); 3 Northeast Bavaria Total Mortality: 1.014 (0.994, 1.034); 0; / 1.023 (1.005, 1.041); 1; 1.013 (0.995, 1.031); 2; / 1.003 (0.985, 1.021); 3 CVD Mortality: 1.018 (0.994, 1.044); 0; / 1.012 (0.987, 1.038); 1; 1.016 (0.991, 1.041); 2; / 1.004 (0.980, 1.029); 3

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Rainham et al. (2003, 053202) **Period of Study:** 1980-1996 **Location:** Toronto, ON, Canada	**Health Outcome (ICD9):** Mortality: Cardiac (390-459); Respiratory (480-519); Total (non-accidental) (<800) **Study Design:** Time-series **Statistical Analyses:**Poisson GAM, natural cubic splines **Age Groups Analyzed:** <65 ≥ 65	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.0 (0.4) ppm **Range (Min, Max):** (0.0, 4.0) **Copollutant:** O_3; NO_2; SO_2	The study did not present quantitative results for CO.
Author: Roemer et al. (2001, 019391) **Period of Study:** 1/1987-11/1998 **Location:** Amsterdam	**Health Outcome (ICD9):** Mortality: Total (non-accidental) (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Air pollution background: 836 µg/m^3 Air pollution traffic: 1805 µg/m^3 **Range (10th, 90th):** Air pollution background: (448, 1315) µg/m^3 Air pollution traffic: (727, 3192) µg/m^3 **Copollutant:** BS; PM_{10}; SO_2; NO_2; NO; O_3	**Increment:** Lag 1 and 2: 100 µg/m^3 Lag 0-6: 50 µg/m^3 **Relative Risk (Lower CI, Upper CI); lag:** Total Population using Background sites 1.002 (1.000-1.004); 1; 1.001 (0.999-1.003); 2; 1.001 (1.000-1.003); 0-6 Traffic Population using Background Sites 1.003 (0.997-1.008); 1; 1.008 (1.003-1.013); 2; 1.003 (0.999-1.007); 0-6 Total population using Traffic Sites 1.000 (1.000-1.001); 1; 1.000 (0.999-1.001); 2; 1.000 (1.000-1.001); 0-6

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Samet et al. (2000, 013132) **Period of Study:** 1987-1994 **Location:** 20 U.S. Cities: Los Angeles, CA; New York, NY; Chicago, IL; Dallas, TX; Houston, TX; San Diego, CA; Anaheim, CA; Phoenix, AZ; Detroit, MI; Miami, FL; Philadelphia, PA; Minneapolis, MN; Seattle, WA; San Jose, CA; Cleveland, OH; San Bernardino, CA; Pittsburgh, PA; Oakland, CA; Atlanta, GA; San Antonio, TX	**Health Outcome (ICD9):** Mortality: Cardiovascular (390-459); Respiratory (460-519); Other (non-accidental) (<800) **Study Design:** Time-series **Statistical Analyses:** Two-stage log linear regression model **Age Groups Analyzed:** <65 65-74 ≥ 75	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Los Angeles: 15.1 ppm New York: 20.4 ppm Chicago: 7.9 ppm Dallas: 7.4 ppm Houston: 8.9 ppm San Diego: 11.0 ppm Anaheim: 12.3 ppm Phoenix: 12.6 ppm Detroit: 6.6 ppm Miami: 10.6 ppm Philadelphia: 11.8 ppm Minneapolis: 11.8 ppm Seattle: 17.8 ppm San Jose: 9.4 ppm Cleveland: 8.5 ppm San Bernardino: 10.3 ppm Pittsburgh: 12.2 ppm Oakland: 9.1 ppm Atlanta: 8.0 ppm San Antonio: 10.1 ppm Range (10th, 90th): Los Angeles: (5.9, 28.3) New York: (14.8, 27.6) Chicago: (4.5, 11.9) Dallas: (3.6, 12.0) Houston: (4.0, 14.2) San Diego: (4.5, 20.5) Anaheim: (3.7, 25.2) Phoenix: (5.4, 22.6) Detroit: (3.2, 11.1) Miami: (6.5, 15.9) Philadelphia: (7.0, 17.2) Minneapolis: (7.0, 17.0) Seattle: (10.5, 26.4) San Jose: (1.7, 21.3) Cleveland: (3.7, 13.8) San Bernardino: (4.0, 17.5) Pittsburgh: (6.1, 19.8) Oakland: (2.9, 17.0) Atlanta: (3.2, 14.3) San Antonio: (4.1, 17.3) **Copollutant correlation:** PM_{10}: r = 0.45; O_3: r = -0.19; NO_2: r = 0.64; SO_2: r = 0.41	This study did not provide quantitative results for CO.
Author: Samoli et al. (2007, 098420) **Period of Study:** 1990-1997 **Location:** 19 European Cities (APHEA2)	**Health Outcome (ICD9):** Mortality: Total (non-accidental) (<800); Cardiovascular (390-459) **Study Design:** Time-series **Statistical Analyses:** Poisson and two-stage hierarchical model **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean Range (unit–mg/m3):** Athens: 6.1; Barcelona: 0.9; Basel: 0.6; Birmingham: 1.0; Budapest: 5.1; Geneva: 1.5; Helsinki: 1.2; Ljubljana: 1.6; London: 1.4; Lyon: 3.8; Milano: 5.4; Netherlands: 0.6; Prague: 0.9; Rome: 4.1; Stockholm: 0.8; Teplice: 0.7; Torino: 5.5; Valencia: 4.1; Zurich: 1.2 **Range (10th, 90th):** Athens: (3.5, 9.2) Barcelona: (0.4, 1.7) Basel: (0.4, 1.1) Birmingham: (0.5, 1.6) Budapest: (3.3, 7.4) Geneva: (0.8, 2.6) Helsinki: (0.7, 1.9) Ljubljana: (0.6, 3.0) London: (0.7, 2.2) Lyon: (2.0, 6.0) Milano: (2.9, 8.7) Netherlands: (0.4, 1.2) Prague: (0.5, 1.5)	**Increment:** 1 mg/m^3 **% Increase (Lower CI, Upper CI); lag:** Non-accidental mortality 8 Degrees of Freedom per yr Fixed Effects: CO: 0.59% (0.41-0.78); 0-1 CO, BS: 0.35% (-0.03 to 0.72); 0-1 CO, PM_{10}: 0.48% (0.24-0.72); 0-1 CO, SO_2: 0.44% (0.21-0.67); 0-1 CO, O_3: 0.66% (0.46-0.86); 0-1 CO, NO_2: 0.27% (0.03-0.51); 0-1 Random Effects: CO: 0.66% (0.27-1.05); 0-1 CO, BS: 0.45% (-0.01 to 0.92); 0-1 CO, PM_{10}: 0.58% (0.12-1.04); 0-1 CO, SO_2: 0.46% (0.07-0.85); 0-1 CO, O_3: 0.76% (0.45-1.06); 0-1 CO, NO_2: 0.30% (-0.11 to 0.71); 0-1 PACF: (Partial Autocorrelation Function) Plot Fixed Effects: CO: 1.00% (0.83-1.18); 0-1 CO, BS: 0.67% (0.30-1.04); 0-1 CO, PM_{10}: 0.78% (0.55-1.00); 0-1 CO, SO_2: 0.68% (0.47-0.90); 0-1 CO, O_3: 1.12% (0.93-1.31); 0-1 CO, NO_2: 0.72% (0.50-0.95); 0-1

Study	Design	Concentrations	Effect Estimates (95% CI)
		Rome: (2.5, 5.9) Stockholm: (0.5, 1.2) Teplice: (0.3, 1.2) Torino: (2.8, 9.1) Valencia: (2.4, 5.9) Zurich: (0.7, 2.0) **Copollutant correlation:** PM_{10}: r = 0.16 to 0.70 BS: r = 0.67 to 0.82 SO_2: r = 0.35 to 0.82 NO_2: r = 0.03 to 0.68 O_3: r = -0.25 to -0.65	Random Effects: CO: 1.20% (0.63-1.77); 0-1 CO, BS: 0.77% (0.28-1.26); 0-1 CO, PM_{10}: 1.09% (0.36-1.83); 0-1 CO, SO_2: 0.75% (0.26-1.26); 0-1 CO, O_3: 1.37% (0.81-1.95); 0-1 CO, NO_2: 0.88% (0.22-1.55); 0-1 Cardiovascular Mortality 8 Degrees of Freedom per Year Fixed Effects: CO: 0.80% (0.53-1.07); 0-1 CO, BS: 0.49% (-0.04 to 1.02); 0-1 CO, PM_{10}: 0.73% (0.39-1.07); 0-1 CO, SO_2: 0.72% (0.39-1.04); 0-1 CO, O_3: 0.91% (0.62-1.20); 0-1 CO, NO_2: 0.44% (0.10-0.79); 0-1 Random Effects: CO: 0.81% (0.36-1.26); 0-1 CO, BS: 0.49% (-0.04 to 1.02); 0-1 CO, PM_{10}: 0.73% (0.39-1.07); 0-1 CO, SO_2: 0.68% (-0.03 to 1.40); 0-1 CO, O_3: 1.02% (0.58-1.46); 0-1 CO, NO_2: 0.43% (-0.06 to 0.93); 0-1 PACF (Partial Autocorrelation Function) Fixed Effects: CO: 1.06% (0.80-1.32); 0-1 CO, BS: 0.83% (0.31-1.35); 0-1 CO, PM_{10}: 0.95% (0.62-1.27); 0-1 CO, SO_2: 0.91% (0.59-1.22); 0-1 CO, O_3: 1.28% (1.01-1.56); 0-1 CO, NO_2: 0.68% (0.35-1.00); 0-1 Random Effects: CO: 1.25% (0.30-2.21); 0-1 CO, BS: 0.83% (0.31-1.35); 0-1 CO, PM_{10}: 1.13% (0.60-1.67); 0-1 CO, SO_2: 0.86% (0.06-1.66); 0-1 CO, O_3: 1.62% (0.72-2.52); 0-1 CO, NO_2: 0.84% (-0.03 to 1.71); 0-1 Effect Modifiers Non-accidental Mortality 8 Degrees of Freedom per Year Number of CO monitors: 25th Percentile: 0.71% (0.48-0.94); 0-1 75th Percentile: 0.54% (0.34-0.74); 0-1 Mean PM_{10} Levels: 25th Percentile: 0.37% (0.08-0.66); 0-1 75th Percentile: 0.49% (0.28-0.69); 0-1 Standardized Mortality Rate: 25th Percentile: 0.79% (0.55-1.03); 0-1 75th Percentile: 0.44% (0.22-0.66); 0-1 Western cities: 0.75% (0.47-1.03); 0-1 Southern cities: 0.61% (0.32-0.91); 0-1 Eastern cities: 0.03% (-0.47 to 0.53); 0-1 PACF (Partial Autocorrelation Function) Number of CO monitors: 25th Percentile: 1.18% (0.96-1.39); 0-1 75th Percentile: 0.92% (0.73-1.11); 0-1 Mean PM_{10} Levels: 25th Percentile: 0.74% (0.46-1.02); 0-1 75th Percentile: 1.07% (0.87-1.27); 0-1 Standardized Mortality Rate: 25th Percentile: 1.29% (1.06-1.52); 0-1 75th Percentile: 0.77% (0.56-0.98); 0-1 Western cities: 1.15% (0.90-1.40); 0-1 Southern cities: 1.08% (0.79-1.38); 0-1 Eastern cities: 0.27% (-0.20 to 0.74); 0-1 Cardiovascular Mortality 8 Degrees of Freedom per Year Mean O_3: 25th Percentile: 1.04% (0.67-1.41); 0-1 75th Percentile: 0.82% (0.55-1.10); 0-1 Standardized Mortality Rate: 25th Percentile: 1.06% (0.71-1.42); 0-1 75th Percentile: 0.61% (0.30-0.93); 0-1

Study	Design	Concentrations	Effect Estimates (95% CI)
			Population >75 yr of age (%): 25th Percentile: 0.58% (0.25-0.92); 0-1 75th Percentile: 0.94% (0.64-1.24); 0-1 Western cities: 1.06% (0.67-1.46); 0-1 Southern cities: 0.70% (0.26-1.14); 0-1 Eastern cities: 0.21% (-0.48 to 0.90); 0-1 PACF (Partial Autocorrelation Function) Mean O_3: 25th Percentile: 1.32% (0.96-1.68); 0-1 75th Percentile: 1.09% (0.83-1.14); 0-1 Standardized Mortality Rate: 25th Percentile: 1.40% (1.06-1.75); 0-1 75th Percentile: 0.85% (0.55-1.14); 0-1 Population >75 yr of age (%): 25th Percentile: 0.74% (0.41-1.06); 0-1 75th Percentile: 1.25% (0.96-1.54); 0-1 Western cities: 1.38% (1.00-1.76); 0-1 Southern cities: 0.90% (0.47-1.33); 0-1 Eastern cities: 0.48% (-0.14 to 1.11); 0-1
Author: Schwartz et al. (1999, 017915) **Period of Study:** 1989-1995 **Location:** Spokane, WA	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 1-h avg **Mean (SD) unit:** Dust Storm Days: 09/08/1990: 6.37 ppm 09/12/1990: 3.40 ppm 10/04/1990: 3.15 ppm 11/09/1990: 2.45 ppm 11/23/1990: 2.50 ppm 09/13/1991: 4.60 ppm 10/16/1991: 2.10 ppm 10/21/1991: 2.20 ppm 09/04/1992: 3.43 ppm 09/12/1992: 1.80 ppm 09/13/1992: 1.65 ppm 09/25/1992: 2.95 ppm 09/26/1992: 4.30 ppm 10/08/1992: 3.85 ppm 09/11/1993: 1.88 ppm 11/3/1993: 5.33 ppm 07/24/1994: 2.10 ppm 08/30/1996: 2.85 ppm **Range (Min, Max):** NR **Copollutant:** PM_{10}	The study did not present quantitative results for CO.
Author: Sharovsky et al. (2004, 156976) **Period of Study:** 1996-1998 **Location:** Sao Paulo, Brazil	**Health Outcome (ICD10):** Mortality: MI (I.21) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** 35-109 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 3.7 (1.6) ppm **Range (Min, Max):** (1.0, 11.8) **Copollutant: correlation** SO_2: r = 0.73; PM_{10}: r = 0.51	**Increment:** NR **β x 100 (SE); lag:** CO: 1.42 (1.01) CO, SO_2, PM_{10}: 0.97 (1.27) **Notes:** The study did not present the lag used for CO.
Author: Slaughter et al. (2005, 073854) **Period of Study:** 1/1995-6/2001 **Location:** Spokane, WA	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory (460-519); asthma (493); COPD (491, 492, 494, 496); pneumonia (480-487); acute upper respirator y tract infections (464-466, 490); cardiac outcomes (390-459) **Study Design:** Time series **Statistical Analyses:** Log-linear Poisson GLM, natural splines for calendar time **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** Areas in Spokane Hamilton St: 1.73 (0.46) ppm Backdoor Tavern: 1.29 (0.23) ppm Spokane Club: 1.41 (0.32) ppm Third and Washington: 1.82 (0.33) ppm Rockwood: 0.42 (0.15) ppm **Range (Min, Max):** NR **Copollutant correlation:** PM_1: r = 0.63; $PM_{2.5}$: r = 0.62; PM_{10}: r = 0.32; $PM_{10-2.5}$: r = 0.32	The study did not present quantitative results for CO.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Stieb et al. (2003, 056908) **Period of Study**: 1985-2000 **Location:** All locations	**Health Outcome (ICD9):** Mortality: Nonaccidental **Study Design:** Meta-analysis **Statistical Analyses:** NR **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** NR IQR (25th, 75th): NR **Copollutant:** NR	**Increment:** 1.1 ppm % Excess Mortality (Lower CI, Upper CI); lag: Non-GAM: Single-pollutant model (4 studies): 4.7% (1.1-8.4) Multi-pollutant model (1 study): 0.0% (-3.8 to 3.8) GAM: Single-pollutant model (18 studies): 1.6% (1.1-2.1) Multi-pollutant model (11 studies): 0.7% (-0.1 to 1.5)
Author: Stölzel et al. (2007, 091374) **Period of Study:** 9/1995-8/2001 **Location:** Erfurt, Germany	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); cardio-respiratory (390-459, 460-519, 785, 786) **Study Design:** Time series **Statistical Analyses:** Poisson GAM **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.47 (0.39) mg/m^3 IQR (25th, 75th): (0.23, 0.57) **Copollutant correlation:** MC0.1-0.5: r = 0.58; MC0.01-2.5: r = 0.57; PM_{10}: r = 0.50; NO: r = 0.70; NO_2: r = 0.71	**Increment:** 0.34 mg/m^3 **Relative Risk (Lower CI, Upper CI); lag:** Total (non-accidental) 1.000 (0.977-1.023); 0; 1.002 (0.980-1.024); 1; 1.013 (0.991-1.035); 2; 1.007 (0.986-1.029); 3; 1.012 (0.990-1.034); 4; 0.995 (0.974-1.017); 5
Author: Sunyer et al. (2001, 019367) **Period of Study:** 1990-1995 **Location:** Barcelona, Spain	**Health Outcome (ICD9):** Mortality: COPD (491, 492, 494, 496) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** >35 yr	**Pollutant:** CO **Averaging Time:** 8-h avg **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** PM_{10}; NO_2; O_3	**Increment:** 4.5 $\mu g/m^3$ **Odds Ratio (Lower CI, Upper CI); lag:** CO: 1.052 (0.990-1.117); 0-2 CO, PM_{10}: 1.017 (0.947-1.091); 0-2
Author: Sunyer et al. (2002, 034835) **Period of Study:** 1985-1995 **Location:** Barcelona, Spain	**Health Outcome (ICD9):** Mortality: Respiratory mortality **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** >14 yr **Study population:** Asthmatic individuals: 5,610	**Pollutant:** CO **Averaging Time:** 24-h avg **Median (SD) unit:** 7.7 $\mu g/m^3$ **Range (Min, Max):** (0.6, 66.0) **Copollutant:** PM_{10}; BS; NO_2; O_3; SO_2	**Increment:** 7.2 $\mu g/m^3$ **Odds Ratio (Lower CI, Upper CI); lag:** Asthmatic individuals with 1 ED visit 1.127 (0.895-1.418); 0-2 Asthmatic individuals with >1 ED visit 1.125 (0.773-1.638); 0-2 Asthma/COPD individuals with >1 ED visit 0.815 (0.614-1.082); 0-2
Author: Tsai et al. (2003, 050480) **Period of Study:** 1994-2000 **Location:** Kaohsiung, Taiwan	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory (460-519); circulatory (390-459) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.827 ppm **Range (Min, Max):** (0.226, 1.770) **Copollutant:** PM_{10}; SO_2; NO_2; O_3	**Increment:** 0.313 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Total (nonaccidental): 1.003 (0.968-1.039); 0-2 Respiratory: 1.011 (0.883-1.159); 0-2 Circulatory: 0.986 (0.914-1.063); 0-2
Author: Tsai et al. (2006, 090709) **Period of Study:** 1994-2000 **Location:** Kaohsiung, Taiwan	Health Outcome (ICD9): Mortality: Total (nonaccidental) (<800) **Study Design:** Case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** 27 days old to <1 yr of age	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit**: 8.27 ppm **Range (Min, Max):** (2.26, 17.70) **Copollutant:** PM_{10}; SO_2; O_3; NO_2	**Increment:** 0.31 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Postneonatal Mortality 1.051 (0.304-3.630); 0-2

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Vedal et al. (2003, 039044) **Period of Study:** 1/1994-12/1996 **Location:** Vancouver, BC, Canada	**Health Outcome (ICD9):** Mortality: Total (nonaccidental) (<800); respiratory (460-519); cardiovascular (390-459) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.6 (0.2) ppm **Range (Min, Max):** (0.3, 1.9) **Copollutant correlation:** Summer: PM_{10}:r = 0.71; O_3: r = 0.12; NO_2: r = 0.81; SO_2: r = 0.67 Winter: PM_{10}: r = 0.76; O_3: r = -0.65; NO_2: r = 0.78; SO_2: r = 0.83	The study did not present quantitative results for CO.
Author: Villeneuve et al. (2003, 055051) **Period of Study:** 1986-1999 **Location:** Vancouver, BC, Canada	Health Outcome (ICD9): Mortality: Nonaccidental (<800); cardiovascular (401-440); respiratory (460-519); cancer (140-239) **Study Design:** Time series **Statistical Analyses:** Poisson, natural splines **Age Groups Analyzed:** ≥ 65 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.0 ppm **Range (Min, Max):** (0.2, 4.9) **Copollutant:** $PM_{2.5}$; PM_{10}; $PM_{10-2.5}$; TSP; SO_4; CO; COH; O_3; NO_2; SO_2	**Increment:** 1.1 ppb **% Increase (Lower CI, Upper CI); lag:** Non-accidental 0.5% (-1.9 to 2.9); 0-2; / -0.3% (-2.2 to 1.7); 0; 0.6% (-1.3 to 2.6); 1; / 0.5% (-1.4 to 2.5); 2 Cardiovascular 2.3% (-1.6 to 6.3); 0-2; / 1.6% (-1.5 to 4.7); 0; 1.2% (-2.0 to 4.5); 1; / 1.5% (-1.5 to 4.4); 2 Respiratory -1.0% (-7.3 to 5.8); 0-2; / 1.3% (-4.4 to 7.3); 0; -0.1% (-5.3 to 5.4); 1; -/ 2.8% (-7.8 to 2.6); 2 Cancer -2.8% (-7.6 to 2.4); 0-2; / -3.0% (-6.9 to 1.1); 0; -1.6% (-5.6 to 2.4); 1; / -0.5% (-4.7 to 3.8); 2
Author: Wang et al. (2008, 179974) **Period of Study:** Daily CO content: 2000-2005 (data from Beijing Environment Protection Bureau), Death rate: 2000-2003 **Location:** Beijing, China	**Health Outcome:** Mortality **Study Design:** Time series, Granger causality, Back propagation neural network model, MIV **Statistical Analyses:** Eviews 3.1, SAS 9.0, Matlab 7.0 **Age Groups Analyzed:** NR **Sample Description:** Death rate of respiratory diseases in Beijing from China Centers for Disease Control and Prevention	**Averaging Time:** NR **Mean (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** NR	**Increment:** NR Granger causality: Acute respiratory diseases probability: 0.03122 COPD probability: 0.00047 Change of death rate of acute respiratory diseases: Increasing 10%: +0.437, Decreasing 10%: -0.386 Change of death rate of COPD: Increasing 10%: +0.181, Decreasing 10%: -0.316 **Lags examined:** 10

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Wichmann et al. (2000, 013912) **Period of Study:** 9/1995-12/1998 **Location:** Erfurt, Germany	**Health Outcome (ICD9):** Mortality: Nonaccidental (<800); cardiovascular (401-440); respiratory (460-519) **Study Design:** Time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups Analyzed:** <70 70-79 ≥ 80	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 0.6 (0.5) mg/m^3 **Range (Min, Max):** (0.10, 2.50) **Copollutant:** correlation $PM_{2.5}$: r = 0.62; PM_{10}: r = 0.58; TSP: r = 0.57; SO_2: r = 0.59; NO_2: r = 0.71	**Increment:** 0.5 ppm **Relative Risk (Lower CI, Upper CI); lag:** Single-Day Lag CO: 1.055 (1.003-1.110); 4 Polynomial Distributed Lag Multi-pollutant model: 1.076 (1.017-1.138); 4 Total Mortality CO: 1.012 (0.977-1.049); 0 Log-transformed: 1.016 (0.962-1.073); 0 1.004 (0.969-1.040); 1 Log-transformed: 1.027 (0.973-1.083); 1 1.020 (0.984-1.057); 2 Log-transformed: 1.024 (0.970-1.081); 2 1.019 (0.984-1.055); 3 Log-transformed: 1.037 (0.984-1.093); 3 1.029 (0.995-1.063); 4 Log-transformed: 1.055 (1.003-1.110); 4 0.997 (0.965-1.031); 5 Log-transformed: 1.014 (0.966-1.065); 5 Total Mortality (Season-specific): Log-transformed Winter: 1.002 (0.922-1.088); 4 Spring: 1.019 (0.942-1.102); 4 Summer: 1.085 (1.018-1.156); 4 Fall: 1.111 (1.039-1.188); 4 Winter-specific: Log-transformed 10/95-3/96: 1.046 (0.949-1.153); 4 10/96-3/97: 1.091 (0.998-1.193); 4 10/97-3/98: 1.028 (0.966-1.095); 4 One-pollutant Model: Log-transformed CO: 1.055 (1.003-1.110); 4
Author: Yang et al. (2004, 055603) **Period of Study:** 1994-1998 **Location:** Taipei, Taiwan	**Health Outcome (ICD9):** Mortality: Nonaccidental (<800); circulatory (390-459); respiratory (460-519) **Study Design:** Bidirectional case crossover **Statistical Analyses:** Conditional logistic regression **Age Groups Analyzed:** All ages	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1.16 ppm **Range (Min, Max):** (0.24, 4.42) **Copollutant:** PM_{10}; SO_2; NO_2; O_3	**Increment:** 0.52 ppm **Odds Ratio (Lower CI, Upper CI); lag:** Non-accidental: 1.005 (0.980-1.031); 0-2 Respiratory: 1.014 (0.925-1.110); 0-2 Circulatory: 0.996 (0.948-1.046); 0-2

Table C-8. Studies of long-term CO exposure and mortality.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Krewski et al. (2009, 191193) **Period of Study:** 1983-2000 **Location:** United States	**Health Outcome:** Mortality **Study Design:** Cohort **Statistical Analyses:** Random effects Cox model **Age Groups Analyzed:** 30+ yrs **Sample Description:** 508,538 adults living in large US cities	**Averaging Time:** 1980 annual avg **Mean (SD) unit:** 1.68 (0.66) ppm **Range (min, max):** 0.19, 3.95 **Copollutant:** PM_{15}, $PM_{2.5}$, SO_2, SO_4, TSP, O_3, NO_2	**Increment:** 1ppm HR Estimate [Lower CI, Upper CI]: **Lags examined:** NR All Causes: 1.00 (0.99, 1.01) Cardiopulmonary: 1.00 (0.99, 1.01) IHD: 1.01 (0.99, 1.03) Lung Cancer: 0.99 (0.97, 1.03) All Other Causes: 0.99 (0.98, 1.01)
Author: Lipfert et al. (2000, 004087) **Period of Study:** 1975-1996 **Location:** 32 Veterans Hospitals, USA	Mortality **Health Outcome (ICD9):** Nonaccidental **Study Design:** Cohort **Study Population:** ~90,000 hypertensive male U.S. veterans **Statistical Analyses:** Staged regression **Age Groups Analyzed:** NR	**Pollutant:** CO **Averaging Time:** 95th Percentile Annual avg **Mean (SD) unit:** 1960-1974: 10.82 (5.15) ppm 1975-1981: 7.64 (2.94) ppm 1982-1988: 3.42 (0.95) ppm 1989-1996: 2.36 (0.67) ppm **Range (Min, Max):** 1960-1974: (0.94, 35.30) 1975-1981: (0.43, 22.38) 1982-1988: (0.30, 15.20) 1989-1996: (0.30, 7.10) **Copollutants; correlation:** 1960-1974: O_3: r = 0.004; NO_2: r = 0.690; SO_4^{2-}: r = 0.469 1975-1981: O_3: r = 0.109; NO_2: r = 0.249; SO_4^{2-}: r = -0.155; IP SO_4^{2-}: r = 0.356; $PM_{2.5}$: r = 0.634; $PM_{10-2.5}$: r = 0.498; PM_{15}: r = 0.626 1982-1988 O_3: r = 0.158; NO_2: r = 0.413; SO_4^{2-}: r = -0.518; IP SO_4^{2-}: r = 0.075; $PM_{2.5}$: r = 0.296; $PM_{10-2.5}$: r = 0.135 PM_{15}: r = 0.284 1989-1996 O_3: r = 0.397; NO_2: r = 0.492; SO_4^{2-}: r = -0.551	**Increment:** NR Coefficient: Baseline Model Exposure Period: up to 1975 Single Period: -0.000 Deaths, 1976-81: 0.0043 Deaths, 1982-88: -0.0002 Deaths after 1988: -0.0041 Exposure Period: 1975-81 Single Period: -0.013 Deaths, 1976-81: -0.0170 Deaths, 1982-88: -0.0217 Deaths after 1988: -0.0240 Exposure Period: 1982-88 Single Period: -0.028 Deaths, 1976-81: -0.0294 Deaths, 1982-88: -0.0484 Deaths after 1988: -0.0424 Exposure Period: 1989-96 Single Period: -0.046 Deaths, 1976-81: -0.0590 Deaths, 1982-88: -0.0581 Deaths after 1988: -0.0536 Final Model w/ Ecological Variables Exposure Period: up to 1975 Single Period: -0.001 Deaths, 1976-81: 0.0013 Deaths, 1982-88: -0.0022 Deaths after 1988: -0.0061 Exposure Period: 1975-81 Single Period: -0.008 Deaths, 1976-81: -0.0128 Deaths, 1982-88: -0.0186 Deaths after 1988: -0.0203 Exposure Period: 1982-88 Single Period: -0.009 Deaths, 1976-81: -0.0007 Deaths, 1982-88: -0.0246 Deaths after 1988: -0.0216 Exposure Period: 1989-96 Single Period: -0.009 Deaths, 1976-81: -0.0106 Deaths, 1982-88: -0.0136 Deaths after 1988: -0.0078 **Notes:** Mortality risks based on mean concentrations of pollutants less estimated background weighted by the number of subjects in each county, but The study did not present this value for each pollutant.

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Lipfert and Morris (2002, 019217) **Period of Study:** 1960-1997 **Location:** U.S. counties	Mortality **Health Outcome (ICD9):** Nonaccidental **Study Design:** Ecological/ cross sectional **Statistical Analyses:** Staged regression **Age Groups Analyzed:** 15-44 yr 45-64 yr 65-74 yr 75-84 yr ≥ 85 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 1960-1969: 13.81 (8.47) ppm 1970-1974:9.64 (5.63) ppm 1979-1981:5.90 (3.54) ppm 1989-1991:2.69 (1.22) ppm 1995-1997:1.72 (0.76) ppm R**ange (Min, Max):** NR **Copollutant:** TSP SO_4^{2-} SO_2 NO_2 O_3	**Increment:** NR Attributable risk (SE): Attributable Risks of mortality (1960-4) Peak CO 1960-1964, All locations Ages 15-44: 0.1299 (0.0341) Ages 45-64: 0.0340 (0.0280) Ages 65-74: -0.0058 (0.0220) Ages 75-84: 0.0121 (0.0188) Ages ≥ 85: 0.0374 (0.0225) Log Mean: 0.0365 (0.0149) Attributable Risks of mortality (1970-4) Peak CO 1970-1974, All locations Ages 15-44: 0.0553 (0.0240) Ages 45-64: 0.0181 (0.0148) Ages 65-74: -0.0146 (0.0134) Ages 75-84: -0.0128 (0.0098) Ages ≥ 85: -0.0151 (0.0093) Log Mean: 0.0038 (0.0086) Attributable Risks of mortality (1979-81) Peak CO 1979-1981, All locations Ages 15-44: 0.0054 (0.0174) Ages 45-64: -0.0060 (0.0141) Ages 65-74: -0.0251 (0.0105) Ages 75-84: -0.0331 (0.0086) Ages ≥ 85: -0.0123 (0.0079) Log Mean: -0.0183 (0.0077) Peak CO 1970-1974, All locations Ages 15-44: 0.0218 (0.0200) Ages 45-64: 0.0327 (0.0161) Ages 65-74: -0.0136 (0.0119) Ages 75-84: -0.0250 (0.0105) Ages ≥ 85: -0.0202 (0.0085) Log Mean: -0.0048 (0.0077) Peak CO 1960-1969, All locations Ages 15-44: 0.0506 (0.0478) Ages 45-64: 0.0704 (0.0337) Ages 65-74: 0.0100 (0.0211) Ages 75-84: -0.0124 (0.0143) Ages ≥ 85: 0.0187 (0.0135) Log Mean: 0.0084 (0.0149) Peak CO 1979-1981, CO 1970-1974 Ages 15-44: 0.0244 (0.0209) Ages 45-64: 0.0016 (0.0181) Ages 65-74: -0.0183 (0.0128) Ages 75-84: -0.0382 (0.0108) Ages ≥ 85: -0.0201 (0.0089) Log Mean: -0.0165 (0.0089) Peak CO 1979-1981, CO 1960-1969 Ages 15-44: 0.0748 (0.0679) Ages 45-64: 0.0844 (0.0496) Ages 65-74: 0.0144 (0.0259) Ages 75-84: -0.0158 (0.0168) Ages ≥ 85: -0.0073 (0.0170) Log Mean: 0.0109 (0.0218) Peak CO 1979-1981, CO 1960-1969 Ages 15-44: 0.1191 (0.0709) Ages 45-64: 0.1163 (0.0491) Ages 65-74: 0.0177 (0.0310) Ages 75-84: -0.0120 (0.0212) Ages ≥ 85: -0.0040 (0.0202) Log Mean: 0.0211 (0.0231) Attributable Risks of mortality (1989-91) Peak CO 1989-1991, All locations Ages 15-44: 0.0404 (0.0322) Ages 45-64: -0.0262 (0.0162) Ages 65-74: -0.0397 (0.0115) Ages 75-84: -0.0464 (0.0097) Ages ≥ 85: -0.0209 (0.0073) Log Mean: -0.0178 (0.0098) Peak CO 1979-1981, All locations

Study	Design	Concentrations	Effect Estimates (95% CI)
			Ages 15-44: 0.0522 (0.0227) Ages 45-64: -0.0047 (0.0121) Ages 65-74: -0.0165 (0.0078) Ages 75-84: -0.0268 (0.0068) Ages ≥ 85: -0.0027 (0.0055) Log Mean: -0.0020 (0.0065) Peak CO 1970-1974, All locations Ages 15-44: 0.0685 (0.0274) Ages 45-64: 0.0022 (0.0148) Ages 65-74: -0.0051 (0.0091) Ages 75-84: -0.0158 (0.0079) Ages ≥ 85: -0.0069 (0.0060) Log Mean: 0.0038 (0.0077) Peak CO 1960-1969, All locations Ages 15-44: 0.0578 (0.0713) Ages 45-64: 0.0583 (0.0347) Ages 65-74: 0.0007 (0.0174) Ages 75-84: -0.0245 (0.0130) Ages ≥ 85: -0.0138 (0.0113) Log Mean: 0.0041 (0.0176) Attributable Risks of mortality (1995-97) Peak CO 1995-1997, All locations Ages 15-44: 0.0344 (0.0256) Ages 45-64: -0.0203 (0.0198) Ages 65-74: -0.0346 (0.0146) Ages 75-84: -0.0378 (0.0161) Ages ≥ 85: -0.0283 (0.0119) Log Mean: -0.0188 (0.0103) Peak CO 1989-1991, All locations Ages 15-44: 0.0289 (0.0248) Ages 45-64: -0.0192 (0.0192) Ages 65-74: -0.0466 (0.0140) Ages 75-84: -0.0497 (0.0147) Ages ≥ 85: -0.0301 (0.0108) Log Mean: -0.0240 (0.0096) Peak CO 1979-1981, All locations Ages 15-44: 0.0336 (0.0176) Ages 45-64: -0.0037 (0.0135) Ages 65-74: -0.0298 (0.0096) Ages 75-84: -0.0301 (0.0105) Ages ≥ 85: -0.0087 (0.0078) Log Mean: -0.0094 (0.0071) Peak CO 1970-1974, All locations Ages 15-44: 0.0464 (0.0202) Ages 45-64: 0.0202 (0.0155) Ages 65-74: -0.0032 (0.0112) Ages 75-84: -0.0157 (0.0122) Ages ≥ 85: -0.0142 (0.0084) Log Mean: 0.0007 (0.0077) Peak CO 1960-1969, All locations Ages 15-44: 0.0679 (0.0441) Ages 45-64: 0.0772 (0.0405) Ages 65-74: 0.0059 (0.0173) Ages 75-84: -0.0085 (0.0213) Ages ≥ 85: -0.0158 (0.0162) Log Mean: 0.0162 (0.0149)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Lipfert et al. (2006, 088218) **Period of Study:** 1976-2001 **Location:** 32 Veterans Hospitals, USA	Mortality **Health Outcome (ICD9):** Nonaccidental **Study Design:** Cohort **Study Population:** ~70,000 hypertensive male U.S. veterans **Statistical Analyses:** Cox proportional-hazards model **Age Groups Analyzed:** NR	**Pollutant:** CO **Averaging Time:** 95th Percentile Annual avg **Mean (SD) unit:** 1976-1981: 7.6 (2.9) ppm 1982-1988: 3.4 (9.5) ppm 1989-1996: 2.4 (0.67) ppm 1997-2001: 1.6 (5.6) ppm **Range (Min, Max):** NR **Copollutants correlation:** ln(VKTA): r = -0.06 Avg NO_2: r = 0.43 Peak O_3: r = 0.08 Peak SO_2: r = -0.05 $PM_{2.5}$: r = 0.08 SO_4^{2-}: r = -0.16 **Note:** VKTA = annual vehicle-km traveled/km^2	**Increment**: 2 ppm **Relative risk (Lower CI, Upper CI):** CO: 1.032 (0.954-1.117) CO, lnVKTA: 0.999 (0.923-1.081) CO, lnVKTA, NO_2: 1.012 (0.923-1.110) CO, lnVKTA, NO_2+O_3: 1.023 (0.939-1.115)
Author: Lipfert et al. (2006, 088756) **Period of Study:** 1997-2002 **Location:** 32 Veterans Hospitals, USA	Mortality **Health Outcome (ICD9):** Nonaccidental **Study Design:** Cohort **Study Population:** ~18,000 hypertensive male U.S. veterans **Statistical Analyses:** Cox proportional-hazards model **Age Groups Analyzed:** NR	Pollutant: CO **Averaging Time:** 95th Percentile Annual avg **Mean (SD) unit:** 1999-2001: 1.63 (0.84) ppm 1999-2001 (STN sites only): 1.73 (0.77) Range (Min, Max): 1999-2001: (0.40, 6.7) 1999-2001 (STN sites only): (0.47, 4.2) **Copollutants correlation:** ln(traffic density): r = -0.199 $PM_{2.5}$: r = 0.040; As: r = 0.148 Cr: r = 0.448; Cu: r = 0.177 Fe: r = -0.138; Pb: r = 0.420 Mn: r = 0.357; Ni: r = 0.090 Se: r = -0.110; V: r = 0.230 Zn: r = 0.472; OC: r = 0.470 EC: r = 0.234; SO_4^{2-}: r = -0.123 NO_3-: r = -0.088 $PM_{2.5}$ comp.: r = 0.133 NO_2: r = 0.418 Peak O_3: r = 0.172 Peak SO_2: r = 0.405	**Increment:** NR **β coefficient (SE); t-statistic:** -0.00000536 (0.0000324); -0.165
Author: Jerrett et al. (2003, 087380) **Period of Study:** 1982-1989 **Location:** 107 U.S. cities	Mortality **Health Outcome (ICD9):** Cardiovascular; CHD; Cerebrovascular disease **Study Design:** Cohort **Study Population:** 65,893 postmenopausal women without previous CVD **Statistical Analyses:** Cox proportional-hazards model **Age Groups Analyzed:** ≥ 30 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit:** 1.56 ppm **Range (Min, Max):** (0.19, 3.95) **Copollutants correlation:** Sulfates: r = -0.07 NO_2 O_3 SO_2	**Increment:** 1 ppm Relative risk (Lower CI, Upper CI): CO: 0.98 (0.92-1.03) CO, Sulfates: 0.97 (0.92-1.03)

Study	Design	Concentrations	Effect Estimates (95% CI)
Author: Miller et al. (2007, 090130) **Period of Study:** 1994-1998 **Location:** 36 U.S. cities	Mortality **Health Outcome (ICD9):** Cardiovascular; CHD; Cerebrovascular disease **Study Design:** Cohort **Study Population:** 65,893 postmenopausal women without previous CVD **Statistical Analyses:** Cox proportional-hazards model **Age Groups Analyzed:** 50-79 yr	**Pollutant:** CO **Averaging Time:** Annual avg **Mean (SD) unit**: NR **Range (Min, Max):** NR **Copollutants:** $PM_{2.5}$ $PM_{10-2.5}$ SO_2 NO_2 O_3	**Increment:** 1 ppm **Hazard ratio (Lower CI, Upper CI):** All subjects CO: 1.0 (0.81-1.22) Only subjects with non-missing exposure data CO: 0.92 (0.71-1.21) CO, $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2, O_3: 0.93 (0.67, 1.30)
Author: Pope et al. (2002, 024689) **Period of Study:** 1980-1998 **Location:** All 50 States, Washington DC, and Puerto Rico (ACS-CPS-II)	Mortality **Health Outcome** (ICD9): Total (nonaccidental) (<800); lung cancer (162); cardiopulmonary (401-440, 460-519) **Study Design:** Prospective cohort **Statistical Analyses:** Cox proportional hazards model **Age Groups Analyzed:** ≥ 30 yr	**Pollutant:** CO **Averaging Time:** 24-h avg **Mean (SD) unit:** 1980: 1.7 (0.7) ppm 1982-1998: 1.1 (0.4) ppm **Range (Min, Max):** NR **Copollutant:** $PM_{2.5}$; PM_{10}; TSP; SO_2; NO_2; O_3	The study presents results for CO graphically.

References

Abe T; Tokuda Y; Ohde S; Ishimatsu S; Nakamura T; Birrer RB (2009). The relationship of short-term air pollution and weather to ED visits for asthma in Japan. Am J Emerg Med, 27: 153-159. 190536

Andersen ZJ; Loft S; Ketzel M; Stage M; Scheike T; Mette MN; Bisgaard H (2008). Ambient Air Pollution Triggers Wheezing Symptoms in Infants. Thorax, 63: 710-716. 096150

Andersen ZJ; Wahlin P; Raaschou-Nielsen O; Scheike T; Loft S (2007). Ambient particle source apportionment and daily hospital admissions among children and elderly in Copenhagen. J Expo Sci Environ Epidemiol, 17: 625-636. 093201

Anderson HR; Bremner SA; Atkinson RW; Harrison RM; Walters S (2001). Particulate matter and daily mortality and hospital admissions in the west midlands conurbation of the United Kingdom: associations with fine and coarse particles, black smoke and sulphate. Occup Environ Med, 58: 504-510. 017033

Atkinson RW; Bremner SA; Anderson HR; Strachan DP; Bland JM; Ponce de Leon A (1999). Short-term associations between emergency hospital admissions for respiratory and cardiovascular disease and outdoor air pollution in London. Arch Environ Occup Health, 54: 398-411. 007882

Baccarelli A; Zanobetti A; Martinelli I; Grillo P; Hou L; Giacomini S; Bonzini M; Lanzani G; Mannucci PM; Bertazzi PA; Schwartz J (2007). Effects of exposure to air pollution on blood coagulation. J Thromb Haemost, 5: 252-260. 090733

Ballester F; Rodriguez P; Iniguez C; Saez M; Daponte A; Galan I; Taracido M; Arribas F; Bellido J; Cirarda FB; Canada A; Guillen JJ; Guillen-Grima F; Lopez E; Perez-Hoyos S; Lertxundi A; Toro S (2006). Air pollution and cardiovascular admisisons association in Spain: results within the EMECAS project. J Epidemiol Community Health, 60: 328-336. 088746

Ballester F; Tenias JM; Perez-Hoyos S (2001). Air pollution and emergency hospital admissions for cardiovascular diseases in Valencia, Spain. J Epidemiol Community Health, 55: 57-65. 013257

Barnett AG; Williams GM; Schwartz J; Best TL; Neller AH; Petroeschevsky AL; Simpson RW (2006). The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in Australian and New Zealand cities. Environ Health Perspect, 114: 1018-1023. 089770

Bedeschi E; Campari C; Candela S; Collini G; Caranci N; Frasca G; Galassi C; Francesca G; Vigotti MA (2007). Urban air pollution and respiratory emergency visits at pediatric unit, Reggio Emilia, Italy. J Toxicol Environ Health A Curr Iss, 70: 261-265. 090712

Bell ML; Ebisu K; Belanger K (2007). Ambient air pollution and low birth weight in Connecticut and Massachusetts. Environ Health Perspect, 115: 1118-24. 091059

Bell ML; Levy JK; Lin Z (2008). The effect of sandstorms and air pollution on cause-specific hospital admissions in Taipei, Taiwan. Occup Environ Med, 65: 104-111. 091268

Bell ML; Peng RD; Dominici F; Samet JM (2009). Emergency admissions for cardiovascular disease and ambient levels of carbon monoxide: Results for 126 U.S. urban counties, 1999-2005. Circulation, 120: 949-955. 193780

Bellini P; Baccini M; Biggeri A; Terracini B (2007). The meta-analysis of the Italian studies on short-term effects of air pollution (MISA): Old and new issues on the interpretation of the statistical evidences. Environmetrics, 18: 219-229. 097787

Berger A; Zareba W; Schneider A; Ruckerl R; Ibald-Mulli A; Cyrys J; Wichmann HE; Peters A (2006). Runs of ventricular and supraventricular tachycardia triggered by air pollution in patients with coronary heart disease. J Occup Environ Med, 48: 1149-58. 098702

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Berglind N; Bellander T; Forastiere F; von Klot S; Aalto P; Elosua R; Kulmala M; Lanki T; Löwel H; Peters A; Picciotto S; Salomaa V; Stafoggia M; Sunyer J; Nyberg F (2009). Ambient air pollution and daily mortality among survivors of myocardial infarction. Epidemiology, 20: 110-118. 190068

Bhattacharyya N (2009). Air quality influences the prevalence of hay fever and sinusitis. Laryngoscope, 119: 429-433. 180154

Biggeri A; Baccini M; Bellini P; Terracini B (2005). Meta-analysis of the Italian studies of short-term effects of air pollution (MISA), 1990-1999. Int J Occup Environ Health, 11: 107-122. 087395

Botter DA; Jorgensen B; Peres AAQ (2002). A longitudinal study of mortality and air pollution for Sao Paulo, Brazil. J Expo Sci Environ Epidemiol, 12: 335-343. 011922

Braga ALF; Saldiva PHN; Pereira LAA; Menezes JJC; Conceicao GMC; Lin CA; Zanobetti A; Schwartz J; Dockery DW (2001). Health effects of air pollution exposure on children and adolescents in Sao Paulo, Brazil. Pediatr Pulmonol, 31: 106-113. 016275

Brauer M; Lencar C; Tamburic L; Koehoorn M; Demers P; Karr C (2008). A cohort study of traffic-related air pollution impacts on birth outcomes. Environ Health Perspect, 116: 680-686. 156292

Bremner SA; Anderson HR; Atkinson RW; McMichael AJ; Strachan DP; Bland JM; Bower JS (1999). Short term associations between outdoor air pollution and mortality in London 1992-4. Occup Environ Med, 56: 237-244. 007601

Briet M; Collin C; Laurent S; Tan A; Azizi M; Agharazii M; Jeunemaitre X; Alhenc-Gelas F; Boutouyrie P (2007). Endothelial function and chronic exposure to air pollution in normal male subjects. Hypertension, 50: 970-976. 093049

Burnett RT; Brook J; Dann T; Delocla C; Philips O; Cakmak S; Vincent R; Goldberg MS; Krewski D (2000). Association between particulate- and gas-phase components of urban air pollution and daily mortality in eight Canadian cities. Inhal Toxicol, 12: 15-39. 010273

Burnett RT; Smith-Doiron M; Stieb D; Cakmak S; Brook JR (1999). Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. Arch Environ Occup Health, 54: 130-139. 017269

Burnett RT; Smith-Doiron M; Stieb D; Raizenne ME; Brook JR; Dales RE; Leech JA; Cakmak S; Krewski D (2001). Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. Am J Epidemiol, 153: 444-452. 093439

Burnett RT; Stieb D; Brook JR; Cakmak S; Dales R; Raizenne M; Vincent R; Dann T (2004). Associations between short-term changes in nitrogen dioxide and mortality in Canadian cities. Arch Environ Occup Health, 59: 228-236. 086247

Cakmak S; Dales RE; Judek S (2006). Respiratory health effects of air pollution gases: modification by education and income. Arch Environ Occup Health, 61: 5-10. 093272

Cakmak S; Dales RE; Vidal CB (2007). Air pollution and mortality in Chile: Susceptibility among the elderly. Environ Health Perspect, 115: 524-7. 091170

Chan C-C; Chuang K-J; Chien L-C; Chen W-J; Chang W-T (2006). Urban air pollution and emergency admissions for cerebrovascular diseases in Taipei, Taiwan. Eur Heart J, 27: 1238-1244. 090193

Chan C-C; Chuang K-J; Su T-C; Lin L-Y (2005). Association between nitrogen dioxide and heart rate variability in a susceptible population. Eur J Cardiovasc Prev Rehabil, 12: 580-586. 088988

Chang C-C; Tsai S-S; Ho S-C; Yang C-Y (2005). Air pollution and hospital admissions for cardiovascular disease in Taipei, Taiwan. Environ Res, 98: 114-119. 080086

Chen L; Jennison BL; Yang W; Omaye ST (2000). Elementary school absenteeism and air pollution. Inhal Toxicol, 12: 997-1016. 011931

Chen L; Yang W; Jennison BL; Goodrich A; Omaye ST (2002). Air pollution and birth weight in northern Nevada, 1991-1999. Inhal Toxicol, 14: 141-157. 024945

Chen P-C; Lai Y-M; Chan C-C; Hwang J-S; Yang C-Y; Wang J-D (1999). Short-term effect of ozone on the pulmonary function of children in primary school. Environ Health Perspect, 107: 921-925. 011149

Cheng M-F; Tsai S-S; Wu T-N; Chen P-S; Yang C-Y (2007). Air pollution and hospital admissions for pneumonia in a tropical city: Kaohsiung, Taiwan. J Toxicol Environ Health A Curr Iss, 70: 2021-2026. 093034

Chiu HF; Cheng MH; Yang CY (2009). Air pollution and hospital admissions for pneumonia in a subtropical city: Taipei, Taiwan. Inhal Toxicol, 21: 32-37. 190249

Cho B; Choi J; Yum YT (2000). Air pollution and hospital admissions for respiratory disease in certain areas of Korea. J Occup Health, 42: 185-191. 099051

Chock DP; Winkler SL; Chen C (2000). A study of the association between daily mortality and ambient air pollutant concentrations in Pittsburgh, Pennsylvania. J Air Waste Manag Assoc, 50: 1481-1500. 010407

Chuang KJ; Coull BA; Zanobetti A; Suh H; Schwartz J; Stone PH; Litonjua A; Speizer FE; Gold DR (2008). Particulate Air Pollution as a Risk Factor for ST-Segment Depression in Patients With Coronary Artery Disease. Circulation, 118: 1314-1320. 155731

Cifuentes LA; Vega J; Kopfer K; Lave LB (2000). Effect of the fine fraction of particulate matter versus the coarse mass and other pollutants on daily mortality in Santiago, Chile. J Air Waste Manag Assoc, 50: 1287-1298. 010351

Conceicao GMS; Miraglia SGEK; Kishi HS; Saldiva PHN; Singer JM (2001). Air pollution and child mortality: a time-series study in Sao Paulo, Brazil. Environ Health Perspect, 1093: 347-350. 016628

D'Ippoliti D; Forastiere F; Ancona C; Agabiti N; Fusco D; Michelozzi P; Perucci CA (2003). Air pollution and myocardial infarction in Rome: a case-crossover analysis. Epidemiology, 14: 528-535. 074311

Dales R (2004). Ambient carbon monoxide may influence heart rate variability in subjects with coronary artery disease. J Occup Environ Med, 46: 1217-1221. 099036

Delfino RJ: Staimer N; Tjoa T; Gillen DL; Polidori A; Arhami M; Kleinman MT; Vaziri ND; Longhurst J; Sioutas C (2009). Air pollution exposures and circulating biomarkers of effect in a susceptible population: clues to potential causal component mixtures and mechanisms. Environ Health Perspect, 117: 1232-1238. 200844

Delfino RJ; Gone H; Linn WS; Pellizzari ED; Hu Y (2003). Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. Environ Health Perspect, 111: 647-656. 050460

Delfino RJ; Staimer N; Tjoa T; Polidori A; Arhami M; Gillen DL; Kleinman MT; Vaziri ND; Longhurst J; Zaldivar F; Sioutas C (2008). Circulating biomarkers of inflammation, antioxidant activity, and platelet activation are associated with primary combustion aerosols in subjects with coronary artery disease. Environ Health Perspect, 116: 898-906. 156390

De Hartog JJ; Hoek G; Peters A; Timonen KL; Ibald-Mulli A; Brunekreef B; Heinrich J; Tiittanen P; Van Wijnen JH; Kreyling W; Kulmala M; Pekkanen J (2003). Effects of fine and ultrafine particles on cardiorespiratory symptoms in elderly subjects with coronary heart disease: the ULTRA study. Am J Epidemiol, 157: 613-623. 001061

De Leon SF; Thurston GD; Ito K (2003). Contribution of respiratory disease to nonrespiratory mortality associations with air pollution. Am J Respir Crit Care Med, 167: 1117-1123. 055688

Dockery DW; Luttmann-Gibson H; Rich DQ; Link MS; Mittleman MA; Gold DR; Koutrakis P; Schwartz JD; Verrier RL (2005). Association of air pollution with increased incidence of ventricular tachyarrhythmias recorded by implanted cardioverter defibrillators. Environ Health Perspect, 113: 670-674. 078995

Dominici F; McDermott A; Daniels M; Zeger SL; Samet JM (2003). Mortality among residents of 90 cities. In: Revised analyses of time-series studies of air pollution and health. Health Effects Institute. Boston, MA. HEI Special Report. http://www.healtheffects.org/Pubs/TimeSeries.pdf. 056116

Estrella B; Estrella R; Oviedo J; Narvaez X; Reyes MT; Gutierrez M; Naumova EN (2005). Acute respiratory diseases and carboxyhemoglobin status in school children of Quito, Ecuador. Environ Health Perspect, 113: 607-11. 099124

Fairley D (1999). Daily mortality and air pollution in Santa Clara County, California: 1989-1996. Environ Health Perspect, 107: 637-641. 000896

Farhat SCL; Paulo RLP; Shimoda TM; Conceicao GMS; Lin CA; Braga ALF; Warth MPN; Saldiva PHN (2005). Effect of air pollution on pediatric respiratory emergency room visits and hospital admissions. Braz J Med Biol Res, 38: 227-235. 089461

Fischer P; Hoek G; Brunekreef B; Verhoeff A; van Wijnen J (2003). Air pollution and mortality in the Netherlands: are the elderly more at risk? Eur Respir J, 40: 34S-38S. 043739

Fischer PH; Steerenberg PA; Snelder JD; Van Loveren H; Van Amsterdam JGC (2002). Association between exhaled nitric oxide, ambient air pollution and respiratory health in school children. Int Arch Occup Environ Health, 75: 348-353. 025731

Forastiere F; Stafoggia M; Picciotto S; Bellander T; D'Ippoliti D; Lanki T; Von Klot S; Nyberg F; Paatero P; Peters A; Pekkanen J; Sunyer J; Perucci CA (2005). A case-crossover analysis of out-of-hospital coronary deaths and air pollution in Rome, Italy. Am J Respir Crit Care Med, 172: 1549-1555. 086323

Forastiere F; Stafoggia M; Tasco C; Picciotto S; Agabiti N; Cesaroni G; Perucci CA (2007). Socioeconomic status, particulate air pollution, and daily mortality: differential exposure or differential susceptibility. Am J Ind Med, 50: 208-216. 090720

Fung KY; Khan S; Krewski D; Chen Y (2006). Association between air pollution and multiple respiratory hospitalizations among the elderly in Vancouver, Canada. Inhal Toxicol, 18: 1005-1011. 089789

Fung KY; Luginaah I; Gorey KM; Webster G (2005). Air pollution and daily hospital admissions for cardiovascular diseases in Windsor, Ontario. Can J Public Health, 96: 29-33. 074322

Fusco D; Forastiere F; Michelozzi P; Spadea T; Ostro B; Arca M; Perucci CA (2001). Air pollution and hospital admissions for respiratory conditions in Rome, Italy. Eur Respir J, 17: 1143-1150. 020631

Gilboa SM; Mendola P; Olshan AF; Langlois PH; Savitz DA; Loomis D; Herring AH; Fixler DE (2005). Relation between ambient air quality and selected birth defects, seven county study, Texas, 1997-2000. Am J Epidemiol, 162: 238-252. 087892

Gold DR; Litonjua A; Schwartz J; Lovett E; Larson A; Nearing B; Allen G; Verrier M; Cherry R; Verrier R (2000). Ambient pollution and heart rate variability. Chest, 101: 1267-1273. 011432

Gold DR; Litonjua AA; Zanobetti A; Coull BA; Schwartz J; MacCallum G; Verrier RL; Nearing BD; Canner MJ; Suh H; Stone PH (2005). Air pollution and ST-segment depression in elderly subjects. Environ Health Perspect, 113: 883-887. 087558

Goldberg MS; Burnett RT; Bailar JC III; Brook J; Bonvalot Y; Tamblyn R; Singh R; Valois M-F (2001). The association between daily mortality and ambient air particle pollution in Montreal, Quebec 1 Nonaccidental mortality. Environ Res, 86: 12-25. 016548

Goldberg MS; Burnett RT; Valois M-F; Flegel K; Bailar JC III; Brook J; Vincent R; Radon K (2003). Associations between ambient air pollution and daily mortality among persons with congestive heart failure. Environ Res, 91: 8-20. 035202

Goldberg MS; Burnett RT; Yale JF; Valois MF; Brook JR (2006). Associations between ambient air pollution and daily mortality among persons with diabetes and cardiovascular disease. Environ Res, 100: 255-267. 088641

Goldberg MS; Giannetti N; Burnett RT; Mayo NE; Valois MF; Brophy JM (2008). A panel study in congestive heart failure to estimate the short-term effects from personal factors and environmental conditions on oxygen saturation and pulse rate. Occup Environ Med, 65: 659-666. 180380

Goss CH; Newsom SA; Schildcrout JS; Sheppard L; Kaufman JD (2004). Effect of ambient air pollution on pulmonary exacerbations and lung function in cystic fibrosis. Am J Respir Crit Care Med, 169: 816-821. 055624

Gouveia N; Bremner SA; Novaes HMD (2004). Association between ambient air pollution and birth weight in Sao Paulo, Brazil. J Epidemiol Community Health, 58: 11-17. 055613

Gouveia N; Fletcher T (2000). Respiratory diseases in children and outdoor air pollution in Sao Paulo, Brazil: a time series analysis. Occup Environ Med, 57: 477-483. 010436

Gouveia N; Fletcher T (2000). Time series analysis of air pollution and mortality: effects by cause, age and socioeconomic status. J Epidemiol Community Health, 54: 750-755. 012132

Guo YL; Lin Y-C; Sung F-C; Huang S-L; Ko Y-C; Lai J-S; Su H-J; Shaw C-K; Lin R-S; Dockery DW (1999). Climate, traffic-related air pollutants, and asthma prevalence in middle-school children in Taiwan. Environ Health Perspect, 107: 1001-1006. 010937

Gwynn RC; Burnett RT; Thurston GD (2000). A time-series analysis of acidic particulate matter and daily mortality and morbidity in the Buffalo, New York, region. Environ Health Perspect, 108: 125-133. 074109

Ha E-H; Hong Y-C; Lee B-E; Woo B-H; Schwartz J; Christiani DC (2001). Is air pollution a risk factor for low birth weight in Seoul? Epidemiology, 12: 643-648. 019390

Ha E-H; Lee J-T; Kim H; Hong Y-C; Lee (2003). Infant susceptibility of mortality to air pollution in Seoul, South Korea. Pediatrics, 111: 284-290. 042552

Hajat S; Anderson HR; Atkinson RW; Haines A (2002). Effects of air pollution on general practitioner consultations for upper respiratory diseases in London. Occup Environ Med, 59: 294-299. 030358

Hajat S; Armstrong B; Wilkinson P; Busby A; Dolk H (2007). Outdoor air pollution and infant mortality: Analysis of daily time-series data in 10 English cities. J Epidemiol Community Health, 61: 719-722. 093276

Hajat S; Haines A; Goubet SA; Atkinson RW; Anderson HR (1999). Association of air pollution with daily GP consultations for asthma and other lower respiratory conditions in London. Thorax, 54: 597-605. 000924

Hapcioglu B; Issever H; Kocyigit E; Disci R; Vatansever S; Ozdilli K (2006). The effect of air pollution and meteorological parameters on chronic obstructive pulmonary disease at an Istanbul hospital. Indoor Built Environ, 15: 147-153. 093263

Henrotin JB; Besancenot JP; Bejot Y; Giroud M (2007). Short-term effects of ozone air pollution on ischaemic stroke occurrence: A case-crossover analysis from a 10-year population-based study in Dijon, France. Occup Environ Med, 64: 439-445. 093270

Hinwood AL; De Klerk N; Rodriguez C; Jacoby P; Runnion T; Rye P; Landau L; Murray F; Feldwick M; Spickett J (2006). The relationship between changes in daily air pollution and hospitalizations in Perth, Australia 1992-1998: A case-crossover study. Int J Environ Health Res, 16: 27-46. 088976

Hirsch T; Weiland SK; Von Mutius E; Safeca AF; Grafe H; Csaplovics E; Duhme H; Keil U; Leupold W (1999). Inner city air pollution and respiratory health and atopy in children. Eur Respir J, 14: 669-677. 003537

Ho W-C; Hartley WR; Myers L; Lin M-H; (2007). Air pollution, weather, and associated risk factors related to asthma prevalence and attack rate. Environ Res, 104: 402-409. 093265

Hoek G; Brunekreef B; Fischer P; Van Wijnen J (2001). The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. Epidemiology, 12: 355-357. 016550

Hoek G; Brunekreef B; Verhoeff A; Van Wijnen J; Fischer P (2000). Daily mortality and air pollution in the Netherlands. J Air Waste Manag Assoc, 50: 1380-1389. 010350

Holguin F; Tellez-Rojo MM; Hernandez M; Cortez M; Chow JC; Watson JG; Mannino D; Romieu I (2003). Air pollution and heart rate variability among the elderly in Mexico City. Epidemiology, 14: 521-527. 057326

Honda Y; Nitta H; Ono M (2003). Low level carbon monoxide and mortality of persons aged 65 or older in Tokyo, Japan 1976-1990. Eisei Kagaku, 49: 454-458. 193774

Hong Y-C; Lee J-T; Kim H; Ha E-H; Schwartz J; Christiani DC (2002). Effects of air pollutants on acute stroke mortality. Environ Health Perspect, 110: 187-191. 024690

Hong Y-C; Lee J-T; Kim H; Kwon H-J (2002). Air pollution: A new risk factor in ischemic stroke mortality. Stroke, 33: 2165-2169. 035060

Hong Y-C; Leem J-H; Ha E-H; Christiani DC (1999). PM10 exposure, gaseous pollutants, and daily mortality in Inchon, South Korea. Environ Health Perspect, 107: 873-8. 008087

Hong YC; Leem JH; Ha EH (1999). Air pollution and daily mortality in Inchon, Korea. J Korean Med Sci, 14: 239-244. 011195

Hosseinpoor AR; Forouzanfar MH; Yunesian M; Asghari F; Naieni KH; Farhood D (2005). Air pollution and hospitalization due to angina pectoris in Tehran, Iran: A time-series study. Environ Res, 99: 126-131. 087413

Huynh M; Woodruff TJ; Parker JD; Schoendorf KC (2006). Relationships between air pollution and preterm birth in California. Paediatr Perinat Epidemiol, 20: 454-461. 091240

Hwang B-F; Jaakkola JJK; Lee Y-L; Lin Y-C; Guo Y-LL (2006). Relation between air pollution and allergic rhinitis in Taiwanese schoolchildren. Respir Res, 7: 23. 088971

Hwang B-F; Lee Y-L; Lin Y-C; Jaakkola JJK; Guo YL (2005). Traffic related air pollution as a determinant of asthma among Taiwanese school children. Thorax, 60: 467-473. 089454

Hwang BF; Jaakkola JJ (2008). Ozone and other air pollutants and the risk of oral clefts. Environ Health Perspect, 116: 1411-1415. 193794

Hwang J-S; Chan C-C (2002). Effects of air pollution on daily clinic visits for lower respiratory tract illness. Am J Epidemiol, 155: 1-10. 023222

Ibald-Mulli A; Stieber J; Wichmann H-E; Koenig W; Peters A (2001). Effects of air pollution on blood pressure: A population-based approach. Am J Public Health, 91: 571-577. 016030

Ibald-Mulli A; Timonen KL; Peters A; Heinrich J; Wolke G; Lanki T; Buzorius G; Kreyling WG; De Hartog J; Hoek G; Ten Brink HM; Pekkanen J (2004). Effects of particulate air pollution on blood pressure and heart rate in subjects with cardiovascular disease: a multicenter approach. Environ Health Perspect, 112: 369-377. 087415

Ito K; Thurston GD; Silverman RA; (2007). Association between coarse particles and asthma emergency department (ED) visits in New York City. Presented at American Thoracic Society international conference 2007, San Francisco, CA. 091262

Jalaludin B; Mannes T; Morgan G; Lincoln D; Sheppeard V; Corbett S (2007). Impact of ambient air pollution on gestational age is modified by season in Sydney, Australia. Environ Health, 6: 16. 156601

Jalaludin B; Morgan G; Lincoln D; Sheppeard V; Simpson R; Corbett S (2006). Associations between ambient air pollution and daily emergency department attendances for cardiovascular disease in the elderly (65+ years), Sydney, Australia. J Expo Sci Environ Epidemiol, 16: 225-237. 189416

Jayaraman G; Nidhi (2008). Air pollution and associated respiratory morbidity in Delhi. Health Care Manag Sci, 11: 132-138. 180352

Jerrett M; Burnett RT; Willis A; Krewski D; Goldberg MS; DeLuca P; Finkelstein N (2003). Spatial analysis of the air pollution-mortality relationship in the context of ecologic confounders. J Toxicol Environ Health A Curr Iss, 66: 1735-1777. 087380

Karr C; Lumley T; Schreuder A; Davis R; Larson T; Ritz B; Kaufman J (2007). Effects of subchronic and chronic exposure to ambient air pollutants on infant bronchiolitis. Am J Epidemiol, 165: 553-560. 090719

Karr C; Lumley T; Shepherd K; Davis R; Larson T; Ritz B; Kaufman J (2006). A case-crossover study of wintertime ambient air pollution and infant bronchiolitis. Environ Health Perspect, 114: 277-281. 088751

Keatinge WR; Donaldson GC (2001). Mortality related to cold and air pollution in London after allowance for effects of associated weather patterns. Environ Res, 86: 209-216. 017063

Kettunen J; Lanki T; Tiittanen P; Aalto PP; Koskentalo T; Kulmala M; Salomaa V; Pekkanen J (2007). Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. Stroke, 38: 918-922. 091242

Kim SY; O'Neill MS; Lee JT; Cho Y; Kim J; Kim H (2007). Air pollution, socioeconomic position, and emergency hospital visits for asthma in Seoul, Korea. Int Arch Occup Environ Health, 80: 701-710. 092837

Klemm RJ; Lipfert FW; Wyzga RE; Gust C (2004). Daily mortality and air pollution in Atlanta: two years of data from ARIES. Inhal Toxicol, 16 Suppl 1: 131-141. 056585

Knox EG (2008). Atmospheric pollutants and mortalities in English local authority areas. J Epidemiol Community Health, 62: 442-447. 193776

Koken PJM; Piver WT; Ye F; Elixhauser A; Olsen LM; Portier CJ (2003). Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. Environ Health Perspect, 111: 1312-1317. 049466

Kontos AS; Fassois SD; Deli MF (1999). Short-term effects of air pollution on childhood respiratory illness in Piraeus, Greece, 1987-1992: nonparametric stochastic dynamic analysis. Environ Res, 81: 275-296. 011326

Krewski D; Jerrett M; Burnett RT; Ma R; Hughes E; Shi Y; Turner MC; Pope AC III; Thurston G; Calle EE; Thun MJ (2009). Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. Health Effects Institute. Cambridge, MA. Report Nr. 140. 191193

Kwon H-J; Cho S-H; Nyberg F; Pershagen G (2001). Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. Epidemiology, 12: 413-419. 016699

Lagorio S; Forastiere F; Pistelli R; Iavarone I; Michelozzi P; Fano V; Marconi A; Ziemacki G; Ostro BD (2006). Air pollution and lung function among susceptible adult subjects: a panel study. Environ Health, 5: 11. 089800

Lanki T; Pekkanen J; Aalto P; Elosua R; Berglind N; D'Ippoliti D; Kulmala M; Nyberg F; Peters A; Picciotto S; Salomaa V; Sunyer J; Tiittanen P; Von Klot S; Forastiere F; for the HEAPSS Study Group (2006). Associations of traffic-related air pollutants with hospitalisation for first acute myocardial infarction: the HEAPSS study. Occup Environ Med, 63: 844-851. 089788

Lee BE; Ha EH; Park HS; Kim YJ; Hong YC; Kim H; Lee JT (2003). Exposure to air pollution during different gestational phases contributes to risks of low birth weight. Hum Reprod, 18: 638-643. 043202

Lee I-M; Tsai S-S; Chang C-C; Ho C-K; Yang C-Y (2007). Air pollution and hospital admissions for chronic obstructive pulmonary disease in a tropical city: Kaohsiung, Taiwan. Inhal Toxicol, 19: 393-398. 090707

Lee J-T; Kim H; Song H; Hong Y-C; Cho Y-S; Shin S-Y; Hyun Y-J; Kim Y-S (2002). Air pollution and asthma among children in Seoul, Korea. Epidemiology, 13: 481-484. 034826

Lee J-T; Son J-Y; Cho Y-S (2007). A comparison of mortality related to urban air particles between periods with Asian dust days and without Asian dust days in Seoul, Korea, 2000-2004. Environ Res, 105: 409-13. 093042

Lee JT; Kim H; Cho YS; Hong YC; Ha EH; Park H (2003). Air pollution and hospital admissions for ischemic heart diseases among individuals 64+ years of age residing in Seoul, Korea. Arch Environ Health, 58: 617-623. 095552

Lee JT; Son JY; Kim H; Kim SY (2006). Effect of air pollution on asthma-related hospital admissions for children by socioeconomic status associated with area of residence. Arch Environ Occup Health, 61: 123-130. 098248

Lee Y-L; Shaw C-K; Su H-J; Lai J-S; Ko Y-C; Huang S-L; Sung F-C; Guo Y-L (2003). Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. Eur Respir J, 21: 964-970. 049201

Leem J-H; Kaplan BM; Shim YK; Pohl HR; Gotway CA; Bullard SM; Rogers JF; Smith MM; Tylenda CA (2006). Exposures to air pollutants during pregnancy and preterm delivery. Environ Health Perspect, 114: 905-910. 089828

Levy D; Sheppard L; Checkoway H; Kaufman J; Lumley T; Koenig J; Siscovick D (2001). A case-crossover analysis of particulate matter air pollution and out-of-hospital primary cardiac arrest. Epidemiology, 12: 193-199. 017171

Liao D; Duan Y; Whitsel EA; Zheng Z-J; Heiss G; Chinchilli VM; Lin H-M (2004). Association of higher levels of ambient criteria pollutants with impaired cardiac autonomic control: a population-based study. Am J Epidemiol, 159: 768-777. 056590

Liao D; Heiss G; Chinchilli VM; Duan Y; Folsom AR; Lin HM; Salomaa V (2005). Association of criteria pollutants with plasma hemostatic/inflammatory markers: a population-based study. J Expo Sci Environ Epidemiol, 15: 319-328. 088677

Lin C-M; Li C-Y; Yang G-Y; Mao I-F (2004). Association between maternal exposure to elevated ambient sulfur dioxide during pregnancy and term low birth weight. Environ Res, 96: 41-50. 089503

Lin CA; Martins MA; Farhat SCL; Pope CA III; Conceicao GMS; Anastacio VM; Hatanaka M; Andrade WC; Hamaue WR; Bohm GM; Saldiva PHN (1999). Air pollution and respiratory illness of children in Sao Paulo, Brazil. Paediatr Perinat Epidemiol, 13: 475-488. 040437

Lin CA; Pereira LAA; Nishioka DC; Conceicao GMS; Graga ALF; Saldiva PHN (2004). Air pollution and neonatal deaths in Sao Paulo, Brazil. Braz J Med Biol Res, 37: 765-770. 095787

Lin M; Chen Y; Burnett RT; Villeneuve PJ; Krewski D (2003). Effect of short-term exposure to gaseous pollution on asthma hospitalisation in children: a bi-directional case-crossover analysis. J Epidemiol Community Health, 57: 50-55. 042549

Lin M; Chen Y; Villeneuve PJ; Burnett RT; Lemyre L; Hertzman C; McGrail KM; Krewski D (2004). Gaseous air pollutants and asthma hospitalization of children with low household income in Vancouver, British Columbia, Canada. Am J Epidemiol, 159: 294-303. 055600

Lin M; Stieb DM; Chen Y (2005). Coarse particulate matter and hospitalization for respiratory infections in children younger than 15 years in Toronto: a case-crossover analysis. Pediatrics, 116: 235-240. 087828

Linn WS; Szlachcic Y; Gong H Jr; Kinney PL; Berhane KT (2000). Air pollution and daily hospital admissions in metropolitan Los Angeles. Environ Health Perspect, 108: 427-434. 002839

Lipfert FW; Baty JD; Miller JP; Wyzga RE (2006). PM2.5 constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans. Inhal Toxicol, 18: 645-657. 088756

Lipfert FW; Morris SC (2002). Temporal and spacial relationships between age-specific mortality and ambient air quality in the United States: preliminary results for counties, 1960-97. Occup Environ Med, 59: 156-174. 019217

Lipfert FW; Morris SC; Wyzga RE (2000). Daily mortality in the Philadelphia metropolitan area and size-classified particulate matter. J Air Waste Manag Assoc, 50: 1501-1513. 004088

Lipfert FW; Perry HM Jr; Miller JP; Baty JD; Wyzga RE; Carmody SE (2000). The Washington University-EPRI veterans' cohort mortality study: preliminary results. Inhal Toxicol, 4: 41-73. 004087

Lipfert FW; Wyzga RE; Baty JD; Miller JP (2006). Traffic density as a surrogate measure of environmental exposures in studies of air pollution health effects: long-term mortality in a cohort of US veterans. Atmos Environ, 40: 154-169. 088218

Lippmann M; Ito K; Nadas A; Burnett RT (2000). Association of particulate matter components with daily mortality and morbidity in urban populations. Health Effects Institute. Cambridge, MA. 011938

Liu S; Krewski D; Shi Y; Chen Y; Burnett R (2007). Association between maternal exposure to ambient air pollutants during pregnancy and fetal growth restriction. J Expo Sci Environ Epidemiol, 17: 426-432. 090429

Liu S; Krewski D; Shi Y; Chen Y; Burnett RT (2003). Association between gaseous ambient air pollutants and adverse pregnancy outcomes in Vancouver, Canada. Environ Health Perspect, 111: 1773-1778. 089548

Ljungman P; Bellander T; Schneider A; Breitner S; Forastiere F; Hampel R; Illig T; Jacquemin B; Katsouyanni K; von Klot S (2009). Modification of the interleukin-6 response to air pollution by interleukin-6 and fibrinogen polymorphisms. Environ Health Perspect, 117: 1373-1379. 191983

Luginaah IN; Fung KY; Gorey KM; Webster G; Wills C (2005). Association of ambient air pollution with respiratory hospitalization in a government designated "area of concern": the case of Windsor, Ontario. Environ Health Perspect, 113: 290-296. 057327

Maheswaran R; Haining RP; Brindley P; Law J; Pearson T; Fryers PR; Wise S; Campbell MJ (2005). Outdoor air pollution and stroke in Sheffield, United Kingdom: A small-area level geographical study. Stroke, 36: 239-243. 088683

Maheswaran R; Haining RP; Brindley P; Law J; Pearson T; Fryers PR; Wise S; Campbell MJ (2005). Outdoor air pollution, mortality, and hospital admissions from coronary heart disease in Sheffield, UK: A small-area level ecological study. Eur Heart J, 26: 2543-2549. 090769

Maisonet M; Bush TJ; Correa A; Jaakkola JJK (2001). Relation between ambient air pollution and low birth weight in the northeastern United States. Environ Health Perspect, 1093: 351-356. 016624

Mann JK; Tager IB; Lurmann F; Segal M; Quesenberry CP Jr; Lugg MM; Shan J; Van den Eeden SK (2002). Air pollution and hospital admissions for ischemic heart disease in persons with congestive heart failure or arrhythmia. Environ Health Perspect, 110: 1247-1252. 036723

Mannes T; Jalaludin B; Morgan G; Lincoln D; Sheppeard V; Corbett S (2005). Impact of ambient air pollution on birth weight in Sydney, Australia. Occup Environ Med, 62: 524-530. 087895

Mar TF; Norris GA; Koenig JQ; Larson TV (2000). Associations between air pollution and mortality in Phoenix, 1995-1997. Environ Health Perspect, 108: 347-353. 001760

Martins LC; Latorre MRDO; Saldiva PHN; Braga ALF (2002). Air pollution and emergency room visits due to chronic lower respiratory diseases in the elderly: An ecological time-series study in Sao Paulo, Brazil. J Occup Environ Med, 44: 622-627. 035059

Masjedi MR; Jamaati HR; Dokouhaki P; Ahmadzadeh Z; Taheri SA; Bigdeli M; Izadi S; Rostamian A; Aagin K; Ghavam SM (2003). The effects of air pollution on acute respiratory conditions. Respirology, 8: 213-230. 052100

McGowan JA; Hider PN; Chacko E; Town GI (2002). Particulate air pollution and hospital admissions in Christchurch, New Zealand. Aust N Z J Public Health, 26: 23-29. 030325

Medeiros A; Gouveia N (2005). Relacao entre baixo peso ao nascer e a poluicao do ar no Municipio de Sao Paulo [Relationship between low birthweight and air pollution in the city of Sao Paulo, Brazil]. Rev Saude Publica, 39: 965-972. 089824

Meng YY; Wilhelm M; Rull RP; English P; Ritz B (2007). Traffic and outdoor air pollution levels near residences and poorly controlled asthma in adults. Ann Allergy Asthma Immunol, 98: 455-463. 093275

Metzger KB; Klein M; Flanders WD; Peel JL; Mulholland JA; Langberg JJ; Tolbert PE (2007). Ambient air pollution and cardiac arrhythmias in patients with implantable defibrillators. Epidemiology, 18: 585-592. 092856

Metzger KB; Tolbert PE; Klein M; Peel JL; Flanders WD; Todd KH; Mulholland JA; Ryan PB; Frumkin H (2004). Ambient air pollution and cardiovascular emergency department visits. Epidemiology, 15: 46-56. 044222

Migliaretti G; Dalmasso P; Gregori D (2007). Air pollution effects on the respiratory health of the resident adult population in Turin, Italy. Int J Environ Health Res, 17: 369-379. 193772

Miller KA; Siscovick DS; Sheppard L; Shepherd K; Sullivan JH; Anderson GL; Kaufman JD (2007). Long-term exposure to air pollution and incidence of cardiovascular events in women. N Engl J Med, 356: 447-458. 090130

Min JY; Paek D; Cho SI; Min KB (2009). Exposure to environmental carbon monoxide may have a greater negative effect on cardiac autonomic function in people with metabolic syndrome. Sci Total Environ, 407: 4807-4811. 199514

Moolgavkar SH (2000). Air pollution and daily mortality in three US counties. Environ Health Perspect, 108: 777-784. 012054

Moolgavkar SH (2000). Air pollution and hospital admissions for chronic obstructive pulmonary disease in three metropolitan areas in the United States. Inhal Toxicol, 12: 75-90. 010274

Moolgavkar SH (2003). Air pollution and daily deaths and hospital admissions in Los Angeles and Cook counties. Health Effects Institute. Boston, MA. 042864

Moolgavkar SH (2003). Air pollution and daily mortality in two US counties: season-specific analyses and exposure-response relationships. Inhal Toxicol, 15: 877-907. 051316

Moon JS; Kim YS; Kim JH; Son BS; Kim DS; Yang W (2009). Respiratory health effects among schoolchildren and their relationship to air pollutants in Korea. Int J Environ Health Res, 19: 31-48. 190297

Mortimer K; Neugebauer R; Lurmann F; Alcorn S; Balmes J; Tager I (2008). Air pollution and pulmonary function in asthmatic children: Effects of prenatal and lifetime exposures. Epidemiology, 19: 550-557. 122163

Mortimer K; Neugebauer R; Lurmann F; Alcorn S; Balmes J; Tager I (2008). Early-Lifetime exposure to air pollution and allergic sensitization in children with asthma. J Asthma, 45: 874-881. 187280

Nautiyal J 3rd; Garg ML; Kumar MS; Khan AA; Thakur JS; Kumar R (2007). Air pollution and cardiovascular health in Mandi-Gobindgarh, Punjab, India - a pilot study. Int J Environ Health Res, 4: 268-82. 190301

Neidell MJ (2004). Air pollution, health, and socio-economic status: The effect of outdoor air quality on childhood asthma. J Health Econ, 23: 1209-1236. 057330

Nkwocha EE; Egejuru RO (2008). Effects of industrial air pollution on the respiratory health of children. Int J Environ Sci Tech, 5: 509-516. 190304

Norris G; Young-Pong SN; Koenig JQ; Larson TV; Sheppard L; Stout JW (1999). An association between fine particles and asthma emergency department visits for children in Seattle. Environ Health Perspect, 107: 489-493. 040774

O'Connor GT; Neas L; Vaughn B; Kattan M; Mitchell H; Crain EF; Evans R 3rd; Gruchalla R; Morgan W; Stout J; Adams GK; Lippmann M (2008). Acute respiratory health effects of air pollution on children with asthma in US inner cities. J Allergy Clin Immunol, 121: 1133-1139. 156818

Ostro BD; Hurley S; Lipsett MJ (1999). Air pollution and daily mortality in the Coachella Valley, California: A study of PM10 dominated by coarse particles. Environ Res, 81: 231-238. 006610

Park H; Lee B; Ha E-H; Lee J-T; Kim H; Hong Y-C (2002). Association of air pollution with school absenteeism due to illness. Arch Pediatr Adolesc Med, 156: 1235-1239. 093798

Park JW; Lim YH; Kyung SY; An CH; Lee SP; Jeong SH; Ju S-Y (2005). Effects of ambient particulate matter on peak expiratory flow rates and respiratory symptoms of asthmatics during Asian dust periods in Korea. Respirology, 10: 470-476. 088673

Park SK; O'Neill MS; Vokonas PS; Sparrow D; Schwartz J (2005). Effects of air pollution on heart rate variability: The VA normative aging study. Environ Health Perspect, 113: 304-309. 057331

Parker JD; Woodruff TJ; Basu R; Schoendorf KC (2005). Air pollution and birth weight among term infants in California. Pediatrics, 115: 121-128. 087462

Peel JL; Metzger KB; Klein M; Flanders WD; Mulholland JA; Tolbert PE (2007). Ambient air pollution and cardiovascular emergency department visits in potentially sensitive groups. Am J Epidemiol, 165: 625-633. 090442

Peel JL; Tolbert PE; Klein M; Metzger KB; Flanders WD; Knox T; Mulholland JA; Ryan PB; Frumkin H (2005). Ambient air pollution and respiratory emergency department visits. Epidemiology, 16: 164-174. 056305

Pekkanen J; Brunner EJ; Anderson HR; Tiittanen P; Atkinson RW (2000). Daily concentrations of air pollution and plasma fibrinogen in London. Occup Environ Med, 57: 818-822. 013250

Penttinen P; Tiittanen P; Pekkanen J (2004). Mortality and air pollution in metropolitan Helsinki, 1988-1996. Scand J Work Environ Health, 2: 19-27. 087432

Penttinen P; Timonen KL; Tiittanen P; Mirme A; Ruuskanen J; Pekkanen J (2001). Ultrafine particles in urban air and respiratory health among adult asthmatics. Eur Respir J, 17: 428-435. 030335

Pereira Filho MA; Pereira LAA; Arbex FF; Arbex M; Conceição GM; Santos UP; Lopes AC; Saldiva PHN; Braga ALF; Cendon S (2008). Effect of air pollution on diabetes and cardiovascular diseases in São Paulo, Brazil. Braz J Med Biol Res, 41: 526-532. 190260

Peters A; Dockery DW; Muller JE; Mittleman MA (2001). Increased particulate air pollution and the triggering of myocardial infarction. Circulation, 103: 2810-2815. 016546

Peters A; Liu E; Verrier RL; Schwartz J; Gold DR; Mittleman M; Baliff J; Oh JA; Allen G; Monahan K; Dockery DW (2000). Air pollution and incidence of cardiac arrhythmia. Epidemiology, 11: 11-17. 011347

Peters A; Perz S; Doring A; Stieber J; Koenig W; Wichmann H-E (1999). Increases in heart rate during an air pollution episode. Am J Epidemiol, 150: 1094-1098. 011554

Peters A; Skorkovsky J; Kotesovec F; Brynda J; Spix C; Wichmann HE; Heinrich J (2000). Associations between mortality and air pollution in central Europe. Environ Health Perspect, 108: 283-287. 001756

Pope CA III; Burnett RT; Thun MJ; Calle EE; Krewski D; Ito K; Thurston GD (2002). Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA, 287: 1132-1141. 024689

Rabinovitch N; Zhang LN; Murphy JR; Vedal S; Dutton SJ; Gelfand EW (2004). Effects of wintertime ambient air pollutants on asthma exacerbations in urban minority children with moderate to severe disease. J Allergy Clin Immunol, 114: 1131-1137. 096753

Rainham DGC; Smoyer-Tomic KE (2003). The role of air pollution in the relationship between a heat stress index and human mortality in Toronto. Environ Res, 93: 9-19. 053202

Ranzi A; Gambini M; Spattini A; Galassi C; Sesti D; Bedeschi M; Messori A; Baroni A; Cavagni G; Lauriola P (2004). Air pollution and respiratory status in asthmatic children: Hints for a locally based preventive strategy AIRE study. Eur J Epidemiol, 19: 567-576. 089500

Rich DQ; Kim MH; Turner JR; Mittleman MA; Schwartz J; Catalano PJ; Dockery DW (2006). Association of ventricular arrhythmias detected by implantable cardioverter defibrillator and ambient air pollutants in the St Louis, Missouri metropolitan area. Occup Environ Med, 63: 591-596. 089814

Rich DQ; Mittleman MA; Link MS; Schwartz J; Luttmann-Gibson H; Catalano PJ; Speizer FE; Gold DR; Dockery DW (2006). Increased risk of paroxysmal atrial fibrillation episodes associated with acute increases in ambient air pollution. Environ Health Perspect, 114: 120-123. 088427

Rich DQ; Schwartz J; Mittleman MA; Link M; Luttmann-Gibson H; Catalano PJ; Speizer FE; Dockery DW (2005). Association of short-term ambient air pollution concentrations and ventricular arrhythmias. Am J Epidemiol, 161: 1123-1132. 079620

Rich KE; Petkau J; Vedal S; Brauer M (2004). A case-crossover analysis of particulate air pollution and cardiac arrhythmia in patients with implantable cardioverter defibrillators. Inhal Toxicol, 16: 363-372. 055631

Riojas-Rodriguez H; Escamilla-Cejudo JA; Gonzalez-Hermosillo JA; Tellez-Rojo MM; Vallejo M; Santos-Burgoa C; Rojas-Bracho L (2006). Personal PM2.5 and CO exposures and heart rate variability in subjects with known ischemic heart disease in Mexico City. J Expo Sci Environ Epidemiol, 16: 131-137. 156913

Ritz B; Wilhelm M; Hoggatt KJ; Ghosh JK (2007). Ambient air pollution and preterm birth in the environment and pregnancy outcomes study at the University of California, Los Angeles. Am J Epidemiol, 166: 1045-1052. 096146

Ritz B; Wilhelm M; Zhao Y (2006). Air pollution and infant death in southern California, 1989-2000. Pediatrics, 118: 493-502. 089819

Ritz B; Yu F; Chapa G; Fruin S (2000). Effect of air pollution on preterm birth among children born in Southern California between 1989 and 1993. Epidemiology, 11: 502-511. 012068

Ritz B; Yu F; Fruin S; Chapa G; Shaw GM; Harris JA (2002). Ambient air pollution and risk of birth defects in Southern California. Am J Epidemiol, 155: 17-25. 023227

Rodriguez C; Tonkin R; Heyworth J; Kusel M; De Klerk N; Sly PD; Franklin P; Runnion T; Blockley A; Landau L; Hinwood AL (2007). The relationship between outdoor air quality and respiratory symptoms in young children. Int J Environ Health Res, 17: 351-360 . 092842

Roemer WH; Van Wijnen JH (2001). Daily mortality and air pollution along busy streets in Amsterdam, 1987-1998. Epidemiology, 12: 649-653. 019391

Rosenlund M; Bellander T; Nordquist T; Alfredsson L (2009). Traffic-generated air pollution and myocardial infarction. Epidemiology, 20: 265-71. 190309

Rosenlund M; Berglind N; Pershagen G; Hallqvist J; Jonson T; Bellander T (2006). Long-term exposure to urban air pollution and myocardial infarction. Epidemiology, 17: 383-390. 089796

Ruckerl R; Greven S; Ljungman P; Aalto P; Antoniades C; Bellander T; Berglind N; Chrysohoou C; Forastiere F; Jacquemin B; von Klot S; Koenig W; Kuchenhoff H; Lanki T; Pekkanen J; Perucci CA; Schneider A; Sunyer J; Peters A (2007). Air pollution and inflammation (interleukin-6, C-reactive protein, fibrinogen) in myocardial infarction survivors. Environ Health Perspect, 115: 1072-1080. 156931

Ruckerl R; Ibald-Mulli A; Koenig WSchneider A; Woelke G; Cyrys J; Heinrich J; Marder V; Frampton M; Wichmann HE; Peters A (2006). Air pollution and markers of inflammation and coagulation in patients with coronary heart disease. Environ Health Perspect, 173: 432-441. 088754

Rudez G; Janssen NA; Kilinc E; Leebeek FW; Gerlofs-Nijland ME; Spronk HM; ten Cate H; Cassee FR; de Maat MP (2009). Effects of ambient air pollution on hemostasis and inflammation. Environ Health Perspect, 117: 995-1001. 193783

Salam MT; Millstein J; Li Y-F; Lurmann FW; Margolis HG; Gilliland FD (2005). Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the Children's Health Study. Environ Health Perspect, 113: 1638-1644. 087885

Samet JM; Dominici F; Curriero FC; Coursac I; Zeger SL (2000). Fine particulate air pollution and mortality in 20 US cities, 1987-1994. N Engl J Med, 343: 1742-1749. 013132

Samoli E; Touloumi G; Schwartz J; Anderson HR; Schindler C; Forsberg B; Vigotti MA; Vonk J; Kosnik M; Skorkovsky J; Katsouyanni K (2007). Short-term effects of carbon monoxide on mortality: An analysis within the APHEA project. Environ Health Perspect, 115: 1578-1583. 098420

Sari I; Zengin S; Ozer O; Davutoglu V; Yildirim C; Aksoy M (2008). Chronic carbon monoxide exposure increases electrocardiographic P-wave and QT dispersion. Inhal Toxicol, 20: 879-84. 190315

Sarnat SE; Suh HH; Coull BA; Schwartz J; Stone PH; Gold DR (2006). Ambient particulate air pollution and cardiac arrhythmia in a panel of older adults in Steubenville, Ohio. Occup Environ Med, 63: 700-706. 090489

Sauerzapf V; Jones AP; Cross J (2009). Environmental factors and hospitalisation for chronic obstructive pulmonary disease in a rural county of England. J Epidemiol Community Health, 63: 324-328. 180082

Schildcrout JS; Sheppard L; Lumley T; Slaughter JC; Koenig JQ; Shapiro GG (2006). Ambient air pollution and asthma exacerbations in children: An eight-city analysis. Am J Epidemiol, 164: 505-517. 089812

Schwartz J; Litonjua A; Suh H; Verrier M; Zanobetti A; Syring M; Nearing B; Verrier R; Stone P; MacCallum G; Speizer FE; Gold DR (2005). Traffic related pollution and heart rate variability in a panel of elderly subjects. Thorax, 60: 455-461. 074317

Schwartz J; Norris G; Larson T; Sheppard L; Claiborne C; Koenig J (1999). Episodes of high coarse particle concentrations are not associated with increased mortality. Environ Health Perspect, 107: 339-342. 017915

Sharovsky R; Cesar LA; Ramires JA (2004). Temperature, air pollution, and mortality from myocardial infarction in Sao Paulo, Brazil. Braz J Med Biol Res, 37: 1651-1657. 156976

Sheppard L; Levy D; Norris G; Larson TV; Koenig JQ (1999). Effects of ambient air pollution on nonelderly asthma hospital admissions in Seattle, Washington, 1987-1994. Epidemiology, 10: 23-30. 086921

Silkoff PE; Zhang L; Dutton S; Langmack EL; Vedal S; Murphy J; Make B (2005). Winter air pollution and disease parameters in advanced chronic obstructive pulmonary disease panels residing in Denver, Colorado. J Allergy Clin Immunol, 115: 337-344. 087471

Singh V; Khandelwal R; Gupta AB (2003). Effect of air pollution on peak expiratory flow rate variability. J Asthma, 40: 81-86. 052686

Slaughter JC; Kim E; Sheppard L; Sullivan JH; Larson TV; Claiborn C (2005). Association between particulate matter and emergency room visits, hospital admissions and mortality in Spokane, Washington. J Expo Sci Environ Epidemiol, 15: 153-159. 073854

Slaughter JC; Lumley T; Sheppard L; Koenig JQ; Shapiro GG (2003). Effects of ambient air pollution on symptom severity and medication use in children with asthma. Ann Allergy Asthma Immunol, 91: 346-353. 086294

Sole D; Camelo-Nunes IC; Wandalsen GF; Pastorino AC; Jacob CMA; Gonzalez C; Wandalsen NF; Rosario Filho NA; Fischer GB; Naspitz CK (2007). Prevalence of symptoms of asthma, rhinitis, and atopic eczema in Brazilian adolescents related to exposure to gaseous air pollutants and socioeconomic status. J Investig Allergol Clin Immunol, 17: 6-13. 090706

Son JY; Cho YS; Lee JT (2008). Effects of air pollution on postneonatal infant mortality among firstborn infants in Seoul, Korea: case-crossover and time-series analyses. Arch Environ Occup Health, 63: 108-13. 190323

Steerenberg PA; Nierkens S; Fischer PH; Van Loveren H; Opperhuizen A; Vos JG; Van Amsterdam JG (2001). Traffic-related air pollution affects peak expiratory flow, exhaled nitric oxide, and inflammatory nasal markers. Arch Environ Occup Health, 56: 167-174. 017157

Steinvil A; Kordova-Biezuner L; Shapira I; Berliner S; Rogowski O (2008). Short-term exposure to air pollution and inflammation-sensitive biomarkers. Environ Res, 106: 51-61. 188893

Stieb DM; Beveridge RC; Brook JR; Smith-Doiron M; Burnett RT; Dales RE; Beaulieu S; Judek S; Mamedov A (2000). Air pollution, aeroallergens and cardiorespiratory emergency department visits in Saint John, Canada. J Expo Sci Environ Epidemiol, 10: 461-477. 011675

Stieb DM; Judek S; Burnett RT (2003). Meta-analysis of time-series studies of air pollution and mortality: Update in relation to the use of generalized additive models. J Air Waste Manag Assoc, 53: 258-261. 056908

Stölzel M; Breitner S; Cyrys J; Pitz M; Wolke G; Kreyling W; Heinrich J; Wichmann H-E; Peters A (2007). Daily mortality and particulate matter in different size classes in Erfurt, Germany. J Expo Sci Environ Epidemiol, 17: 458-467. 091374

Strickland MJ; Klein M; Correa A; Reller MD; Mahle WT; Riehle-Colarusso TJ; Botto LD; Flanders WD; Mulholland JA; Siffel C; Marcus M; Tolbert PE (2009). Ambient air pollution and cardiovascular malformations in Atlanta, Georgia, 1986-2003. Am J Epidemiol, 169: 1004-14. 190324

Sullivan J; Ishikawa N; Sheppard L; Siscovick D; Checkoway H; Kaufman J (2003). Exposure to ambient fine particulate matter and primary cardiac arrest among persons with and without clinically recognized heart disease. Am J Epidemiol, 157: 501-509. 043156

Sun HL; Chou MC; Lue KH (2006). The relationship of air pollution to ED visits for asthma differ between children and adults. Am J Emerg Med, 24: 709-713. 090768

Sunyer J; Basagana X (2001). Particles, and not gases, are associated with the risk of death in patients with chronic obstructive pulmonary disease. Int J Epidemiol, 30: 1138-1140. 019367

Sunyer J; Basagana X; Belmonte J; Anto JM (2002). Effect of nitrogen dioxide and ozone on the risk of dying in patients with severe asthma. Thorax, 57: 687-693. 034835

Symons JM; Wang L; Guallar E; Howell E; Dominici F; Schwab M; Ange BA; Samet J; Ondov J; Harrison D; Geyh A (2006). A case-crossover study of fine particulate matter air pollution and onset of congestive heart failure symptom exacerbation leading to hospitalization. Am J Epidemiol, 164: 421-433. 091258

Szyszkowicz M (2007). Air pollution and emergency department visits for ischemic heart disease in Montreal, Canada. Int J Occup Med Environ Health, 20: 167-173. 193793

Tarkiainen TH; Timonen KL; Vanninen EJ; Alm S; Hartikainen JEK; Pekkanen J (2003). Effect of acute carbon monoxide exposure on heart rate variability in patients with coronary artery disease. Clin Physiol Funct Imaging, 23: 98-102. 053625

Tenias JM; Ballester F; Perez-Hoyos S; Rivera ML (2002). Air pollution and hospital emergency room admissions for chronic obstructive pulmonary disease in Valencia, Spain. Arch Environ Occup Health, 57: 41-47. 026077

Thompson AJ; Shields MD; Patterson CC (2001). Acute asthma exacerbations and air pollutants in children living in Belfast, Northern Ireland. Arch Environ Occup Health, 56: 234-241. 073513

Timonen KL; Pekkanen J; Tiittanen P; Salonen RO (2002). Effects of air pollution on changes in lung function induced by exercise in children with chronic respiratory symptoms. Occup Environ Med, 59: 129-134. 025653

Timonen KL; Vanninen E; De Hartog J; Ibald-Mulli A; Brunekreef B; Gold DR; Henrich J; Hoek G; Lanki T; Peters A; Tarkiainen T; Tiittanen P; Kreyling W; Pekkanen J (2006). Effects of ultrafine and fine particulate and gaseous air pollution on cardiac autonomic control in subjects with coronary artery disease: The ULTRA study. J Expo Sci Environ Epidemiol, 16: 332-341. 088747

Tolbert PE; Klein M; Peel JL; Sarnat SE; Sarnat JA (2007). Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. J Expo Sci Environ Epidemiol, 17: S29-S35. 090316

Trapasso LM; Keith L (1999). Relationships between selected meteorological/pollution parameters and hospital admissions for asthma in south central kentucky . J Ky Acad Sci, 60: 73-77. 180127

Tsai S-S; Chen C-C; Hsieh H-J; Chang C-C; Yang C-Y (2006). Air pollution and postneonatal mortality in a tropical city: Kaohsiung, Taiwan. Inhal Toxicol, 18: 185-189. 090709

Tsai S-S; Cheng M-H; Chiu H-F; Wu T-N; Yang C-Y (2006). Air pollution and hospital admissions for asthma in a tropical city: Kaohsiung, Taiwan. Inhal Toxicol, 18: 549-554. 089768

Tsai S-S; Goggins WB; Chiu H-F; Yang C-Y (2003). Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. Stroke, 34: 2612-2616. 080133

Tsai S-S; Huang C-H; Goggins WB; Wu T-N; Yang C-Y (2003). Relationship between air pollution and daily mortality in a tropical city: Kaohsiung, Taiwan. J Toxicol Environ Health A Curr Iss, 66: 1341-1349. 050480

Vedal S; Brauer M; White R; Petkau J (2003). Air pollution and daily mortality in a city with low levels of pollution. Environ Health Perspect, 111: 45-51. 039044

Vedal S; Rich K; Brauer M; White R; Petkau J (2004). Air pollution and cardiac arrhythmias in patients with implantable cardiovascular defibrillators. Inhal Toxicol, 16: 353-362. 055630

Vigotti MA; Chiaverini F; Biagiola P; Rossi G (2007). Urban air pollution and emergency visits for respiratory complaints in Pisa, Italy. J Toxicol Environ Health A Curr Iss, 70: 266-269. 090711

Villeneuve PJ; Burnett RT; Shi Y; Krewski D; Goldberg MS; Hertzman C; Chen Y; Brook J (2003). A time-series study of air pollution, socioeconomic status, and mortality in Vancouver, Canada. J Expo Sci Environ Epidemiol, 13: 427-435. 055051

Villeneuve PJ; Chen L; Stieb D; Rowe BH (2006). Associations between outdoor air pollution and emergency department visits for stroke in Edmonton, Canada. Eur J Epidemiol, 21: 689-700. 090191

Villeneuve PJ; Doiron M-S; Stieb D; Dales R; Burnett RT; Dugandzic R (2006). Is outdoor air pollution associated with physician visits for allergic rhinitis among the elderly in Toronto, Canada? Allergy, 61: 750-758. 091179

Von Klot S; Wolke G; Tuch T; Heinrich J; Dockery DW; Schwartz J; Kreyling WG; Wichmann HE; Peters A (2002). Increased asthma medication use in association with ambient fine and ultrafine particles. Eur Respir J, 20: 691-702. 034706

Von Klot S; Peters A; Aalto P; Bellander T; Berglind N; D'Ippoliti D; Elosua R; Hormann A; Kulmala M; Lanki T; Lowel H; Pekkanen J; Picciotto S; Sunyer J; Forastiere F; Health Effects of Particles on Susceptible Subpopulations (HEAPSS) Study Group (2005). Ambient air pollution is associated with increased risk of hospital cardiac readmissions of myocardial infarction survivors in five European cities. Circulation, 112: 3073-3079. 088070

Wang Q; Liu Y; Pan X (2008). Atmosphere pollutants and mortality rate of respiratory diseases in Beijing. Sci Total Environ, 391: 143-148. 179974

Wang T-N; Ko Y-C; Chao Y-Y; Huang C-C; Lin R-S (1999). Association between indoor and outdoor air pollution and adolescent asthma from 1995 to 1996 in Taiwan. Environ Res, 81: 239-247. 008105

Wellenius GA; Bateson TF; Mittleman MA; Schwartz J (2005). Particulate air pollution and the rate of hospitalization for congestive heart failure among medicare beneficiaries in Pittsburgh, Pennsylvania. Am J Epidemiol, 161: 1030-1036. 087483

Wellenius GA; Schwartz J; Mittleman MA (2005). Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries. Stroke, 36: 2549-2553. 088685

Wellenius GA; Yeh GY; Coull BA; Suh HH; Phillips RS; Mittleman MA (2007). Effects of ambient air pollution on functional status in patients with chronic congestive heart failure: a repeated-measures study. Environ Health, 6: 1-7. 092830

Wheeler A; Zanobetti A; Gold DR; Schwartz J; Stone P; Suh HH (2006). The relationship between ambient air pollution and heart rate variability differs for individuals with heart and pulmonary disease. Environ Health Perspect, 114: 560-566. 088453

Wichmann H-E; Spix C; Tuch T; Wolke G; Peters A; Heinrich J; Kreyling WG; Heyder J (2000). Daily mortality and fine and ultrafine particles in Erfurt, Germany Part I: role of particle number and particle mass. Health Effects Institute. Boston, MA. 013912

Wilhelm M; Meng YY; Rull RP; English P; Balmes J; Ritz B (2008). Environmental public health tracking of childhood asthma using California health interview survey, traffic, and outdoor air pollution data. Environ Health Perspect, 116: 1254-1260. 191912

Wilhelm M; Ritz B (2005). Local variations in CO and particulate air pollution and adverse birth outcomes in Los Angeles County, California, USA. Environ Health Perspect, 113: 1212-1221. 088668

Woodruff TJ; Darrow LA; Parker JD (2008). Air pollution and postneonatal infant mortality in the United States, 1999-2002. Environ Health Perspect, 116: 110-115. 098386

Xirasagar S; Lin HC; Liu TC (2006). Seasonality in pediatric asthma admissions: the role of climate and environmental factors. Eur J Pediatr, 165: 747-752. 093267

Yang C-Y; Chang C-C; Chuang H-Y; Tsai S-S; Wu T-N; Ho C-K (2004). Relationship between air pollution and daily mortality in a subtropical city: Taipei, Taiwan. Environ Int, 30: 519-523. 055603

Yang C-Y; Chen Y-S; Yang C-H; Ho S-C (2004). Relationship between ambient air pollution and hospital admissions for cardiovascular diseases in Kaohsiung, Taiwan. J Toxicol Environ Health A Curr Iss, 67: 483-493. 094376

Yang CY (2008). Air pollution and hospital admissions for congestive heart failure in a subtropical city: Taipei, Taiwan. J Toxicol Environ Health A Curr Iss, 71: 1085-1090. 157160

Yang CY; Chen CC; Chen CY; Kuo HW (2007). Air pollution and hospital admissions for asthma in a subtropical city: Taipei, Taiwan. J Toxicol Environ Health A Curr Iss, 70: 111-117. 092848

Yang CY; Chen CJ (2007). Air pollution and hospital admissions for chronic obstructive pulmonary disease in a subtropical city: Taipei, Taiwan. J Toxicol Environ Health A Curr Iss, 70: 1214-1219. 092847

Yang Q; Chen Y; Krewski D; Burnett RT; Shi Y; McGrail KM (2005). Effect of short-term exposure to low levels of gaseous pollutants on chronic obstructive pulmonary disease hospitalizations. Environ Res, 99: 99-105. 090184

Yang Q; Chen Y; Krewski D; Shi Y; Burnett RT; McGrail KM (2004). Association between particulate air pollution and first hospital admission for childhood respiratory illness in Vancouver, Canada. Arch Environ Occup Health, 59: 14-21. 087488

Yang Q; Chen Y; Shi Y; Burnett RT; McGrail KM; Krewski D (2003). Association between ozone and respiratory admissions among children and the elderly in Vancouver, Canada. Inhal Toxicol, 15: 1297-1308. 055621

Yu O; Sheppard L; Lumley T; Koenig JQ; S (2000). Effects of ambient air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP study. Environ Health Perspect, 108: 1209-1214. 013254

Zanobetti A; Canner MJ; Stone PH; Schwartz J; Sher D; Eagan-Bengston E; Gates KA; Hartley LH; Suh H; Gold DR (2004). Ambient pollution and blood pressure in cardiac rehabilitation patients. Circulation, 110: 2184-2189. 087489

Zanobetti A; Schwartz J (2006). Air pollution and emergency admissions in Boston, MA. J Epidemiol Community Health, 60: 890-895. 090195

Annex D. Controlled Human Exposure Studies

Table D-1. Controlled human exposure studies.

Study	Subjects	Exposure	Findings
Adir et al. (1999, 001026)	15 healthy nonsmokers **Gender:** M **Age:** 22-34 yr	**Inhaled Concentration:** Not provided **Exposure Duration:** 3 min 45 s **COHb Concentration**: 4-6% **COHb Analysis:** CO-oximeter (IL-282) Exposures to CO and room air were separated by 1 mo, with the order of exposure randomly assigned.	Exposure to CO resulted in a decrease in postexposure exercise duration (Bruce protocol) relative to clean air exposure in 13 out of 15 subjects (p = 0.0012). Statistically significant decreases in METs were also reported following CO exposure (p = 0.0001). No CO-induced changes in HR, BP, ECG parameters, or myocardial perfusion were observed.
Bathoorn et al. (2007, 193963)	19 former smokers with COPD **Gender:** 18 M/1 F **Age:** 66-70 yr	**Inhaled Concentration:** 100 ppm (9 subjects) or 125 ppm (10 subjects) **Exposure Duration:** 2 h on each of 4 consecutive days **COHb Concentration**: 2.7% (following 4th day exposure) **COHb Analysis:** Not provided Exposures to CO and room air conducted were separated by at least 1 wk, using a randomized crossover design.	Following the 4th day of exposure, CO inhalation reduced sputum eosinophils relative to room air and also increased the provocative concentration of methacholine required to cause a 20% reduction in FEV_1. Neither of these effects were shown to reach statistical significance. No changes in sputum neutrophils, white blood cell counts or serum C-reactive protein (CRP) were observed. Although this study appears to demonstrate some evidence of an anti-inflammatory effect of CO among subjects with COPD, it must be noted that 2 of these patients experienced exacerbations of COPD during or following CO exposure, with 1 patient requiring hospitalization 2 mo after exposure (initial symptoms first experienced 1 wk postexposure).
Hanada et al. (2003, 193915)	20 healthy adults **Gender:** M **Age:** 26 ± 1 yr	**Inhaled Concentration:** Not provided **Exposure Duration:** 20 min **COHb Concentration**: 20-24% **COHb Analysis:** CO-oximeter (OSM-3) 15 subjects exposed for 20 min (10 min rest, 5 min handgrip exercise, 2 min postexercise ischemia, 3 min recovery) under the following 4 conditions: (1) normoxia (inspiratory O_2 fraction 21.4%); (2) hypoxia (inspiratory O_2 fraction 10.3%); (3) CO + normoxia; and (4) CO + hyperoxia (inspiratory O_2 fraction 95.9%). Trials involving exposure to CO were conducted last in this sequence. Each of the 4 conditions was separated from the next by 20 min of rest. 5 subjects served as controls (4 consecutive 20 min periods of normoxia).	Blood oxygenation, BP, HR and respiratory rate were measured during exposure. Muscle sympathetic nerve activity (MSNA) and leg hemodynamics were evaluated in two subsets of the study group (n = 8 and 7, respectively). Arterial oxygen saturation (pulse oximetry) was significantly lower, and resting HR and ventilation significantly higher during the period of hypoxia compared to the other periods; none of these measures were affected by exposure to CO. MSNA was shown to increase during hypoxia and CO exposure relative to normoxia. Neither hypoxia nor CO was found to affect leg blood flow or vasoconstriction.

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Study	Subjects	Exposure	Findings
Kizakevich et al. (2000, 052691)	16 healthy nonsmokers **Gender:** M **Age:** 18-29 yr	**Inhaled Concentration:** Initial short term (4-6 min) exposure to 1,000 or 3,000 pap, followed by exposures to 27, 55, 83, or 100 ppm to maintain COHb concentration. **Exposure Duration:** 4-6 min at 1,000 or 3,000 pap, followed by 20 min at 27, 55, 83, or 100 ppm. **Target COHb Concentrations**: 5, 10, 15, and 20% **COHb Analysis:** CO-oximeter (IL-282) Subjects exposed on 4 separate days to increasing CO concentrations during either upper-body exercise (hand-crank) or lower-body exercise (treadmill). Targeted COHb concentrations were initially attained using short-term (4-6 min) exposures to CO at concentrations of 1,000 or 3,000 ppm. Chamber exposures were then conducted at CO concentrations required to maintain COHb levels of <2% (room air), 5% (27 ppm), 10% (55 ppm), 15% (83 ppm), and 20% (100 ppm).	At all levels of upper- and lower-body exercise, exposures to CO resulted in increases in HR, cardiac output, and cardiac contractility relative to clean-air exposures. Increases in HR reached statistical significance at COHb concentrations ≥ 5%, and increases in both cardiac output and cardiac contractility reached statistical significance at COHb concentrations ≥ 10%. CO exposure during exercise was not observed to cause ventricular arrhythmias or affect ECG wave shape (no evidence of ST-segment depression) at COHb concentrations ≤ 20%.
Mayr et al. (2005, 193984)	13 healthy nonsmokers **Gender:** M **Age:** 18-38 yr	**Inhaled Concentration:** 500 ppm **Exposure Duration:** 1 h **COHb Concentration**: 7% **COHb Analysis:** CO-oximeter (AVL 912) Subjects exposed to both CO and clean air with exposures separated by a 6-wk period. Immediately following exposure, subjects were administered an intravenous bolus dose (2 ng/kg) of lipopolysaccharide (LPS).	Infusion of LPS significantly increased plasma concentrations of TNF-α, CRP, IL-6, and IL-8, with no difference in the inflammatory response between clean-air and CO exposures.
Morse et al. (2008, 097980)	12 healthy nonsmokers **Gender:** M **Age:** 25 ± 2.9 yr	**Inhaled Concentration:** 3,000 ppm **Exposure Duration:** 3-8 min **COHb Concentration**: 6.2% **COHb Analysis:** Electrochemical sensor (Smokerlyzer) measuring CO in exhaled breath Exposures conducted on2 separate occasions to room air (6 min) and CO. Subjects were exposed to CO until COHb reached 6% (3- to 8-min exposures).	Leg strength and muscle fatigue were evaluated immediately following exposure. CO exposure did not affect muscle strength (maximal voluntary isometric contraction) but did cause a statistically significant increase in muscle fatigue ($p < 0.05$).
Ren et al. (2001, 193850)	12 healthy adults (10 nonsmokers and 1 smoker) **Gender:** 9 M/3 F **Age:** 20-32 yr	**Inhaled Concentration:** 0.4% (4,000 ppm) **Exposure Duration:** 10-30 min at 0.4% followed by ~ 8-h with periodic exposure to maintain COHb concentration **COHb Concentration**: 10% **COHb Analysis:** Not provided Each subject underwent 4 different 8-h experimental protocols: (1) isocapnic hypoxia (end-tidal PO_2 held at 55 mmHg); (2) withdrawal of 500 mL of venous blood at the start of an 8-h period; (3) CO exposure at a concentration required to maintain a COHb level of 10%; and (4) a control exposure where subjects breathed room air with no intervention.	A statistically significant increase in ventilation was observed following hypoxia, but no such increase was found following any of the other 3 protocols, including exposure to CO. One subject felt faint during the blood withdrawal protocol and did not complete the study.

Study	Subjects	Exposure	Findings
Resch et al. (2005, 193853)	15 healthy nonsmokers **Gender:** M **Age:** 27 ± 4 yr	**Inhaled Concentration:** 500 ppm **Exposure Duration:** 1 h **COHb Concentration**: ~ 10% **COHb Analysis:** CO-oximeter (AVL 912) Exposures to CO and synthetic air control were separated by a period of at least 1 wk.	COHb levels averaged 5.6% after 30 min and 9.4% after 60 min of exposure. Statistically significant increases in retinal blood flow, retinal vessel diameter, and choroidal blood flow were observed with CO exposure relative to synthetic air at both time points. Exposure to CO did not affect oxygen saturation of arterial blood.
Vesely et al. (2004, 194000)	10 healthy nonsmokers **Gender:** M **Age:** 22-52 yr	**Inhaled Concentration:** 1,200 ppm **Exposure Duration:** 30-45 min **COHb Concentration**: 10% **COHb Analysis:** CO-oximeter (OSM-3) Prior to and following exposure, subjects performed hypoxic and hyperoxic rebreathing tests. Four subjects were exposed to hypoxic conditions first, while 6 subjects were exposed to hyperoxic conditions first, both prior to and following CO exposure.	Ventilation rate was observed to significantly increase during hypoxic rebreathing relative to hyperoxic rebreathing. However, exposure to CO had no effect on ventilation under either hypoxic or hyperoxic conditions. The authors concluded that exposure to low levels of CO does not significantly affect chemoreflex sensitivity of the CO_2-induced stimulation of ventilation.
Zevin et al. (2001, 021120)	12 healthy smokers **Gender:** M **Age:** 27-47 yr	**Inhaled Concentration:** 1,200-1,500 ppm **Exposure Duration:** 10 min each h, 16 h each day, over 7 days **COHb Concentration**: 5-6% **COHb Analysis:** CO-oximeter (Ciba Corning 2500) Exposures were conducted over 21 consecutive days under3 different protocols, with each protocol lasting 7 days. In 1 protocol, subjects smoked 20 cigarettes per day, 1 every 45 min. In the other 2 protocols, every 45 min (20 times per day) subjects breathed either air or CO from a 1-liter bag once per min for 10 min at a time. Subjects completed all 3 protocols, with 6 subjects exposed sequentially to CO, smoking, then air, and the other 6 exposed sequentially to air, smoking, then CO.	COHb levels were similar during smoking and exposure to CO, with average concentrations of 6% and 5%, respectively. Blood was drawn on day 4 of each exposure and analyzed for CRP, plasma platelet factor 4, and white blood cell count. Plasma levels of CRP and platelet factor 4 were significantly elevated with smoking but not with CO exposure, relative to air control. HR and BP were evaluated on day 3 of each protocol. Cigarette smoke but not CO was observed to significantly increase HR, while no difference in BP was observed between any of the 3 exposures.

References

Adir Y; Merdler A; Haim SB; Front A; Harduf R; Bitterman H (1999). Effects of exposure to low concentrations of carbon monoxide on exercise performance and myocardial perfusion in young healthy men. Occup Environ Med, 56: 535-538. 001026

Bathoorn E; Slebos DJ; Postma DS; Koeter GH; van Oosterhout AJ; van der Toorn M; Boezen HM; Kerstjens HA (2007). Anti-inflammatory effects of inhaled carbon monoxide in patients with COPD: A pilot study. Eur Respir J, 30: 1131-1137. 193963

Hanada A; Sander M; González-Alonso J (2003). Human skeletal muscle sympathetic nerve activity, heart rate and limb haemodynamics with reduced blood oxygenation and exercise. J Physiol, 551: 635-647. 193915

Kizakevich PN; McCartney ML; Hazucha MJ; Sleet LH; Jochem WJ; Hackney AC; Bolick K (2000). Noninvasive ambulatory assessment of cardiac function in healthy men exposed to carbon monoxide during upper and lower body exercise. Eur J Appl Physiol, 83: 7-16. 052691

Mayr FB; Spiel A; Leitner J; Marsik C; Germann P; Ullrich R; Wagner O; Jilma B (2005). Effects of carbon monoxide inhalation during experimental endotoxemia in humans. Am J Respir Crit Care Med, 171: 354-360. 193984

Morse CI; Pritchard LJ; Wust RC; Jones DA; Degens H (2008). Carbon monoxide inhalation reduces skeletal muscle fatigue resistance. Eur Phys J A, 192: 397-401. 097980

Ren X; Dorrington KL; Robbins PA (2001). Respiratory control in humans after 8 h of lowered arterial PO2, hemodilution, or carboxyhemoglobinemia. J Appl Physiol, 90: 1189-1195. 193850

Resch H; Zawinka C; Weigert G; Schmetterer L; Garhofer G (2005). Inhaled carbon monoxide increases retinal and choroidal blood flow in healthy humans. Invest Ophthalmol Vis Sci, 46: 4275-4280. 193853

Vesely AE; Somogyi RB; Sasano H; Sasano N; Fisher JA; Duffin J (2004). The effects of carbon monoxide on respiratory chemoreflexes in humans. Environ Res, 94: 227-233. 194000

Zevin S; Saunders S; Gourlay SG; Jacob P III; Benowitz NL (2001). Cardiovascular effects of carbon monoxide and cigarette smoking. J Am Coll Cardiol, 38: 1633-1638. 021120

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Annex E. Toxicological Studies

Table E-1. Human and animal studies.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Acevedo and Ahmed (1998, 016003)	Human pregnant myometrium			HO-1 and HO-2 (mRNA and protein) were upregulated in pregnant myometrium when compared to nonpregnant myometrium. The HO activator hemin inhibited spontaneous and oxytocin-induced contractility of the myometrium. Progesterone induced HO-1 and HO-2 mRNA expression.
Achouha et al. (2008, 179918)	Human arteries	Until equilibrium	Approximately 30 µM	CO induced endothelium- and NO-independent relaxation of precontracted human ITA and RA graft by partially stimulating cGMP production. The mechanism and extent of relaxation depended upon the tissue.
Ahmed et al. (2000, 193863)	Human placenta			Placental HO-1 was significantly higher at term. HO-1 significantly attenuated TNFα-dependent cellular damage in placental explants. HO-1 was significantly attenuated in pre-eclampsia pregnancies vs non-pre-eclamptic pregnancies. Placental arteries exposed to the HO activator hemin demonstrated reduced vascular tension (i.e., placental blood vessel relaxation).
Ahmed et al. (2005, 193865)	Human placental cotyledons			The source of CO in term human placental chorionic villi was found to be the catalysis of heme by HO and not endogenous lipid peroxidation.
Alexander et al. (2007, 193869)	Rat Sprague Dawley Adult female		.	Modulation of the HO/CO system in the anterior pituitary of the female rat led to altered secretion of gonadotropins and prolactin.
Alexandreanu et al. (2002, 192373)	Rat Sprague Dawley Female			The role of the HO/CO system in estrous cyclicity, pregnancy and lactation was evaluated using HO inhibitors and substrates. The HO inhibitor CrMP decreased time in estrous. Administering HO-inhibitors to pregnant rodents induced total litter loss. CrMP induced decreased litter weight gain during lactation, which the authors attribute to maternal milk production or ejection problems as cross-fostered pups regained weight lost during nursing on CrMP dams.
Alexandreanu and Lawson ((2003, 193871)	Rat Sprague Dawley Adult female			Modulation of the HO/CO system in the anterior pituitary of the female rat led to altered secretion of gonadotropins and prolactin.
Alexandreanu and Lawson (2003, 193876)	Rat Sprague Dawley Adult female ovary			HO-1 and HO-2 were localized in the ovaries in rats, and treatment of rat ovaries in vitro with CrMP, an inhibitor of HO, or with hemin, a substrate for HO induced steroidogenic changes in the ovaries.
Alonso et al. (2003, 193882)	Human muscle tissue mitochondria	5 min	50-500 ppm	CO significantly reduced muscle mitochondrial cytochrome *c* oxidase activity by 20%, 42%, and 55% after treatment with 50, 100, and 500 ppm CO respectively but did not change the activity of 3 other electron transport proteins.
Andersen et al. (2006, 180449)	Rat Long Evans Male Mouse C57BL/6J Male Cerebral vessels		1-100 µM	CO did not dilate rat or mouse cerebral arteries until 100 µM, which is not a physiological concentration. Also, the HO inhibitors constricted vessels in a nonspecific manner.

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Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Antonelli et al. (2006, 194960)	Rat Wistar	GD5-GD20	75 ppm	Pups exposed to CO in utero had significant impairment of cortical neuronal glutamanergic transmission at PND1 in both neurons at rest and in neurons stimulated with depolarization.
Appleton and Marks (2002, 193935)	Human placenta			Endogenous CO production by HO in the human placenta was regulated by O_2 availability. Placental HO activity was directly dependent on O_2 availability; this does not vary between pre-eclamptic and normotensive placentas.
Ashfaq et al. (2003, 194002)	Human placenta			Placentas were collected from smokers and nonsmokers who gave birth to male infants. Premature aging and a statistically significant increase in apoptotic cells were seen in placentas from smokers vs nonsmokers.
Astrup et al. (1972, 011121)	Rabbit (strain not identified)	Continuous CO exposure over gestation	90 or 180 ppm	Skeletal abnormalities: Three pups (from n = 123) in the 180 ppm CO group had deformities in their extremities at birth, whereas no control and no 90 ppm CO-exposed animals manifested with this malformation.
Bainbridge et al. (2002, 043161)	Human placenta		72–3369 nM	Isolated human placenta exposed to solutions containing CO demonstrated a concentration-dependent decrease in perfusion pressure further demonstrating the role of CO in maintaining basal vasculature tone.
Bainbridge et al. (2006, 193949)	Human placenta	6 h	Starting concentrations of CO: 3.9 µM CO in cell culture media (control) and CO-exposed groups: 116 µM, 145 µM, 181 µM. After 3 h, the CO in the culture media was 3.7 µM (control), and CO-exposed cells 10.2, 12, and 15.9 µM.	C-section placentas were collected from healthy term pregnancies. Villous explants of placentas were cultured under hypoxia followed by reoxygenation (H/R). H/R- and CO-exposed placental tissue had decreased apoptosis and decreased PARP (a protein marker of apoptosis) vs control H/R-exposed cells. Secondary necrosis of the placental tissue post H/R was inhibited by CO treatment.
Bainbridge and Smith (2005, 193946)	Human placenta			The role of HO in the placenta and during pregnancy is reviewed in this article. The conflicting data on the activity, localization and expression of HO in the placentas of pre-eclamptic women are presented.
Bamberger et al. (2001, 016271)	Human placenta			Expression and tissue localization of soluble guanylyl cyclase in human placenta using antibody localization were characterized. These tools can be used in future studies to elucidate the NO/CO/cGMP pathway.
Barber et al. (1999, 193953)	Human myometrium			HO and NOS did not maintain human uterine quiescence during pregnancy.
Barber et al. (2001, 193891)	Human placenta			Women who had pregnancies with fetal growth restrictions (FGR) produced term placenta with significant decreases in HO-2 vs healthy pregnancies.
Baum et al. (2000, 016435)	Human			End-tidal CO measurements in women with pregnancy-induced hypertension and pre-eclampsia were significantly lower than in normotensive pregnant women.
Benagiano et al. (2005, 180445)	Rat Wistar Female	GD0-GD20	75 ppm	CO caused a significant reduction in glutamic acid decarboxylase and GABA immunoreactivities in the cerebellar cortex of adult rats prenatally exposed to CO (number of positive neuronal bodies and axon terminals and the area they covered). No difference was found in the microscopic structure of the cerebellar cortex or distribution patterns of GAD or GABA.
Benagiano (2007, 193892)	Rat Wistar Female	GD5-GD20	75 ppm	Prenatal CO reduced GAD and GABA immunoreactivities. There were no structural alterations of the cerebellar cortex.
Bergeron et al. (1998, 193967)	Rat Brain			To address the developmental changes of HO staining in the brain, immunohistochemical staining for HO-1 was performed on the developing rat brain at PND7, PND14, and PND21. HO-1 staining was most intense at PND7, and by PND21 reached its adult pattern of staining localizing to the hippocampus, thalamic and hypothalamic nuclei, with virtually no staining of endothelium, white matter and cortex. HO-2 is the dominant HO isoform in the brain.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Bing et al. (1995, 079418)	Rodent		.	Spatial learning in the Morris water maze was enhanced in rodents exposed to the HO inhibitor tin protoporphyrin (Sn-PP).
Burmester et al. (2000, 099998)	Human Mouse			Nb had a high oxygen affinity similar to Mb, and thus may increase the availability of O_2 to brain tissue.
Bye et al. (2008, 193777)	Rat Wistar Female	100 h/wk for 18 mo	200 ppm	CO-exposed (11-14.7% COHb) rats experienced a 24% decrease in aerobic capacity evidenced by VO_2 max deficits. Left ventricular cardiomyocytes were longer and wider, had increased expression of growth-related proteins, and had impaired contraction-relaxation cycles. CO increased cGMP and impaired cardiomyocyte Ca^{2+} handling. No change in BP was observed.
Cagiano et al. (1998, 087170)	Rat Wistar Female	GD0-GD20	75 or 150 ppm	At 5 mo of age, CO-exposed male offspring showed decrements in sexual behavior, including an increase in mount- to-intromission latency, a decrease in mount-to-intromission frequency, and a decrease in ejaculation frequency. Basal extracellular dopamine concentration in the nucleus accumbens was unchanged after CO-exposure. However, when stimulated with amphetamine administration, control rats had increased release of dopamine that is absent in CO-exposed rats.
Carmines and Rajendran (2008, 188440)	Rat Sprague Dawley	GD6-GD19 of gestation for 2 h/day	600 ppm	Significant decreases in birth weight were reported after CO exposure. Maternal body weight was unchanged during gestation, but corrected terminal body weight (body weight minus uterine weight) was significantly elevated in CO-exposed dams at term.
Carratu et al. (1993, 013812)	Rat Wistar Male pups	GD0-GD20	75 or 150 ppm	Prenatal CO exposure slowed the inactivation kinetics of transient sodium current in the sciatic nerve fibers of 40-day-old male rats. The maximum number of activatable Na channels at normal resting potential was increased in CO exposed rats, and the voltage-current relationship showed a negative shift of sodium equilibrium potential.
Carratu et al. (1995, 079427)	Rat Wistar		150 ppm	Sphingolipid homeostasis was disrupted in male offspring of prenatally exposed rats, without a disruption in motor function.
Carratu et al. (2000, 015935)	Rat Wistar	GD0-GD20	150 ppm	Maternal COHb (mean % ± SEM) was 1.9 ± 0.04 and 16.02 ± 0.98 in control and 150 ppm CO-exposed animals, respectively. Prenatal CO exposure had no effect on brain sphinganine (SA) or sphingosine (SO) levels in male offspring at 90 days of age. However, the sciatic nerve had significant increases in SO after CO exposure, and no changes in SA at 90 days of age. Motor activity, which could be affected by changes in myelination, showed no differences between CO and control animals at 90 days of age.
Carratu et al. (2000, 015839)	Rat Wistar	GD0-GD20	75 or 100 ppm	The myelin sheath thickness of the nerve fibers was significantly decreased in CO-exposed animals (75 and 150 ppm). Axon diameter was not affected by CO exposure. Even though CO affected myelination, it did not significantly affect motor activity of CO-exposed rats at 40 and 90 days.
Carraway et al. (2002, 026018)	Rat model of hypoxic pulmonary vascular remodeling (Strain of rat not stated)	3 wk	Hypobaric hypoxia ± 50 ppm	CO promoted remodeling and increased pulmonary vascular resistance in response to HH. The number of small muscular vessels was increased compared with HH alone. Changes in cell proliferation, apoptosis, actin and HO-1 gene and protein expression correlated with structural changes. COHb levels were <0.5% in controls, 1.5-2.8% in the HH treatment group, and 3.5-3.9% in the HH + CO treatment group.
Cella et al. (2006, 193240)	Rat Sprague Dawley			HO-1 production and HO concentration were shown to be regulated by estrogen in the rat uterus.
Chen (2001, 193985)	Rat Long Evans Male 2 mo	3.5 h	1201 ± 18 ppm	CO potentiates-noise induced hearing loss. The NMDA inhibitor (+)-MK-801 did not block the potentiation of the NIHL by CO.
Cheng et al. (2009, 193775)	Human atherectomy biopsy (clinical carotid artery disease) Mouse model of vulnerable plaque ApoE-/- mouse			HO-1 expression correlated with features of vulnerable human atheromatous plaque.HO-1 expression was upregulated in vulnerable lesions in the mouse model. Induction of HO-1 in the mouse impeded lesion progression into vulnerable plaques. Inhibition of HO-1 augmented plaque vulnerability. Overexpression of HO-1 resulted in plaque stabilization. It was concluded that HO-1 induction was atheroprotective.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Chung et al. (2006, 193987)	Rat Sprague Dawley Male		3-6%	CO inactivation of Mb did not induce any change in the respiration rate, contractile function or high-energy phosphate levels in perfused rat hearts.
Cronje et al. (2004, 180440)	Rat Sprague Dawley Male 240-325 g	45 min	2,500 ppm	Results indicate that tissue and blood (CO) (66-72% COHb) dissociate during CO inhalation, but tissue (CO) does not follow blood (CO) or $1/pO_2$ as in the Warburg theory during intake or elimination. Tissue (CO) increases later during the resolution period and varies significantly among animals and tissues. The deviation from the predicted values in the brain is likely due to the release of heme and increase in NADPH stimulating endogenous CO production by HO. Immediately following exposure, tissue CO concentrations were found to be: Blood: 27,500 (800) pmol/mg Heart: 800 (300) pmol/mg Muscle: 90 (80) pmol/mg Brain: 60 (40) pmol/mg These values are estimates taken from a graph, with control levels in parentheses A later report stated that these tissue CO values were too high due to a computational error (Piantadosi et al., 2006, 180424)
Cudmore et al. (2007, 193991)	Human placenta Human (HUVEC) Mouse (HO-1 deficient mouse on 129/SV × C57BL/6 background) Pig (Porcine aortic endothelial cells)			HUVEC cells, porcine aortic endothelial cells, HO-1 null mice and placental villous explants (normotensive and pre-eclamptic pregnancies) were used in this study. The HO-1/CO system inhibited sFlt-1 and sEng release, two factors upregulated in pre-eclampsia.
D'Amico et al. (2006, 193992)	Human embryonic kidney (HEK293) cells	0-30 min	20 µM	Exogenous CO inhibited respiration in HEK293 cells under ambient O_2 concentration (21%). Inhibition was enhanced under hypoxic conditions. Increased endogenous CO resulting from HO-1 overexpression inhibited respiration by 12% and cytochrome c oxidase activity by 23%. This effect was enhanced under hypoxic conditions.
Dani et al. (2007, 193994)	Human (neonatal blood)			CO was lower at birth and 48-72 h postpartum in infants born by elective C-section and higher in vaginally born infants.
De Luca et al. (1996, 080911)	Rat Wistar Female Male pups	GD0-GD20	75 or 150 ppm	Prenatal CO (150 ppm) delayed development of the ion channels responsible for passive and active membrane electrical properties of skeletal muscle. CO-induced lower values of resting chloride conductance was reversed at PND80. CO-induced delayed developmental reduction of resting potassium conductance was reversed at PND60.
De Salvia et al. (1995, 079441)	Rat Wistar	GD0-GD20	75 or 150 ppm	Animals exposed to the higher dose of CO (150 ppm) in utero had significantly impaired acquisition (at 3 and 18 mo) and reacquisition (at 18 mo) of conditioned avoidance behavior.
Denschlag et al. (2004, 193894)	Human			Genetic polymorphisms in human HO-1 are linked to idiopathic recurrent miscarriages.
Dewilde et al. (2001, 019318)				Nb exists as a reversibly hexacoordinated Hb type with a His-Fe^{2+}-His binding scheme. Dissociation of the internal ligand by O_2 or CO is the rate limiting step.
Di Giovanni et al. (1993, 013822)	Rat Wistar Female	GD0-GD20	75 and 150 ppm	CO (150 ppm) reduced the minimum frequency of ultrasonic calls as well as decreased responsiveness to a challenge dose of diazepam. There was no change in locomotion; however CO impaired learning in a two-way active avoidance task.
Dubois et al. (2002, 193911)	Rat Wistar Adult female 250 g	3 wk	530 ppm	Intrapulmonary resistance artery smooth muscle cells were isolated from control and exposed rats. Electrophysiological recordings provided evidence of increased Ca^{2+}-activated K^+ current consequent to chronic CO exposure. The authors speculated that this could in part explain the vasodilatory effect of CO in the pulmonary circulation.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Dubois et al. (2005, 180435)	Rat Wistar Male	21 days	50 ppm	CO attenuated PAHT by activating BK_{ca} channels in PA myocytes and reduced hemodynamic changes of PAHT.
Dubois et al. (2003, 180439)	Rat Wistar Male	21 days	50 ppm	CO induced relaxation of pulmonary artery rings in normoxic, hypoxic, and hypoxic-CO rats, and it was not endothelium dependent. Chronic hypoxia decreased acute CO sensitivity, while CO-hypoxia increased it. K^+ channel blocker reduced this effect while sGC blocker did not.
Durante et al. (2006, 193778)				Reviews the role of CO in cardiovascular function.
Favory et al. (2006, 184462)	Rat 250-300 g (Strain not stated)	90 min	250 ppm	CO inhibited myocardial permeabilized fiber respiration (complex IV), increased coronary perfusion pressure and left ventricular developed pressure (LVDP) first derivative and decreased the cGMP/cAMP ratio in the heart. These changes were maintained over 24-48 h of recovery in air. Cardiac function and vasodilatory responses were evaluated at 3-h recovery in air. β-adrenergic blockade had no effect on coronary perfusion pressure or LVDP first derivative. Total inhibition of vasodilator response to acetylcholine and partial inhibition of vasodilator response to nitroprusside were observed. An increase in myofilament calcium sensitivity was also observed. Thus CO promotes abnormalities in mitochondrial respiration, coronary vascular relaxation and myocardial contractility. The authors speculated that CO may have a detrimental effect on heart O_2 supply-to-utilization which could potentially lead to myocardial hypoxia because of the increased O_2 demand resulting from increased contractility, the inhibited mitochondrial respiration and the reduced coronary blood-flow reserve resulting from the decreased vasodilatory capacity. COHb was found to be 11% immediately after exposure. COHb levels gradually returned to baseline (1.5%) over the next 96 h.
Fechter and Annau (1977, 010688)	Rat Long Evans	Continuous CO exposure throughout pregnancy	150 ppm CO	The authors found a 5% significantly decreased birth weights at PND1 in gestationally CO-exposed pups vs control animals with weight decrements persisting to weaning; lactational cross fostering did not ameliorate the CO-dependent reduced growth rates. Dams exposed to CO during gestation had COHb over gestation of 15% with control dams having less than 1%. Decreased birth weight and pre-weaning weight were seen in CO-exposed pups despite a lack of weight decrement in CO-exposed dams vs air-exposed control dams.
Fechter et al. (1980, 011294)	Rat Long Evans	Continuous CO exposure throughout pregnancy	150 ppm	CO-exposed animals had cardiomegaly at birth (wet heart weight) that dissipated by PND4.
Fechter and Annau (1980, 011295)	Rat Long Evans	Continuous CO exposure throughout pregnancy	150 ppm	CO-exposed animals had decreased birth weight, impaired righting reflexes, impaired negative geotaxis, and delayed homing behavior.
Fechter et al. (1987, 012194)	Rat Long-Evans Male		1-4 mL/100 g BW (ip)	High-dose CO led to dose-dependent, reversible loss of the compound action potential sensitivity for high frequency tone bursts. Also, CO produced a dose-dependent elevation in the cochlear blood flow.
Fechter et al.(1987, 012259)	Rat Long Evans Male	Continuous CO exposure throughout pregnancy or from GD0 to PND10	75, 150, or 300 ppm	The neostriatum of each PND21 rat brains was collected and showed disrupted development following CO exposure (GD0-PND10 group, 300 ppm CO). Dopamine levels were also significantly elevated in CO-exposed animals (GD0-PND10, 150 and 300 ppm CO).
Fechter et al. (1997, 081322)	Guinea pigs		35 ml/kg gas (ip) 40% COHb	CO impairs high-frequency auditory sensitivity, shown by increased compound action potential threshold at higher test frequencies. Free radical inhibitors blocked this response.
Fechter et al. (1986, 012030)				Reviews the effects of carbon monoxide on brain development.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Garofolo et al. (2002, 193930)	Human infants Rat	Rat: PND2-PND5		Human infants who die from SIDS showed decreased brainstem muscarinic receptor binding vs infants dying from other causes. ß-adrenergic modulation of muscarinic receptors in developing heart was observed. Rodent ß-adrenergic agonists at PND2-PND5 induced muscarinic receptor decrement in adenylyl cyclase.
Gautier et al. (2007, 096471)	Rat Wistar Adult male Model of right ventricular hypertrophy secondary to chronic hypoxia	3 wk of HH ± CO in final wk Or 1 wk of CO	50 ppm	CO altered the right ventricular adaptive response to pulmonary hypertension which occurs secondarily to chronic hypoxia. Right ventricular end-systolic pressure (RVESP) and right ventricular shortening fraction (RVSF) were smaller in rats treated with CO+HH compared with rats treated with HH alone. CO alone had no effect on these measures. Hypobaric hypoxia had no effect on left ventricular function while CO+ HH led to an increased left ventricular shortening fraction (LVSF). CO alone led to a decrease in LVSF and the mitral E-to-A ratio, indicative of an LV-filling impairment. Hypobaric hypoxia decreased the relative RV perfusion and increased the relative LV perfusion. These effects were prevented with concomitant exposure to CO, although exposure to CO alone had no effects on myocardial perfusion. Morphologic and histologic analysis demonstrated RV hypertrophy in both the HH group and the CO+HH group and fibrotic lesions in the CO+HH group. The authors concluded that the 1-wk exposure to 50 ppm CO had a deleterious effect on RV myocardial perfusion adaptation to chronic hypoxia and pressure overload. Although the reduced RV pressure overload was beneficial, it was counterbalanced by impaired RV perfusion and redistribution of perfusion toward the LV.
Gaworski et al. (2004, 193933)	Rat Sprague Dawley	2 h/day, 7 days/wk by nose-only inhalation Males: 4 wk prior to and during mating; and Females: 2 wk prior to mating; during mating; and through weaning to PND21	Cigarette smoke: 150, 300, or 600 mg/m^3 Total Particulate Matter (TPM)	Maternal exposure to high concentrations of cigarette smoke during gestation and lactation reduced pup birth weight and retarded neonatal pup growth. Developmental and neurobehavioral testing of neonates did not show any behavioral effects following parental smoke exposure.
Ghio et al. (2008, 096321)	Rat Sprague Dawley Adult male	24 h	50 ppm	Mild neutrophil accumulation was observed in BALF, accompanied by increases in BALF MIP-2, protein and LDH. Iron status was altered since CO exposure led to an increase in BALF iron and ferritin, a decrease in lung non-heme iron and an increase in liver non-heme iron.
	Human bronchial epithelial cells (BEAS-2B)	2-24 h	10-100 ppm	CO exposure for 24 h led to a dose-dependent decrease in cellular non-heme iron, with the effect at 10 ppm statistically significant and the effect at 50 ppm maximal. This effect was reversible since removing the cells after 2 h of CO and incubating them in air restored non-heme iron concentrations at 24 h. A dose-dependent decrease in cellular ferritin was observed following exposure for 24 h to 50-500 ppm CO. In addition, exposure to 50 ppm CO for 20 h blocked iron uptake by cells, while exposure to 50 ppm CO for 2 h increased iron release from cells. Increased protein expression of the iron transporter DMT-1 was also noted after 24 h exposure to 50 ppm CO. Oxidative stress, mediator release and cell proliferation were also decreased by exposure to 50 ppm for 24 h. This effect was also reversible upon removal to air. Effects of CO on cell proliferation indices were mimicked by with the iron-depleting agent deferoxamine. The authors concluded that CO exposure altered lung iron homeostasis possibly by initially causing heme release from proteins.
Giustino et al. (1999, 011538)	Rat Wistar Male and pregnant female	GD0-GD20	75 or 150 ppm	This study showed that CO- exposed (75 and 150 ppm) male animals at 40 days of age had a significantly decreased time of exploration of novel objects. The 150 ppm CO group showed a lack of habituation after the second exposure to a previously viewed object. Blood COHb concentrations (mean % ± SEM) on GD20 were reported (0 ppm: 1.6 ± 0.1; CO 75 ppm: 7.36 ± 0.2; CO 150 ppm: 16.1 ± 0.9).

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Giustino et al. (1993, 013833)	Rat Wistar	GD0-GD20	75 or 150 ppm	CO exposure in utero led to a reversible and dose-dependent loss of function of splenic macrophages, with decreased killing ability, decreased phagocytosis, and decreased ROS production during the macrophage respiratory burst.
Giustino et al. (1994, 076343)	Rat Wistar Male pups	GD0-GD20	75 or 150 ppm	CO (150 ppm) decreased the number of leukocyte common antigen (LCA+) cells at PND21. This was reversed by PND540. CO (75 ppm), and other measures of immunological changes showed trends toward reduction (macrophages, T cells, B cells, and MHC II cells).
Glabe et al. (1998, 086704)	Rat Sprague Dawley Male, Myocardium		pCO = 0-107 Torr	Increased pCO and increased COMb saturation did not alter high-energy phosphate signals (ATP, phosphocreatine, P_i). MVO_2 began to decline at 87.6% COMb and is likely not due to cytochrome c oxidase inhibition.
Grover et al. (2000, 010465)	Fetal lamb (mixed breed)	10 min	500 ppm	Fetal methoxyhemoglobin (COHb%) ranged from 3.8 ± 0.2 to 8.1 ± 2.0 at 0 and 500 ppm CO, respectively. Inhaled 0-500 ppm CO administered to near-term fetal lambs did not induce pulmonary vasodilation (main pulmonary artery, left pulmonary artery, aorta and left atrium), and the HO inhibitor zinc protoporphyrin IX failed to affect baseline vascular tone.
Hara et al. (2002, 037497)	Rat Sprague Dawley Male	40 min	1,000-3,000 ppm	CO exposure increased extracellular dopamine levels and decreased its major metabolites in a Na^+-dependent pathway. CO withdrawal and reoxygenation caused levels to return to control or overshoot, which may suggest an increase in oxidative metabolism of CO, mediated by MAO-A.
Harada et al. (2004, 193920)	Pig Granulosa cells			In this porcine model, HO was able to augment granulosa cell apoptosis allowing for proper follicular maturation.
Hendler and Baum (2004, 193925)	Human			End-tidal breath CO measurements in pregnant women with contractions (term and pre-term) were lower than those measurements in noncontracting women.
Hofmann and Brittain (1998, 052019)	Human			Partitioning of O_2 and CO in the human embryonic Hb is discussed.
Iheagwara et al. (2007, 193861)	Mouse C57BL/6 Male	3 h	1,000 ppm	CO significantly reduced cytochrome c oxidase activity and V_{max} but not K_m in myocardial mitochondria. Cytochrome c oxidase protein levels and heme content were significantly decreased. The average COHb level was 61%, but no tissue hypoxia was observed in the heart.
Imai et al. (2001, 193864)	HO-1 transgenic mice which specifically over-express HO-1 in smooth muscle			Transgenic mice had a significant increase in arterial pressure and impaired nitrovasodilatory aortic responses. The mice had enhanced NO production and impaired sGC activity. The authors speculated that the effect of HO-1 overexpression was to suppress vasodilatory responses to NO in vascular smooth muscle.
Ischiropoulos et al. (1996, 079491)	Rat Wistar Male 200-290 g	60 min 40-60 min	1,000-3,000 ppm 1,000 ppm	CO poisoning resulted in free NO in brains as measured by electron paramagnetic resonance spectroscopy and in a 10-fold increase in nitrotyrosine as measured by immunohistochemical staining. These responses were blocked by pretreatment with a NOS inhibitor but not by neutrophil depletion. Brain nitrotyrosine formation was blocked by platelet depletion following 40-min but not 60-min exposure to 1,000 ppm CO. Following CO poisoning, myeloperoxidase activity, a measure of leukocyte sequestration, was increased in brain microvessels. This response was blocked by NOS inhibition but not by platelet depletion. Similar effects were noted for xanthine oxidase activation. The authors concluded that perivascular reactions mediated by peroxynitrite are key to CO poisoning effects in brain.
Johnson and Johnson (2003, 053611)	Rat Sprague Dawley Male 250-300 g		0-100 µM	CO produced a concentration-dependent, endothelium-dependent vasoconstriction in isolated gracilis muscle arterioles, evident at 1 µM CO. Pretreatment with a NOS substrate prevented this response, while pretreatment with a NOS inhibitor converted this response to a vasodilation. The authors concluded that exogenous CO was acting through NOS inhibition.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Johnson et al. (2003, 193868)	Rat Dahl/Rapp salt-resistant and salt-sensitive model Male			High-salt diet increased COHb, BP, and aortic HO-1 protein levels in salt-sensitive Dahl rats. Enhanced immunostaining was observed for HO-1 but not HO-2 in isolated gracilis muscle arterioles. Compared with the low-salt diet, the high-salt diet resulted in a smaller vasoconstrictor response when NOS was inhibited. Vasoconstriction was exacerbated in arterioles from both low-salt- and high-salt-treated rats using both NOS and HO inhibitors. Acetylcholine-induced vasodilation was diminished in the high-salt diet group compared with the low-salt diet group. This effect was not seen using the HO inhibitor. The high-salt diet did not alter endothelium-independent vasodilation. The authors concluded that HO-derived CO caused dysfunction of the $NO^{\bullet}$ system in salt-sensitive rats treated with a high-salt diet.
Johnson et al. (2004, 193870)	Rat Sprague Dawley Male Deoxycorticosterone acetate (DOCA)-salt hypertension model Rats WKY Rats Spontaneously hypertensive (SHR)			Salt-sensitive DOCA rats, but not SHR, had elevated aortic HO-1 expression and blood COHb levels. Both had elevated mean arterial BP compared with controls. Acetylcholine-mediated vasodilation of isolated gracilis muscle arterioles was attenuated in DOCA rats but not SHR. Pretreatment with an HO inhibitor restored the response in DOCA rats. The authors concluded that HO-1-derived CO contributes to endothelial dysfunction in DOCA but not SHR.
Johnson et al. (2006, 193874)	Rat Zucker Lean and obese Male		100 µM CO	The obese rats had increased CO expiration and mean arterial pressure, which was decreased by pretreatment with a HO inhibitor. No difference was observed in HO-1 protein between lean and obese rats. Acetylcholine- and flow-mediated vasodilation of isolated gracilis muscle arterioles was attenuated in obese but not lean rats. Pretreatment with a HO inhibitor restored the response in obese rats. Exogenous CO prevented the restoration of flow-induced dilation by the HO inhibitor. The authors concluded that HO-derived CO contributes to endothelial dysfunction in this model of metabolic syndrome.
Katoue et al. (2005, 193896)	Rat Wistar			HO activity in the aorta is significantly increased during pregnancy, but aortic AVP-dependent vasoconstriction appears to be HO/CO independent.
Katoue et al. (2006, 193954)	Rat Wistar			Pregnancy-induced modulation of calcium mobilization and downregulation of Rho-kinase expression contributed to attenuated vasopressin-induced contraction of the rat aorta.
Khan et al. (2006, 193955)	Nb overexpressing BDF × CD1 mice			Cerebral and myocardial infarcts were decreased in neuroglobin overexpressing mice, decreasing ischemic injury.
Kim et al. (2005, 193959)	Primary rat pulmonary artery smooth muscle cells Rat Inbred LEW Sprague Dawley 200-250 g	24 h or pretreatment for 1-2 h followed by 24 h post-treatment	250 ppm	Exposure of cells in culture to 250 ppm CO for 24 h inhibited serum-stimulated cell proliferation, increased expression of p21Waf1/Cip1, and decreased expression of cyclin A. CO also inhibited PDGF-stimulated cell proliferation and reversed the inhibitory effect of PDGF on caveolin-1 expression. Genetic silencing of caveolin-1 using siRNA, prevented the antiproliferative effect of CO. Endogenous CO, derived from HO-1 in an overexpression system, was found to upregulate caveolin-1 expression. Effects of CO on caveolin-1 were found to be mediated by p38 MAPK and cGMP. Experiments in fibroblasts deficient in p38 confirmed a role for p38 in CO-mediated inhibition of cellular proliferation via effects on p21Waf1/Cip1, cyclin A and caveolin-1. Experiments in fibroblasts deficient in caveolin-1 confirmed the role of caveolin-1 in the anti-proliferative effects of CO. In a model of neointimal injuries induced by balloon injuries in intact animals, exposure to CO inhibited neointimal formation and increased caveolin-1 expression in the intima and media.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Kim et al. (2008, 193961)	Primary rat hepatocytes Primary mouse hepatocytes Respiration-deficient human Hep3B cells	10-60 min	250 ppm	Exposure of cells in culture to 250 CO for 1 h twice a day prevented spontaneous hepatocyte death over 6 days in culture. CO also decreased caspase-3 activity. Cell death was determined to be partly due to apoptosis. CO also increased ROS as measured by dichlorofluorescein fluorescence in rat hepatocytes, mouse hepatocytes, and Hep3B cells but not in respiration-deficient Hep3B cells, indicating that ROS were mitochondrial in origin. An increase in mitochondrial oxidized glutathione was noted in rat hepatocytes treated with CO for 30 min. Increased Akt phosphorylation occurred following 10-30 min CO and was diminished by treatment with antioxidants. CO was found to activate NFκB through a PI3K and oxidant-dependent pathway. CO mediated spontaneous cell death was found to be dependent on ROS and Akt phosphorylation. The authors concluded that CO prevents hepatocyte apoptosis through redox mechanisms, leading to cytoprotection.
Kinobe et al. (2006, 188447)	Sheep Gravid and nongravid sheep and their near-term fetuses			There were no significant differences in hypoxic adult and hypoxic fetal sheep when compared to their normoxic controls.
Knuckles et al. (2008, 191987)	Mouse	4 h	Diesel emissions: 350 µg/m^3	Diesel exhaust enhanced vasoconstriction in veins but not arteries. It were suggested that this is through the uncoupling of eNOS.
Korres et al. (2007, 190908)	Human			Transient evoked otoacoustic emissions response and amplitude at 4,000 Hz was lower in neonates with prenatal exposure to cigarette smoke. There was no dose-dependent change in response depending on the amount cigarettes per day that was smoked.
Kreiser et al. (2004, 193948)	Human			End-tidal CO concentrations were lower in pregnant women with gestational hypertension and pre-eclampsia than normotensive women.
Lash et al. (2003, 193849)	Human Term placental chroionic villi from healthy or pre-eclamptic placentas			Infarcted areas of placenta had decreased HO expression (in pre-eclamptic placenta only).
Li et al. (2008, 187003)	Mouse ICR (CD-1) Pregnant			The effect of maternal LPS exposure on fetal liver HO was measured. HO-1 was upregulated in fetal livers post-LPS exposure, and this HO-1 upregulation was attenuated with the spin trap agent PBN, pointing to a ROS-dependent HO-1 upregulation post-maternal LPS treatment.
Liu and Fechter (1995, 076524)	Guinea pig Male		35 mL/kg (ip)	CO increased the compound action potential threshold at high frequencies. This could be blocked by inhibition of the glutamate receptor.
Loennechen et al. (1999, 011549)	Rat Sprague Dawley Female 220-240g	1 wk 1 wk 100 ppm and 1 wk 200 pm	100 ppm 100-200 ppm	Endothelin-1 expression increased by 53% and 54% in the left and right ventricle, respectively, during the 2-wk exposure, and by 43% and 12% in the left and right ventricle, respectively, during the 1-wk exposure. Right ventricular to body weight ratio was increased by 18% and 16% in the 2-wk and 1-wk exposure groups, respectively. COHb levels were 23% and 12% in the 2-wk and 1-wk exposure groups, respectively.
Longo et al. (1999, 011548)	Rat uterine tissue and tail artery rings Sprague Dawley Human uterine biopsies		10^{-4} M	The addition of exogenous CO to isolated human and rat uterine tissue failed to induce relaxation of uterine tissue. Isolated rat aortic rings and tail artery rings from pregnant dams can be relaxed by submersion in exogenous CO solutions.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Lopez et al. (2008, 097343)	Rat Sprague Dawley	Pregnant rats exposed to CO GD5-GD20 (Group A) or GD5-GD20 plus PND5-PND20 (Group B); Group C (control air exposure). 10-18 h/day	25 ppm	CO exposure induced damage to the spiral ganglia neurons and inner hair cells, with oxidative stress seen in cochlear blood vessels. At PND20 groups A and B showed vacuolization of afferent terminals at the base of the cochlea. At PND3, group A showed decreased synapsin-1 staining of the efferent nerve terminals. At PND20, groups A and B showed decreased neurofilament-IR (staining) in type I spiral ganglia neurons and afferent nerve fibers. At PND12 and PND20, group B showed increased HO-1 and SOD-1-IR in blood vessels of the stria vasularis; group A was similar to controls. From PND3-PND20, there was increased iNOS and increased nitrotyrosine-IR in blood vessels of the cochlea.
Lopez et al. (2003, 193901)	Rat Sprague Dawley	PND6 to weaning (PND19-PND20)	12 or 25 ppm	In the cochlea, atrophy or vacuolization of the nerve cells that innervate the inner (not outer) hair cells was seen. Fibers of the 8th cranial nerve (internal auditory canal of the ARCO animals, 25 ppm) had distorted myelination and vacuolization of the axoplasm. In the organ of corti and spiral ganglion neurons, cytochrome c oxidase and NADH-TR were significantly decreased in 25 ppm exposure group vs control. Expression of the calcium-mediated myosin ATPase in the organ of corti and spiral ganglion neurons was significantly decreased in the 25 ppm CO exposure group vs controls.
Lund et al. (2007, 125741)	Mouse ApoE$^{-/-}$ Male High-fat diet	6 h/day, 7days/wk, 7 wk	8, 40, or 60 µg/m^3 PM whole-gasoline exhaust; or filtered exhaust with gases matching the 60 µg/m^3 concentration. CO concentrations were 9, 50, and 80 ppm, corresponding to the 8, 40, and 60 µg/m^3 PM whole-exhaust exposures	Both whole-gasoline and filtered-gasoline exhaust increased aortic mRNA expression of matrix metalloproteinase-3 (MMP-3), MMP-7, and MMP-9, tissue inhibitor of metalloproteinases-2, endothelin-1 and HO-1 at 60 µg/m^3. Aortas also showed increased immunostaining for MMP-9 and nitrotyrosine in 60 µg/m^3 PM whole exhaust and PM-filtered exhaust exposed groups. Aortic TBARS, a measure of lipid peroxidation, was also increased in all treatment groups.
Lund et al. (2009, 180257)	Mouse ApoE$^{-/-}$ Male High-fat diet	6 h/day, 1 or 7 days	Gasoline engine exhaust containing 60 µg/m^3 PM and 80 ppm CO	Gasoline exhaust exposure increased aortic MMP-2/9 activity at 1 and 7 days. Protein levels of aortic MMP-9, MMP-2, TMP-2 and plasma MMP-9 were also increased after 7 days. Lipid peroxidation in aorta, resulting from gasoline exhaust exposure, was inhibited by treatment with the antioxidant Tempol, while increases in mRNA for ET-1 and MMP-9 in aortas were inhibited by treatment with BQ-123, an antagonist of ETA receptor. Treatment with BQ-123 also reduced aortic MMP-2/9 activity in aortas following gasoline exhaust exposure. The authors concluded that ETA receptor pathway is a key mediator of gasoline engine exhaust effects in the vasculature.
Lyall and Myatt (2002, 193971)	Human			Women with pre-eclampsia produced term placenta with significant decreases in HO-2 vs women with healthy pregnancies.
Lyall et al. (2000, 193902)	Human (placentas from 8-to19-wk pregnancy and term placentas)			The use of a HO inhibitor ZnPP increased placental perfusion pressure. HO-1 and HO-2 were expressed in the placenta and placental bed and vary in expression over the course of pregnancy. HO may thus be involved in trophoblast invasion, placental function, and perfusion pressure.
Mactutus and Fechter (1984, 011355)	Rat Long Evans	Continuous exposure to CO over gestation	150 ppm	Acquisition as measured in a two-way conditioned avoidance (flashing light warnings followed by mild footshock) test failed to improve with age of in utero CO-exposed (150 ppm, dam COHb 15%) rats (male and female offspring) in contrast to air-exposed controls who improved with age/maturation, indicating a failure in the associative process of learning. The authors also found impairments in reacquisition performance, an index of retention, in PND31 rats that had received continuous in utero CO exposure. Prenatal CO exposure induced learning and memory deficits in male and female offspring.
McGregor et al. (1998, 085342)	Guinea pig	GD23-GD25 until term (approximately 68 days) 10 h/day	200 ppm	Aberrant respiratory responses (to asphyxia and CO_2) of offspring with prenatal CO exposure. The authors hypothesized that this may be related to changes in the brainstem. COHb was measuerd in maternal (8.53 ± 0.6% vs 0.25 ± 0.1%) and fetal blood (13.0 ± 0.4% vs 1.6 ± 0.1%) from CO-treated vs controls.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
McLaughlin et al. (2001, 193823)	Human placenta			Various pathologies of pregnancy including IUGR and pre-eclampsia are associated with significant decreases in placental HO activity. The endogenous generation of CO in the placenta has been demonstrated in chroionic villi of term placenta.
McLaughlin et al. (2000, 015815)	Human placenta			Placental regional localization of HO was explored. The chorionic plate, chorionic villi, basal plate, and choorio-decidua had significantly higher HO activity than the amnion.
McLaughlin et al. (2003, 193827)	Human placenta			HO expression in various regions of term placentas was explored. Microsomal HO-2 protein content was not different between normotensive and milk pre-eclamptic pregnancies. There was increased expression of microsomal HO-1 protein in chorionic villi and fetal membranes from pre-eclamptic pregnancies vs normotensive pregnancies.
McLean et al. (2000, 016269)	Human placenta			HO activity was highest in the placenta near term.
Melin et al. (2002, 037502)	Rat Dark Agouti Male Model of right ventricle hypertrophy secondary to chronic hypoxia (HH 10 wk)	10 wk	50 ppm alone or concomitant with HH	Hb and hematocrit levels were increased above controls in HH rats, CO rats and HH+CO rats, with the increase due to the combined treatment significantly higher than the increase due to HH. COHb levels were 1.1% in controls, 1.3% in HH rats, 4.7% in CO rats and 9.1% in HH plus CO rats. HH treatment significantly increased right ventricular (RV) heart weight above controls while CO treatment had no effect on any postmortem heart weights. Combined treatment with HH+CO resulted in a significant increase in left ventricular plus septum (LV+S) weight and RV weight compared with HH treatment alone. Echocardiographic left ventricular morphology and mass also showed the greatest changes in the HH+CO group. Hemodynamic measurements of LV function demonstrated significant effects in the HH+CO group for left ventricular end diastolic pressure (LVESP), left ventricular maximal first derived pressure (+dP/dtLV), and left ventricular work (LVW) compared with controls. Hemodynamic measurements of RV function demonstrated significant effects in the HH group for right ventricular end systolic and diastolic pressure (RVESP, RVEDP), right ventricular maximal and minimal first derived pressure (+dP/dtRV, -dP/dtRV) and right ventricular work (RVW). CO significantly enhanced the effects of HH on RVEDP and significantly diminished the effects of HH on dP/dtRV and RVW. The authors concluded that CO intensified the HH-induce RV hypertrophy, increased LV weight, and induced severe hematological responses that could hamper adaptation.
Melin et al. (2005, 193833)	Rat Dark Agouti Male and female Model of right ventricle hypertrophy secondary to chronic hypoxia (HH, 10 wk) Half of the animals were exercise trained to induce LV hypertrophy	10 wk	50 ppm alone or concomitant with HH	In untrained animals, combined treatment with HH+CO led to increased LV+S and RV weights compared with HH treatment alone. HH+CO led to several changes in measured echocardiographic parameters, including increased anterior and posterior wall thickness in diastole (AWTd, PWTd), and to increased fraction of shortening. These effects were not seen with HH alone. In addition, RVEDP was enhanced in HH+CO compared with HH alone. HRV components were altered by HH+CO but not by CO alone.
Mereu et al (2000, 193838)	Rat Wistar	GD0-GD20 continuous CO exposure	150 ppm	In utero exposure to CO disrupted hippocampal LTP with concomitant HO-2 and nNOS reductions. The authors surmised that these changes may be related to the memory deficits seen in animals exposed to CO in utero.
Middendorff et al. (2000, 015842)	Human Adult males aged 65-75 yr Testicular tissue from orchiectomy			Zn protoporphryin (ZnPP) and Hb both significantly reduced seminiferous tubular cGMP generation, suggesting a role for CO in human testicular tissue.
Montagnani et al. (1996, 080902)	Rat Wistar Male pups	GD0-GD20	75 or 150 ppm	CO caused an increase in tetrodotoxin-induced inhibition of perivascular nerve stimulation PNS-evoked vasoconstriction, increased the time to NO-related relaxant effect by ACh, and decreased the contractile response evoked by ACh on resting tone.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Naik and Walker (2003, 193852)	Rat Sprague Dawley Male		210 µL of CO/100 mL of physiological saline solution	Endogenous CO-mediated vasorelaxation involved cGMP-independent activation of vascular smooth muscle large-conductance Ca^{2+}-activated K^+ channels. However, exogenous CO vasodilation was cGMP dependent.
Ndisang et al. (2004, 180425)				Review of CO and hypertension. CO is a vasorelaxant due to activation of the big conductance calcium-activated potassium channels and soluble guanylate cyclase/cGMP pathway. Developmental stage and tissue type will determine which of these pathways plays more of a role in vasorelaxation.
Neggers and Singh (2006, 193964)	Mouse CD-1	GD8-GD18	500 ppm	Developmental toxicitiy of CO was attenuated by protein supplementation, i.e., protein supplemented animals (27%) showed a significantly lower incidence of fetal mortality vs 8% and 16% protein groups. Further, dietary restriction of both protein and zinc with CO exposure to during gestation increased the incidence of pup mortality and malformations including gastroschisis. Zinc supplementation to a protein-deficient diet in CO-exposed mice decreased fetal mortality and malformation.
Newby et al. (2005, 193966)	Human placental cells in culture			Term human placental cells were grown in cell culture under basal and hypoxic conditions to explore changes in HO expression. HO-1 was unchanged in cytotrophoblasts under hypoxia, but HO-1 was significantly decreased in hypoxic syncytiotrophoblasts. HO-2 was unchanged in either cell type with hypoxia. These cell culture data can give insight into what cell types might be responsive to hypoxia through the HO/CO system in the human placenta.
Odrcich et al. (1998, 193958)	Guinea pig			Immunohistochemical localization of HO in guinea pig placentae showed that HO-1 staining was highest near term (PND62) and lesser at term or earlier in pregnancy. HO-1 was localized in the advential layer of fetal blood vessels.
Ozawa et al. (2002, 193841)	Rat Wistar Adult male			The role of HO-1 in spermatogenesis was explored. $CdCl_2$ induced testicular HO-1 and reduced HO-2 protein in rats. Pretreatment with ZnPPIX attenuated $CdCl_2$-dependent apoptosis. Leydig cells use HO-1-derived CO to trigger apoptosis of pre-meiotic germ cells and modulate spermatogenesis under $CdCl_2$ dependent oxidative stress.
Patel et al. (2003, 043155)	Rat Sprague Dawley Male 262 ± 30 g Isolated hearts	30 min	Buffer saturated with 0.01 and 0.05% CO	The ventricular glutathione content, both reduced and oxidized, decreased by 76% and 84% 90 min post-exposure to 0.01% and 0.05% CO, respectively. Treatment with antioxidants partially blocked the decreases in glutathione. Increased creatine kinase activity was observed in heart perfusate during and after treatment.
Penney et al. (1983, 011385)	Rat (strain not reported)	GD17-GD22	157, 166 or 200 ppm	In utero CO exposure induced decreased fetal body weight, decreased placental weight, increased wet heart weight at birth, and altered cardiac enzymes at birth.
Penney et al. (1982, 011387)	Rat COBS	GD0-GD32	350 ppm PND1-PND3, then 425 ppm PND4-PND7, then 500 ppm PND8-PND32	Postnatal CO exposure decreased body weight, to a greater extent in male pups. The heart to body weight ratio and left ventricle plus interventricular septum and right ventricle weight increased after birth in CO exposed pups. This persistent cardiomegaly was not explained by increasing in DNA or hydroxyproline.
Piantadosi (2002, 037463)				Reviews the biochemical activities of CO, including various heme protein binding. The review stresses the importance of the CO/O_2 ratio in determining the physiological effects of CO.
Piantadosi (2008, 180423)				Reviews the physiologic responses to exogenous and endogenous CO and biochemical effects, including the binding to heme proteins, the generation of reactive O_2 species, and activation-related signaling pathways.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Piantadosi et al. (2006, 180424)	Rat Sprague Dawley Adult male	1, 3, or 7 days	50 ppm or HH	COHb produced COHb levels of 4-5% (controls approximately 1%) and liver CO concentration of 30-40 pmol/mg wet weight (controls approximately 10 pmol/mg wet weight). Both CO and HH led to increased expression of hypoxia-sensitive proteins HO-1 and HIF-1α and mitochondrial antioxidant protein SOD-2. CO caused a greater change in mitochondrial GSH/GSSG than HH. Only CO increased mitochondrial 3-nitrotyrosine and protein mixed disulfides. Mitochondria isolated from CO-exposed rats, but not from HH-exposed rats, showed an increase in the calcium sensitivity of the mitochondrial permeability transition (MPT). Exposure to CO or HH resulted in a loss of the ability of adenine nucleotides to protect mitochondria from MPT. This effect was restored in the presence of a strong reductant. The authors concluded that CO caused mitochondrial pore stress independently of its hypoxic effects
Prigge and Hochrainer (1977, 012326)	Rat Wistar, SPF	GD0-GD20	60, 100, 250, 500 ppm	Fetuses were collected by C-section after 21-days exposure. Significant increases in fetal heart weight were seen in fetuses exposed to CO in all dose groups. Fetal body weight was signifi-cantly decreased (NOAEL 125 ppm CO).
(Raub and Benignus, 2002, 041616)				Reviews the physiology of CO and the effects on the nervous system. It is estimated that COHb would have to rise to 15-20% before a 10% reduction in any behavioral or visual measurement could be observed.
Richardson et al. (2002, 037513)	Human Male		20% COHb	20% COHb did not influence O_2Mb binding indicated by unaltered deoxy-myoglobin signal. Resting skeletal muscle metabolic rate was unaffected by 20% COHb. VO_2 max was decreased. No decrement in intracellular PO_2 was found. 20% COHb altered exercising bioenergetics, pH, PCr, and ATP levels.
Ryter et al. (2006, 193765)				Reviews the basic science of exogenous and endogenous CO including HO-1 regulation. It also reviews some therapeutic applications for CO.
Sartiani et al. (2004, 190898)	Rat Wistar	In utero inhalation exposure	150 ppm	At 4 wk of age, the action potential duration APD of isolated cardiac myocytes from CO-exposed animals failed to shorten or mature as did the APD of control animals. Further, the two ion conduction channels Ito (transient outward current, K^+-mediated) and ICa,L (L-type Ca^{2+} current), which largely control the rat APD, were significantly different from control animals after CO exposure at 4 wk of age. All of these CO-dependent changes were no longer different from controls at 8 wk of age, showing a delayed maturation.
Schwetz et al. (1979, 011855)	Mouse CF-1 Rabbit New Zealand	7 or 24-h/day GD6-GD15 (Mice) GD6-GD18 (Rabbits)	250 ppm	In mice there was a significant increase in number of skeletal abnormalities in CO-exposed mice. Decreased birth weight in mice exposed to 24 h/day CO vs control. Increased birth weight in mice exposed to 7 h/day CO vs controls. No similar effects were seen in rabbits.
Singh et al. (1992, 013759)	Mouse CD-1	GD8-GD18	65, 125, or 250 ppm	CO exposure concomitant with a low-protein diet exacerbated the percent of skeletal malformations in offspring. The percent of dead, resorbed, or grossly malformed fetuses was directly related to CO concentration and inversely related to maternal dietary protein levels. CO and maternal dietary protein restriction had a synergistic effect on offspring survival and an additive effect on malformations.
Singh (2006, 190512)	Mouse CD-1	6 h/day during the first 2nd wk of pregnancy	65 or 125 ppm	Modulating dam protein intake during in utero CO exposure altered pup mortality.
Singh et al. (1993, 013892)	Mouse Albino CD-1	GD8-GD18	65, 125, 250, or 500 ppm	Mice were given various protein diets (4, 8, 16, or 27% protein) during pregnancy, along with CO exposure. All concentrations of CO exposure within each maternal dietary protein level significantly increased the percentage of litters with malformations in a dose-dependent manner. CO exposure concomitant with a low protein diet exacerbated the percent of skeletal malformations in offspring. The percent of dead, resorbed, or grossly malformed fetuses was directly related to CO concentration and inversely related to maternal dietary protein levels. CO and maternal dietary protein restriction had a synergistic effect on mouse offspring mortality and an additive effect on malformations.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Singh (2003, 053624)	Mouse Albino CD-1	GD8-GD18	500 ppm	CO decreased the mean implants per litter and increased the incidence of fetal mortality. Under low protein conditions, CO exposure increased the incidence of malformations (9.4% vs 0%) when Zn levels were normal and increased the incidence of gastroschisis (5% vs 0%) when Zn levels were low.
Singh and Scott (1984, 011409)	Mouse Albino CD-1	GD7-GD18	65, 125, 250, or 500 ppm	All concentration of CO decreased fetal weight in mouse pups. Near-term fetal body weight was decreased at GD18 in mice exposed from GD7-GD18 to 125, 250, and 500 ppm CO but not at 65 ppm CO.
Singh (1986, 012827)	Mouse Albino CD-1	GD7-GD18	65 or 125 ppm	Impaired aerial righting score at PND14 (65 and 125 ppm), impaired negative geotaxis at PND10 and righting reflex on PND1 (125 ppm)
Sitdikova et al. (2007, 180417)	Frog neuro-muscular junctions	20 min	96 µM	CO-induced acetylcholine release, without effects on the pre-synaptic action potential or functional properties of post-synaptic receptors in frog neuro-muscular preparations.
Song et al. (2002, 037531)	Human Primary human airway smooth muscle cells	0-48 h	10-250 ppm	CO inhibited SMC proliferation at concentrations from 50-500 ppm. The cell cycle arrest occurred at the G0/G1 phase of the cell cycle. CO increased expression of the cell cycle inhibitor p21Cip1 at 1 h and decreased expression of cyclin D1 over 24-48 h. The antiproliferative actions of CO were found to be independent of sGC, but instead exerted through the inhibition of ERK MAPK activation since 15 min exposure to 250 ppm CO blocked serum-mediated ERK phosphorylation.
Sorhaug et al. (2006, 180414)	Rat Wistar Female 169 ± 4.5 g	20 h/day, x 5 days/wk, x 72 wk	200 ppm	COHb was 14.7% in CO-exposed animals and 0.3% in controls. Total Hb was also increased in following CO exposure. CO caused no changes in lung morphology or pulmonary hypertenstion. No atherosclerotic lesions were found in aorta or femoral artery. Weight increases of 20% and 14% were observed in the right ventricle and left ventricle plus septum, respectively, indicative of ventricular hypertrophy following chronic CO exposure.
Stevens and Wang (1993, 188458)	Mouse C57/Bl-6J Rat Sprague Dawley Hippocampal brain slices			HO inhibition blocked long-term potentiation but not long-term depression.
Stockard-Sullivan et al. (2003, 190947)	Rat Sprague Dawley	22 h/day, PND6-PND22	12, 25, 50, or 100 ppm	Using functional OAE testing and ABR showed that with perinatal CO exposure (50 and 100 ppm CO) there were significant decrements in OAE in CO-exposed animals. ABR showed no functional deficits with CO exposure. Using another otoacoustic test revealed significant attenuation of the AP of the 8th cranial nerve with CO exposure (12, 25, and 50 ppm CO) vs controls at PND22.
Storm and Fechter (1985, 011653)	Rat Long Evans	GD0-parturition	150 ppm	Prenatal CO exposure increased mean and total cerebellar norepinephrine concentration from PND14-PND42 but not in the cortex.
Storm and Fechter (1985, 011652)	Rat Long Evans	GD0-GD20	75, 150, and 300 ppm	CO transiently decreased 5HT and NE in the pons/medulla and increased NE in the cortex and hippocampus at PND42. CO dose-dependently reduced cerebellum wet weight. Maternal COHb: 2.5%, 11.5%, 18.5%, and 26.8% (0, 75, 150, and 300 ppm, respectively).
Storm et al. (1986, 012136)	Rat Long Evans	GD0-PND10	75, 150, and 300 ppm	CO decreased cerebellar weight (150-300 ppm at PND10, 75-300 ppm at PND21) and decreased total cerebellar GABA (150-300 ppm at PND10 and PND21). CO- exposed (300 ppm) cerebella had fewer fissures.
Styka and Penney (1978, 011166)	Rat Charles River Male	6 wk	400 ppm or gradual increase from 500 to 1,100 ppm	CO caused increased heart weight to body weight that regressed within a couple of mo after CO exposure. COHb: 400 ppm – 35%; 1,100 ppm – 58%

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Suliman et al. (2007, 193768)	Mouse C57BL/6 Wild-type and eNOS deficient Male Rat Embryonic cardiomyocytes H9c2 cells	1 h	50-1,250 ppm Or HH Or 100 mM dichloromethane	One-h exposure of mice to 1,250 ppm CO increased cardiac mitochondrial content of all 5 respiratory complexes 24 h later. The volume density of interfibrillar mitochondria was increased by 30% after 24 h demonstrating that CO caused cardiac mitochondrial biogenesis. The CO concentration in heart increased from 9 pmol/mg to 50-150 pmol/mg in mice exposed to 50-1,250 ppm CO for 1 h. These levels declined to baseline by 6 h. Peroxisome proliferator-activated receptor gamma coactivator 1 alpha (PGC-1α) expression was increased 6 h following exposure to 50-1,250 ppm CO. Expression of DNA polymerase and mitochondrial transcription factor A (TFAM) was increased 6 and 24 h after exposure, while mitochondrial DNA was increased two- to threefold 24 h after exposure. CO activated gene expression of these proteins involved in cardiac mitochondrial biogenesis beginning at 2 h postexposure for PGC-1α, nuclear respiratory factors 1 and 2 (NRF-1 and -2) and at 6 h postexposure for TFAM. These effects were independent of NOS and not seen with HH. CO exposure resulted in phosphorylation of p38 MAPK and Akt at 2 and 6 h postexposure to 1,250 ppm CO for 1 h. Inhibition of p38 activation failed to inhibit the CO-mediated increase in cardiac mitochondrial biogenesis. In cell culture experiments, CO derived from dichloromethane metabolism resulted in increased cGMP, protein levels of SOD2, TFAM, NRF-1, NRF-2, PGC-1,mitochondrial ROS, Akt phosphorylation, and mitochondrial DNA. Inhibition of GC or PI3K/Akt but not p38 blocked the responses to CO. A role for mitochondrial H_2O_2 in Akt regulation was demonstrated. Mitochondrial H_2O_2 and the PI3K/Akt pathway were important mediators of TFAM expression. The authors concluded that CO exposure increased mitochondrial ROS, which promoted mitochondrial biogenesis in the heart.
Sun et al. (2001, 026022)	Mouse Neuronal cultures prepared from the cerebral hemispheres of 16-day Charles River CD1 mouse embryos			Nb expression was increased by neuronal hypoxia in vitro and focal cerebral ischemia in vivo. Inhibiting Nb reduced neuronal survival after hypoxia whereas Nb overexpression enhanced neuronal survival.
Tattoli et al. (1999, 011557)	Rat Wistar Male and pregnant female	PND1-PND10	75 and 150 ppm	Cognitive function was assessed in rats after postnatal CO exposure at 3 and 18 mo of age. Postnatal CO exposure did not affect the acquisition and reacquisition of an active avoidance task. This is different from previous findings by the same laboratory, indicating that in utero exposure to CO (75 and 150 ppm) induced long-lasting learning and memory deficits.
Telfer et al. (2001, 193769)	Human Myometrium tissue obtained from gravid (pre-term [25- to 34 wk gestation], term not in labor or term in labor) and non-gravid women			cGMP was monitored in various myometrial tissues. cGMP was significantly higher than that from nonpregnant tissue and decreased at term, especially in tissue from laboring women.
Teran et al. (2005, 193770)	Rat Dahl/Rapp salt-sensitive rats Male		100 µM	A high-salt diet for 1-4 wk resulted in increased aortic HO-1 protein expression, an increase in mean arterial pressure, and time-dependent inhibition of flow- and acetylcholine-mediated vasodilation in isolated gracilis muscle arterioles. A smaller degree of inhibition of acetylcholine-mediated vasodilation was observed with a low-salt diet for 1-4 wk. Pretreatment with a HO inhibitor restored these responses, but this effect was reversed in the presence of exogenous CO. Mean arterial pressure was decreased in intact animals fed a high-salt diet for 4 wk and then treated with a HO inhibitor. The authors concluded that the HO-derived CO contributed to the development of hypertension and the impairment of endothelium-dependent vasodilator responses in this model.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Thom et al. (1994, 076459)	Rat Wistar Male Isolated blood cells	1 h Or >1 h 30 min	1,000 ppm Or 1,000-3,000 and higher ppm 0.5 mL of pure CO	CO poisoning inhibited B_2 integrin-dependent PMN adherence in heparinized blood obtained from rats immediately after exposure. Adherence was restored when platelet number was decreased. Adherence was also decreased when PMN from control animals were incubated with platelets from poisoned animals. Adherence of activated PMN was reduced in the presence of SOD and enhanced by NOS inhibition. Platelet production of NO was significantly greater while platelet NOS activity was significantly inhibited after poisoning. When whole blood or platelet-rich plasma was incubated with CO, PMN adherence was inhibited. The authors concluded that PMN B_2 integrin activity was inhibited by CO-dependent release of NO from the platelets into the blood.
Thom and Ischiropoulos (1997, 085644)	Ra Wistar Male 200-290 g Platelet-rich plasma from rats was used as the source of platelets Bovine pulmonary artery endothelial cells	1 h 30 min or 2 h 1 h	20-1,000 ppm 10-20 ppm 10-100 ppm	Platelets isolated from rats exposed to 20-1,000 ppm CO for 1-h released NO in a dose-dependent manner. COHb levels were 0.7% in controls and 3.2%, 7.8% and 51.0% in 20, 100 and 1,000 ppm exposure groups, respectively. Isolated platelets released NO when incubated for 30 min with 20-100 ppm CO. NOS activity was not enhanced by 100 ppm CO. Platelets released NO in response to 10-100 ppm CO after 30-min pretreatment with a NOS inhibitor, suggesting that CO displaces NO from heme-binding sites. Longer incubations (2 h) with the NOS inhibitor led to a diminished response to 100 ppm CO. There appears to be a discrepancy in the results, depending on howNOwas measured (electrode vs Greiss reaction). Endothelial cells released NO in response to 20-100 ppm CO. NOS inhibition blocked the response to 100 ppm CO. CO was found not to affect arginine transport or NOS activity in endothelial cells. Exposure to 40-100 ppm CO resulted in the release of short-lived oxidants. This response was blocked by NOS inhibition. Lysates from cells exposed to 50 and 100 ppm CO had increased nitrotyrosine content. This response was blocked by NOS inhibition. Cellular reduced sulfhydryls were not decreased by 100 ppm CO. Dihydrorhodamine 123 oxidation, a measure of peroxynitrite formation, was increased by exposure to 100 ppm CO. This effect was blocked by NOS inhibition. Cytotoxicity of CO was evaluated by the release of ^{51}chromium. Cytotoxicity was evident 4 h following a 2-h incubation with 100 ppm CO but not immediately after exposure. This response was not blocked by NOS inhibition, although NOS inhibition had protective effects under conditions of continuous CO exposure of 4 h. Exposure to 20 and 100 ppm CO for 2 h led to the loss of membrane integrity (measured by ethidium homodimer-1 staining) 18 h later. Results demonstrate that 10-20 ppm CO released NO from platelets and endothelial cells in vitro. Platelets from rats that inhaled 20 ppm CO also released NO in vitro. The authors suggested that CO-mediated NO release from platelets and endothelial cells resulted from disrupted intracellular scavenging for NO. They also suggested that peroxynitrite may have been generated in response to CO.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Thom et al. (1997, 084337)	Bovine pulmonary artery endothelial cells	30 min-4 h	10-100 ppm (11-110 nM)	One-h exposure to 111-110 nM CO led to a dose-dependent increase in NO release, as measured by nitrite+nitrate. Significance was achieved at 22 nM (corresponding to an interstitial partial pressure of 20 ppm and a blood COHb level of 7%). NOS inhibition blocked the response to 110 nM CO. A dose-dependent increase in cellular nitrotyrosine was also observed following a 2-h exposure to CO, with significance achieved at 55 nM CO. NOS inhibition blocked the response to 110 nM. CO exposure failed to decrease the concentration of reduced sulfhydryls but did result in the extracellular release of a short-lived oxidant species, which was blocked by NOS inhibition. Dihydrorhodamine oxidation, a measure of peroxynitrite formation, occurred in response to 110 nM CO, an effect which was blocked by NOS inhibition. Cytotoxicity of CO was evaluated by the release of ^{51} chromium. Cytotoxicity was evident 4 h following a 2-h incubation with 110 nM CO but not immediately after exposure. This response was not blocked by NOS inhibition, although NOS inhibition had protective effects under conditions of continuous CO exposure of 4 h. Exposure to 110 nM CO for 2 h led to the loss of membrane integrity (measured by ethidium homodimer-1 staining) 18 h later. This response was blocked by NOS inhibition. Exposure to 110 nM CO had no effect on O_2 consumption, production of intracellular $H2O_2$ or cellular redox activity. Exposure to 110 nM did not alter arginine transport or NOS activity. NO release from cells which had been pretreated with a NOS inhibitor and then exposed briefly to 5% CO was measured using a NO-selective electrode, suggesting that CO competed with intracellular binding sites of NO. The authors concluded that endothelial cells release NO and NO-derived oxidants in response to CO. A delayed cell death occurred following exposures to 22 nM and higher concentrations of CO.
Thom et al. (1999, 016753)	Rat Wistar Male 200-290 g Some rats were fed a high cholesterol diet	1 h	50-1,000 ppm	Nitrotyrosine immunoreactivity was found in aortic intima in rats exposed to CO for 1 h but not in controls. Nitrotyrosine content was quantitated and found to be increased in a dose-dependent manner following 1-h exposure to 50-1,000 ppm CO. The effect was significant at 50 ppm but the COHb content measured immediately after exposure was not different than controls. Platelet and neutrophil depletion did not alter nitrotyrosine content following CO exposure. Leukocyte adherence to the aorta occurred 18 h but not immediately after a 1-h exposure to 100 ppm CO. This effect was blocked by NOS inhibition. The influx of albumin from the microvasculature into skeletal muscle increased during the 3 h after exposure to 100 ppm CO but was not seen 18 h later. This effect was blocked by NOS inhibition. Rats fed a high-cholesterol diet and exposed to 100 ppm CO for 1 h had increased aortic nitrotyrosine content, which was not different than that in CO-exposed rats fed the standard diet. However, rats on the high-cholesterol diet had a six-fold increase in LDL oxidation immediately after 1-h exposure to 100 ppm CO. This effect was not blocked by NOS inhibition. The authors concluded that CO can alter vascular status by several mechanisms linked to NO-derived oxidants.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Thom et al. (1999, 016757)	Rat Wistar Male 200-290 g	1 h	50-1,000 ppm	Leakage of albumin into lung parenchyma occurred 18 h after rats were exposed to 100 ppm CO for 1 h. This response was not observed at earlier timepoints following CO exposure. This response was also observed using 50 and 1,000 ppm but not 20 ppm CO. Leakage resolved by 48 h. Furthermore, no leakage occurred when rats which were exposed to 100 ppm CO were pretreated with a NOS inhibitor. COHb levels were 0.9% in controls and 4.8%, 10.6% and 53.7% following 1-h exposure to 50, 100 and 1,000 ppm CO, respectively. Elevated free NO (determined by EPR) was observed in lungs of rats exposed to 100 ppm CO for 1 h. This effect was blocked when rats were pretreated with a NOS inhibitor. Lung H_2O_2 was elevated by exposure to 100 ppm CO for 1 h, and this effect was blocked when rats were pretreated with a NOS inhibitor. Elevated nitrotyrosine content was observed in lung homogenates 2-4 h following 1-h exposure of rats to 100 ppm CO. This effect was also blocked by pretreatment with a NOS inhibitor. No leukocyte sequestration was observed in lungs 18 h following exposure to 100 ppm CO. CO-induced lung leak was not affected by neutrophil depletion. The authors concluded that CO causes lung vascular injury which is dependent on NO.
Thom et al. (2000, 011574)	Bovine pulmonary artery endothelial cells	40 min-2 h	11-110 nM (10-100 ppm)	Increased uptake of ethidium homodimer-1, a measure of decreased membrane integrity and cell death, was observed in endothelial cells 18 h after exposure to 110 nM for 60-120 min. Exposures of 20-40 nM were ineffective in this regard. Ethidium uptake was also increased by 2-h exposure to 88 nM CO. Preincubation for 2 h with an inhibitor of eNOS, an antioxidant, and an inhibitor of peroxynitrite reactions blocked the CO-mediated cell death. Morphological changes in cells were observed 2 h following a 2-h exposure to 110 nM CO. Cell death induced by 110 nM CO was also blocked by inhibition of protein synthesis and inhibition of caspase-1 but of caspase-3. Caspase-1 activity was increased following 2-h exposure to 110 nM CO; this effect was blocked by inhibiting eNOS. Pre-exposure of cells to 11 nM CO for 40 min followed by a 3-h incubation period resulted in an increased level of MnSOD and protection against cell death 18 h following a 2-h exposure to 110 nM CO. The authors concluded that exposure to 11 nM CO led to an adaptive response which protected cells from injury and apoptosis resulting from NO-derived oxidants.
Thom et al. (2001, 193779)	Rat	Until lost consciousness	1,000-3,000 ppm	Neutrophils sequestration was observed in the brain vessels of rats exposed to high-dose CO. CO also led to increased nitrotyrosine formation in the brain vessels. These events were blocked by pretreatment with a peroxynitrite scavenger or a PAF receptor antagonist.
Thom et al. (2006, 098418)	Human Rat Wistar Male Mouse C57B6J MPO-deficient Blood samples and brain tissue	1 h	Humans: Acute CO poisoning Rats and mice: 1,000-3,000 ppm	In humans, COHb was 20-30.5%. Increased cell surface expression of CD18 and PAC1 was observed in neutrophils from people with CO poisoning. Increased surface-bound myeloperoxidase (MPO, indicative of neutrophil degranulation), increased plasma MPO, and more numerous platelet-neutrophil aggregates were also observed. Similar changes were observed in blood of CO-poisoned rats. Platelet depletion, inhibition of NOS, and inhibition of platelet integrin-dependent adhesion blocked these responses. Brains from poisoned rats had significant elevations in MPO, which could reflect either an increase number of neutrophils or an increase in neutrophil degranulation. Perivascular MPO and nitrotyrosine were CO-localized in brain. CO poisoning also resulted in altered brain myelin basic protein. Similar changes were observed in blood of CO-poisoned mice. MPO deficiency blocked the CO-mediated alteration in brain myelin basic protein. The authors concluded that exposure to CO triggers intravascular interactions between platelets and neutrophils that lead to neutrophil degranulation in experimental animals and people with CO poisoning.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Thorup et al. (1999, 193782)	Rat Sprague Dawley Male 200-250 g		0.01-10 µM	Perfusion of isolated rat renal resistance arteries with CO-containing buffer (0.001-10 µM) led to the biphasic release of NO, peaking at 100 nM and declining to undetectable responses at 10 µM. Sequential pulses of 100 nM resulted in a blunting of NO release with consecutive pulses, consistent with a depletion of intracellular NO stores. NO release was dependent on arginine concentrations and was inhibited by pretreatment with a NOS inhibitor. Perfusion with 100 nM CO blocked carbachol-dependent NO release from vessels. Rats were treated with a HO-1 inducer, and renal resistance arteries were isolated 12 h later. Carbachol-induced NO release was smaller in the HO-1-induced rats compared with controls, suggesting that endogenous CO has a similar effect as 100 nM exogenous CO. This effect was reversed in the presence of excess arginine. Vasodilation was measured in blood-perfused afferent arterioles perfused with CO in solution. A biphasic vasodilatory response was observed as well as a blunted muscarinic vasorelaxation. CO (0.1-10 µM) suppressed the release of NO from purified recombinant eNOS in solution. The authors concluded that low levels of CO may release NO and elicit vasorelaxation and modulate basal vascular tone, while higher levels of CO may inhibit eNOS and NO generation.
Tolcos et al. (2000, 015997)	Guinea pig	10 h/day over the last 60% of gestation	200 ppm	Fetal nd maternal COHb were 13% and 8.5%, respectively. Neurotransmitter systems were affected after CO exposure. The catecholaminergic system of the brainstem displayed significant decreases in immunoreactivity for tyrosine hydroxylase (TH), which was likely due to decreased cell number in specific medullar regions. The cholinergic system was also affected by prenatal CO exposure with significant increases in ChAT immunoreactivity of the medulla and no changes in muscarinic acetylcholine receptor.
Tolcos et al. (2000, 010468)	Guinea pig	10 h/day for the last 60% of gestation	200 ppm	Brains were collected at 1 and 8 wk of age. These data showed that CO exposure in utero sensitized the brain to hyperthermia at PND4 leading to generation of necrotic lesions in the brain and changes in neurotransmitter levels.
Toyada et al. (1996, 079945)				
Tschugguel et al. (2001, 193785)	Human HUVEC			CO was generated by primary endothelial cells from human umbilical veins and uterine arteries after exogenous 17-ß estradiol administration.
Vallone et al. (2004, 193993)	Mouse protein			The authors presented the X-ray structure of CO-bound ferrous murine Nb. When CO binds, the heme group slides deeper into the protein crevice.
Villamor et al. (2000, 015838)				
Vreman et al. (2000, 096915)	Human Umbilical cord (artery and vein) Rat Aorta, vena cavae, liver and heart			HO activity was quantified in human umbilical cord and in the rat vasculature (aorta and vena cavae). Human umbilical artery and vein HO activity were equal. The rat aorta and vena cavae produced equal amounts of HO activity (wet weight/g tissue) but generated 3 times greater HO than the heart and 0.2 times of the liver. HO activity in rat vasculature was 3 times that of the human cord tissues. Use of the HO inhibitor CrMP effectively blocked HO activity in the rat liver and heart but was less effective at blocking HO activity in the human umbilical cord or the rat vasculature (only 50% effective). The activity of HO in the umbilical vessels may provide a role for CO in control of vasculature tone during pregnancy.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Vreman et al. (2005, 193786)	Mouse BALB/c	30 min	500 ppm OR Heme arginate 30 µmol/kg body weight i.v.	Following CO exposure, COHb levels were 28%. Tissue concentrations of CO were as follows with control levels in parenthesis. Blood: 2648 ± 400 (45) pmol/mg Heart: 100 ±18 (6) pmol/mg Muscle: 14 ± 1 (10) pmol/mg Brain: 18 ± 4 (2) pmol/mg Kidney: 120 ± 12 (7) pmol/mg Spleen: 229 ± 55 (6) pmol/mg Liver: 115 ± 31 (5) pmol/mg Lung: 250 ± 2 (3) pmol/mg Intestine: 9 ± 7 (4) pmol/mg Testes: 6 ± 3 (2) pmol/mg CO concentration relative to 100% blood: Lung: 9.4%, Spleen: 8.6% Kidney: 4.5%, Liver: 4.3%, Heart: 3.8%, Brain: 0.7%, Muscle: 0.5%, Intestine: 0.3%, Testes: 0.2% Injection of heme arginate resulted in a threefold increase in CO excretion, reaching a maximum at 60 min. Animals were sacrificed at 90 min. COHb levels were 0.9%. Tissue concentrations of CO were as follows with control levels in parenthesis: Blood: 88 ±10 (45) pmol/mg Heart: 14 ± 3 (6) pmol/mg Muscle: 7 ± 1 (10) pmol/mg Brain: 2 ± 0 (2) pmol/mg Kidney: 7 ± 2 (7) pmol/mg Spleen: 11 ± 1 (6) pmol/mg Liver: 8 ± 3 (5) pmol/mg Lung: 8 ± 3 (3) pmol/mg Intestine: 3 ± 1 (4) pmol/mg Testes: 2 ± 0 (2) pmol/mg CO concentration relative to 100% blood: Heart: 16% Spleen: 13% Lung: 9% Liver: 9% Kidney: 8% Muscle: 8% Intestine: 3% Brain: 2% Testes: 2%
Weaver et al. (2007, 193939)	Human		Acute CO poisoning	Mean COHb in humans with acute CO poisoning was 35%. Hyperbaric O_2 reduces cognitive sequelae in a randomized clinical trial of CO-poisoned patients. Risk factors for cognitive sequelae without hyperbaric O_2 included older age and longer CO exposures. Patients with loss of consciousness or high initial COHb levels should also be treated with hyperbaric O_2.
Webber et al. (2003, 190515)	Rat (Strain not stated)	PND8-PND22	12.5, 25, or 50 ppm	Immunostaining of c-Fos, a marker of neuronal activation in the nervous system, was followed. C-Fos immunoreactivity in the central IC was significantly decreased in the CO-exposed animals at both PND27 and PND75-PND77 over all dose groups of CO; immnunostaining of other subregions of the IC were not affected by CO. These studies show exposure to CO during development can lead to permanent changes in the auditory system of rats that persist into adulthood.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Webber et al. (2005, 190514)	Rat (Strain not stated)	PND9-PND24	25 or 100 ppm	Neurofilament loss from the spiral ganglion neurons and somas after ARCO treatment was rescued (no detectable neurofilament loss) with low iron+CO (ARIDCO); ARID (low iron) treatment induced no change in neurofilaments. CuZn superoxide dismutase (SOD1) was significantly increased with CO exposure (ARCO) and rescued in ARIDCO animals; SOD1 was unchanged in low-iron-only animals (ARID). Low-iron treatment or CO exposure alone led to significant decreases in c-fos positive cell numbers of the central IC, but c-fos levels were unchanged after low-iron diet concomitant with CO exposure (ARIDCO).
Wellenius et al. (2004, 087874)	Rat Sprague Dawley 250 g Diazepam-sedated Model of acute MI induced by thermocoagulation	1 h, 12-18 h after surgery	35 ppm	CO exposure decreased ventricular premature beat frequency by 60.4% during the exposure period compared to controls. 1-h exposure to CAPs (318 $\mu g/m^3$) decreased ventricular premature beat frequency in specific subgroups. Neither CAPs nor CO had an effect on heart rate. There were no significant interactions between their effects when rats were exposed to both CO and CAPs.
Wellenius et al. (2006, 156152)	Rat Sprague Dawley 250 g Diazepam-sedated Model of acute MI induced by thermocoagulation	1 h, 12-18 h after surgery	35 ppm	Exposure to CO failed to increase the probability of observing supraventricular ectopic beats (SVEB). Exposure to CAPs (646 $\mu g/m^3$) for 1 h decreased the frequency of SVEB. There were no significant effects observed when rats were exposed to both CO and CAPs. Among a subset of rats with one or more SVEB at baseline, a significant decrease in number of SVEB during the exposure period was observed with either CO or CAPs exposure compared with controls.
Yoshiki et al.(2001, 193790)	Human			HO localization in human endometrium and its changes in expression over the menstrual cycle were explored in this study. HO-1 was constitutively expressed throughout the menstrual cycle, and HO-2 was greater in the secretory than the proliferative phase of the menstrual cycle. HO-1 was localized to the epithelial cells and macrophages. HO-2 was found in endothelial cells and smooth muscle cells of endometrial blood vessels.
Yu et al. (2008, 192384)	Guinea pig Allergic rhinitis model using nasal ovalbumin sensitization			Indicators of allergic rhinitis were enhanced by treatment with a HO-1 inducer and decreased by treatment with a HO-1 inhibitor. Immunoreactivity for HO-1 was shown in the lamina of mucosa of sensitized guinea pigs. Endogenous CO may play a role in the inflammation process of allergic rhinitis.
Zamudio et al. (1995, 193908)	Human			Women living at high altitude had an increased risk of adverse pregnancy outcomes vs women living at lower altitudes.
Zenclussen et al. (2006, 193873)	Mouse CBA/J x DBA/2J			To evaluate the role of HO-1 in spontaneous abortion, a mouse model that spontaneously undergoes abortion (CBA/J x DBA/2J mice) was used with and without HO adenovirus treatment to see if pregnancy outcome could be modulated by changing HO concentration. Pregnancy outcome was significantly better (abortion rate significantly decreased) in mice overexpressing HO due to adenovirus transfer.
Zhang et al. (2005, 184460)	Rat Pulmonary artery endothelial cells	8-28 h	15 ppm	Exposure to 15 ppm CO during anoxia resulted in decreased phosphorylation of STAT1 and increased phosphorylation of STAT3 at 8-24 h. Similar responses were observed when 24-h anoxia was followed by a period of reoxygenation (0.5-4 h). DNA binding of STAT1 was decreased while that of STAT3 was enhanced by CO treatment during anoxia/reoxygenation. Exposure to 15 ppm during 8-24-h anoxia or 24 h anoxia followed by 0.5-4 h reoxygenation resulted in increased phosphorylation of Akt and p38 MAPK. Inhibitor studies demonstrated that activation of the PI3K pathway by CO was upstream of p38 MAPK activation during anoxia/reoxygenation. Similarly, the PI3K and p38 MAPK pathways were found to be upstream of STAT modulation. The anti-apoptotic effects of 15 ppm CO during anoxia-reoxygenation involved decreased FAS expression and decreased caspase 3 acvitiry. These effects were dependent on activation of the PI3K, p38 MAPK and STAT3 pathways. The authors concluded that CO blocks anoxia-reoxygenation mediated apoptosis through modulation of PI3K/Akt/p38 MAPK and STAT1 and STAT3.

Reference	Species / Model	Exposure Duration	CO Concentration	Findings
Zhang et al. (2007, 193879)	Mouse			A single dose of LPS administered to pregnant mice induced up-regulation of HO-1 but not HO-2 in the mouse placenta 12-48 h postLPS treatment. Pretreatment of mice with the spin trap agent PBN or the TNF α inhibitor pentoxifylline prevented the LPS-dependent HO-1 upregulation. Thus ROS may mediate the LPS-dependent upregulation of HO-1.
Zhao et al. (2008, 193883)	Mouse FVB			With pregnancy, there was an increased blood volume without a concurrent increase in systemic BP; this was accomplished by a decrease in total vascular resistance, to which CO contributed as determined by using HO inhibitors.
Zhuo et al. (1993, 013905)	Guinea pig Adult male			Hippocampal LTP of brain sections is significantly affected by CO exposure with ZnPP IX, a HO inhibitor, blocking hippocampal LTP.
Zuckerbraun et al. (2007, 193884)	Macrophages RAW 264.7 THP-1 cells, wild-type and respiration-deficient	10 min-24 h	50-500 ppm	Exposure of RAW macrophages to 250 ppm CO for 10-60 min increased ROS generation, measured as dichlorofluorescein (DCF) fluorescence. ROS generation at 1 h was dose dependent with significant effects observed at 50, 250 and 500 ppm CO. This response was not blocked with a NOS inhibitor. A 1-h exposure to 250 ppm resulted in decreased intracellular glutathione levels. CO treatment was found to block TNFα production and to enhance p38 MAPK phosphorylation in LPS-stimulated cells. These effects were diminished by pretreatment with antioxidants. The source of CO-derived oxidants was determined to be mitochondrial since respiration-deficient THP-1 macrophages, unlike wild-type cells, failed to generate ROS in response to 250 ppm CO. Furthermore, treatment of RAW cells with the mitochondrial complex III inhibitor antimycin C, blocked ROS generation in response to 250 ppm CO. Exposure of RAW cells to 250 ppm CO for 1 h inhibited cytochrome c oxidase activity by 50%. Exposure to 250 ppm CO for 6 h had no effect on cellular ATP levels or mitochondrial membrane potential. Antimycin C treatment was found to reverse the effects of CO on LPS-mediated responses (TNFα and p38 MAPK), suggesting that mitochondrial-derived ROS mediated the effects of CO. The authors concluded that CO increased the generation of mitochondrial-derived ROS.

References

Acevedo CH; Ahmed A (1998). Hemeoxygenase-1 inhibits human myometrial contractility via carbon monoxide and is upregulated by progesterone during pregnancy. J Clin Invest, 101: 949-955. 016003

Achouh PE; Simonet S; Fabiani JN; Verbeuren TJ (2008). Carbon monoxide induces relaxation of human internal thoracic and radial arterial grafts. Interact Cardiovasc Thorac Surg, 7: 959-963. 179918

Ahmed A; Rahman M; Zhang X; Acevedo CH; Nijjar S; Rushton I; Bussolati B; St John J (2000). Induction of placental heme oxygenase-1 is protective against TNFalpha-induced cytotoxicity and promotes vessel relaxation. Mol Med, 6: 391-409. 193863

Ahmed H; McLaughlin BE; Soong J; Marks GS; Brien JF; Nakatsu K (2005). The source of endogenous carbon monoxide formation in human placental chorionic villi. Cell Mol Biol Incl Cyto Enzymol, 51: 447-451. 193865

Alexander PG; Chau L; Tuan RS (2007). Role of nitric oxide in chick embryonic organogenesis and dysmorphogenesis. Birth Defects Res A Clin Mol Teratol, 79: 581-594. 193869

Alexandreanu IC; Lawson DM (2002). Effects of chronic administration of a heme oxygenase substrate or inhibitor on progression of the estrous cycle, pregnancy and lactation of Sprague-Dawley rats. Life Sci, 72: 153-162. 192373

Alexandreanu IC; Lawson DM (2003). Heme oxygenase in the rat anterior pituitary: Immunohistochemical localization and possible role in gonadotropin and prolactin secretion. Exp Biol Med, 228: 64-69. 193871

Alexandreanu IC; Lawson DM (2003). Heme oxygenase in the rat ovary: Immunohistochemical localization and possible role in steroidogenesis. Exp Biol Med, 228: 59-63. 193876

Alonso JR; Cardellach F; Lopez S; Casademont J; Miro O (2003). Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. Pharmacol Toxicol, 93: 142-146. 193882

Andresen JJ; Shafi NI; Durante W; Bryan RM Jr (2006). Effects of carbon monoxide and heme oxygenase inhibitors in cerebral vessels of rats and mice. Am J Physiol Heart Circ Physiol, 291: H223-H230. 180449

Antonelli T; Tomasini MC; Tattoli M; Cassano T; Finetti S; Mazzoni E; Trabace L; Carratu MR; Cuomo V; Tanganelli S; Ferraro L (2006). Prenatal exposure to the cannabinoid receptor agonist WIN 55,212-2 and carbon monoxide reduces extracellular glutamate levels in primary rat cerebral cortex cell cultures. Neurochem Int, 49: 568-76. 194960

Appleton SD; Marks GS; Nakatsu K; Brien JF; Smith GN; Graham CH (2002). Heme oxygenase activity in placenta: Direct dependence on oxygen availability. Am J Physiol Heart Circ Physiol, 282: 2055-2059. 193935

Ashfaq M; Janjua MZ; Nawaz M (2003). Effects of maternal smoking on placental morphology . JAMC, 15: 1-5. 194002

Astrup P; Olsen HM; Trolle D; Kjeldsen K (1972). Effect of moderate carbon-monoxide exposure on fetal development. Lancet, 7789: 1220-1222. 011121

Bainbridge SA; Belkacemi L; Dickinson M; Graham CH; Smith GN (2006). Carbon monoxide inhibits hypoxia/reoxygenation-induced apoptosis and secondary necrosis in syncytiotrophoblast. Am J Pathol, 169: 774-783. 193949

Bainbridge SA; Farley AE; McLaughlin BE; Graham CH; Marks GS; Nakatsu K; Brien JF; Smith GN (2002). Carbon monoxide decreases perfusion pressure in isolated human placenta. Placenta, 23: 563-569. 043161

Bainbridge SA; Smith GN (2005). HO in pregnancy. Free Radic Biol Med, 38: 979-988. 193946

Bamberger A-M; Koglin M; Kempfert J; Loning T; Scholz H; Behrends S (2001). Expression and tissue localization of soluble guanylyl cyclase in the human placenta using novel antibodies directed against the alpha2 subunit. J Clin Endocrinol Metab, 86: 909-912. 016271

Barber A; Robson SC; Lyall F (1999). Hemoxygenase and nitric oxide synthase do not maintain human uterine quiescence during pregnancy. Am J Pathol, 155: 831-840. 193953

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISAs) and the Integrated Risk Information System (IRIS).

Barber A; Robson SC; Myatt L; Bulmer JN; Lyall F (2001). Heme oxygenase expression in human placenta and placental bed: reduced expression of placenta endothelial HO-2 in preeclampsia and fetal growth restriction. FASEB J, 15: 1158-68. 193891

Baum M; Schiff E; Kreiser D; Dennery PA; Stevenson DK; Rosenthal T; Seidman DS (2000). End-tidal carbon monoxide measurements in women with pregnancy-induced hypertension and preeclampsia. Am J Obstet Gynecol, 183: 900-903. 016435

Benagiano V; Lorusso L; Coluccia A; Tarullo A; Flace P; Girolamo F; Bosco L; Cagiano R; Ambrosi G (2005). Glutamic acid decarboxylase and GABA immunoreactivities in the cerebellar cortex of adult rat after prenatal exposure to a low concentration of carbon monoxide. Neuroscience, 135: 897-905. 180445

Benagiano V; Lorusso L; Flace P; Girolamo F; Rizzi A; Sabatini R; Auteri P; Bosco L; Cagiano R; Ambrosi G (2007). Effects of prenatal exposure to the CB-1 receptor agonist WIN 55212-2 or CO on the GABAergic neuronal systems of rat cerebellar cortex. Neuroscience, 149: 592-601. 193892

Bergeron M; Ferriero DM; Sharp FR (1998). Developmental expression of heme oxygenase-1 (HSP32) in rat brain: An immunocytochemical study. Dev Brain Res, 105: 181-194. 193967

Bing O; Grundemar L; Ny L; Moller C; Heilig M (1995). Modulation of carbon monoxide production and enhanced spatial learning by tin protoporphyrin. Neuroreport, 6: 1369-1372. 079418

Burmester T; Weich B; Reinhardt S; Hankeln T (2000). A vertebrate globin expressed in the brain. Nature, 407: 520-523. 099998

Bye A; Sørhaug S; Ceci M; Høydal MA; Stølen T; Heinrich G; Tjønna AE; Najjar SM; Nilsen OG; Catalucci D; Grimaldi S; Contu R; Steinshamn S; Condorelli G; Smith GL; Ellingsen O; Waldum H; Wisløff U (2008). Carbon monoxide levels experienced by heavy smokers impair aerobic capacity and cardiac contractility and induce pathological hypertrophy. Inhal Toxicol, 20: 635-646. 193777

Cagiano R; Ancona D; Cassano T; Tattoli M; Trabace L; Cuomo V (1998). Effects of prenatal exposure to low concentrations of carbon monoxide on sexual behaviour and mesolimbic dopaminergic function in rat offspring. Br J Pharmacol, 125: 909-915. 087170

Carmines E; Rajendran N (2008). Evidence for carbon monoxide as the major factor contributing to lower fetal weights in rats exposed to cigarette smoke. Toxicol Sci, 102: 383. 188440

Carratu MR; Cagiano R; De Salvia MA; Trabace L; Cuomo V (1995). Developmental neurotoxicity of carbon monoxide. Presented at In: Degen, G. H.; Seiler, J. P.; Bentley, P., eds. Toxicology in transition: proceedings of the 1994 EUROTOX congress; August 1994; Basel, Switzerland. Arch. Toxicol. Suppl. 17: 295-301. 079427

Carratu MR; Cagiano R; Desantis S; Labate M; Tattoli M; Trabace L; Cuomo V (2000). Prenatal exposure to low levels of carbon monoxide alters sciatic nerve myelination in rat offspring. Life Sci, 67: 1759-1772. 015839

Carratu MR; Cagiano R; Tattoli M; Trabace L; Borracci P; Cuomo V (2000). Prenatal exposure model simulating CO inhalation in human cigarette smokers: sphingomyelin alterations in the rat sciatic nerve. Toxicol Lett, 117: 101-106. 015935

Carratu MR; Renna G; Giustino A; De Salvia MA; Cuomo V (1993). Changes in peripheral nervous system activity produced in rats by prenatal exposure to carbon monoxide. Arch Toxicol, 67: 297-301. 013812

Carraway MS; Ghio AJ; Suliman HB; Carter JD; Whorton AR; Piantadosi CA (2002). Carbon monoxide promotes hypoxic pulmonary vascular remodeling. Am J Physiol, 282: L693-L702. 026018

Cella M; Farina MG; Sarmiento MIK; Chianelli M; Rosenstein RE; Franchi AM (2006). Heme oxygenase-carbon monoxide (HO-CO) system in rat uterus : Effect of sexual steroids and prostaglandins. J Steroid Biochem Mol Biol, 99: 59-66 . 193240

Chen GH; Kong J; Reinhard K; Fechter LD (2001). NMDA receptor blockage protects against permanent noise-induced hearing loss but not its potentiation by carbon monoxide . Hear Res, 154: 108-115. 193985

Cheng C; Noordeloos AM; Jeney V; Soares MP; Moll F; Pasterkamp G; Serruys PW; Duckers HJ (2009). Heme oxygenase 1 determines atherosclerotic lesion progression into a vulnerable plaque. Circulation, 119: 3017-3027. 193775

Chung Y; Huang SJ; Glabe A; Jue T (2006). Implication of CO inactivation on myoglobin function. Am J Physiol Lung Cell Mol Physiol, 290: 1616-1624. 193987

Cronje FJ; Carraway MS; Freiberger JJ; Suliman HB; Piantadosi CA (2004). Carbon monoxide actuates O2-limited heme degradation in the rat brain. Free Radic Biol Med, 37: 1802-1812. 180440

Cudmore M; Ahmad S; Al-Ani B; Fujisawa T; Coxall H; Chudasama K; Devey LR; Wigmore SJ; Abbas A; Hewett PW; Ahmed A (2007). Negative regulation of soluble Flt-1 and soluble endoglin release by heme oxygenase-1. Circulation, 36: 2973-2979. 193991

D'Amico G; Lam F; Hagen T; Moncada S (2006). Inhibition of cellular respiration by endogenously produced carbon monoxide. J Cell Sci, 119: 2291-2298. 193992

Dani C; Giannini L; Bertini G; Pratesi S; Corsini I; Longini M; Buonocore G; Masini E; Rubaltelli FF (2007). Changes of nitric oxide, carbon monoxide and oxidative stress in term infants at birth. Free Radic Res, 41: 1358-1363. 193994

Denschlag D; Marculescu R; Unfried G; Hefler LA; Exner M; Hashemi A; Riener EK; Keck C; Tempfer CB; Wagner O (2004). The size of a microsatellite polymorphism of the haem oxygenase 1 gene is associated with idiopathic recurrent miscarriage. Mol Hum Reprod, 10: 211-4. 193894

Dewilde S; Kiger L; Burmester T; Hankeln T; Baudin-Creuza V; Aerts T; Marden MC; Caubergs R; Moens L (2001). Biochemical characterization and ligand binding properties of neuroglobin, a novel member of the globin family. J Biol Chem, 276: 38949-38955. 019318

De Luca A; Pierno S; Tricarico D; Carratu MR; Cagiano R; Cuomo V; Camerino DC (1996). Developmental changes of membrane electrical properties of rat skeletal muscle fibers produced by prenatal exposure to carbon monoxide. Environ Toxicol Pharmacol, 2: 213-221. 080911

De Salvia MA; Cagiano R; Carratu MR; Di Giovanni V; Trabace L; Cuomo V (1995). Irreversible impairment of active avoidance behavior in rats prenatally exposed to mild concentrations of carbon monoxide. Psychopharmacology, 122: 66-71. 079441

Di Giovanni V; Cagiano R; De Salvia MA; Giustino A; Lacomba C; Renna G; Cuomo V (1993). Neurobehavioral changes produced in rats by prenatal exposure to carbon monoxide. Brain Res, 616: 126-131. 013822

Dubuis E; Gautier M; Melin A; Rebocho M; Girardin C; Bonnet P; Vandier C (2002). Chronic carbon monoxide enhanced IbTx-sensitive currents in rat resistance pulmonary artery smooth muscle cells. Am J Physiol Lung Cell Mol Physiol, 283: L120-L129. 193911

Dubuis E; Gautier M; Melin A; Rebocho M; Girardin C; Bonnet P; Vandier C (2003). Chronic carbon monoxide exposure of hypoxic rats increases in vitro sensitivity of pulmonary artery smooth muscle. Can J Physiol Pharmacol, 81: 711-719. 180439

Dubuis E; Potier M; Wang R; Vandier C (2005). Continuous inhalation of carbon monoxide attenuates hypoxic pulmonary hypertension development presumably through activation of BKCa channels. Cardiovasc Res, 65: 751-761. 180435

Durante W; Johnson FK; Johnson RA (2006). Role of carbon monoxide in cardiovascular function. J Cell Mol Med, 10: 672-686. 193778

Favory R; Lancel S; Tissier S; Mathieu D; Decoster B; Neviere R (2006). Myocardial dysfunction and potential cardiac hypoxia in rats induced by carbon monoxide inhalation. Am J Respir Crit Care Med, 174: 320-325. 184462

Fechter LD; Annau Z (1977). Toxicity of mild prenatal carbon monoxide exposure. Science, 197: 680-682. 010688

Fechter LD; Annau Z (1980). Prenatal carbon monoxide exposure alters behavioral development. Neurotoxicol Teratol, 2: 7-11. 011295

Fechter LD; Karpa MD; Proctor B; Lee AG; Storm JE (1987). Disruption of neostriatal development in rats following perinatal exposure to mild, but chronic carbon monoxide. Neurotoxicol Teratol, 9: 277-281. 012259

Fechter LD; Liu Y; Pearce TA (1997). Cochlear protection from carbon monoxide exposure by free radical blockers in the guinea pig. Toxicol Appl Pharmacol, 142: 47-55. 081322

Fechter LD; Mactutus CF; Storm JE (1986). Carbon monoxide and brain development. Neurotoxicology, 7: 463-473. 012030

Fechter LD; Thakur M; Miller B; Annau Z; Srivastava U (1980). Effects of prenatal carbon monoxide exposure on cardiac development. Toxicol Appl Pharmacol, 56: 370-375. 011294

Fechter LD; Thorne PR; Nuttall AL (1987). Effects of carbon monoxide on cochlear electrophysiology and blood flow. Hear Res, 27: 37-45. 012194

Garofolo MC; Seidler FJ; Auman JT; Slotkin TA (2002). beta-Adrenergic modulation of muscarinic cholinergic receptor expression and function in developing heart. Am J Physiol Regul Integr Comp Physiol, 282: R1356-1363. 193930

Gautier M; Antier D; Bonnet P; Le Net JL; Hanton G; Eder V (2007). Continuous inhalation of carbon monoxide induces right ventricle ischemia and dysfunction in rats with hypoxic pulmonary hypertension. Am J Physiol Heart Circ Physiol, 293: H1046-52. 096471

Gaworski CL; Carmines EL; Faqi AS; Rajendran N (2004). In utero and lactation exposure of rats to 1R4F reference cigarette mainstream smoke: Effect on prenatal and postnatal development. Toxicol Sci, 79: 157-169. 193933

Ghio AJ; Stonehuerner JG; Dailey LA; Richards JH; Madden MD; Deng Z; Nguyen NB; Callaghan KD; Yang F; Piantadosi CA (2008). Carbon monoxide reversibly alters iron homeostasis and respiratory epithelial cell function. Am J Respir Cell Mol Biol, 38: 715-723. 096321

Giustino A; Cagiano R; Carratu MR; Cassano T; Tattoli M; Cuomo V (1999). Prenatal exposure to low concentrations of carbon monoxide alters habituation and non-spatial working memory in rat offspring. Brain Res, 844: 201-205. 011538

Giustino A; Cagiano R; Carratu MR; De Salvia MA; Panaro MA; Jirillo E; Cuomo V (1993). Immunological changes produced in rats by prenatal exposure to carbon monoxide. Basic Clin Pharmacol Toxicol, 73: 274-278. 013833

Giustino A; Carratu MR; Brigiani GS; De Salvia MA; Pellegrino NM; Steardo L; Jirillo E; Cuomo V (1994). Changes in the frequency of splenic immunocompetent cells in rats exposed to carbon monoxide during gestation. Immunopharmacol Immunotoxicol, 16: 281-292. 076343

Glabe A; Chung Y; Xu D; Jue T (1998). Carbon monoxide inhibition of regulatory pathways in myocardium. Am J Physiol, 274: H2143-2151. 086704

Grover TR; Rairigh RL; Zenge JP; Abman SH; Kinsella JP (2000). Inhaled carbon monoxide does not cause pulmonary vasodilation in the late-gestation fetal limb. Am J Physiol, 278: L779-L784. 010465

Hara S; Mukai T; Kurosaki K; Kuriiwa F; Endo T (2002). Modification of the striatal dopaminergic neuron system by carbon monoxide exposure in free-moving rats, as determined by in vivo brain microdialysis. Arch Toxicol, 76: 596-605. 037497

Harada T; Koi H; Kubota T; Aso T (2004). Haem oxygenase augments porcine granulosa cell apoptosis in vitro. J Endocrinol, 181: 191-205. 193920

Hendler I; Baum M; Kreiser D; Schiff E; Druzin M; Stevenson DK; Seidman DS (2004). End-tidal breath carbon monoxide measurements are lower in pregnant women with uterine contractions. J Perinatol, 24: 275-278. 193925

Hofmann OM; Brittain T (1998). Partitioning of oxygen and carbon monoxide in the three human embryonic hemoglobins. Hemoglobin, 22: 313-319. 052019

Iheagwara KN; Thom SR; Deutschman CS; Levy RJ (2007). Myocardial cytochrome oxidase activity is decreased following carbon monoxide exposure. Biochim Biophys Acta, 1772: 1112-1116. 193861

Imai T; Morita T; Shindo T; Nagai R; Yazaki Y; Kurihara H; Suematsu M; Katayama S (2001). Vascular smooth muscle cell-directed overexpression of heme oxygenase-1 elevates blood pressure through attenuation of nitric oxide-induced vasodilation in mice. Circ Res, 89: 55-62. 193864

Ischiropoulos H; Beers MF; Ohnishi ST; Fisher D; Garner SE; Thom SR (1996). Nitric oxide production and perivascular tyrosine nitration in brain after carbon monoxide poisoning in the rat. J Clin Invest, 97: 2260-2267. 079491

Johnson FK; Durante W; Peyton KJ; Johnson RA (2003). Heme oxygenase inhibitor restores arteriolar nitric oxide function in Dahl rats. Hypertension, 41: 149-155. 193868

Johnson FK; Durante W; Peyton KJ; Johnson RA (2004). Heme oxygenase-mediated endothelial dysfunction in DOCA-salt, but not in spontaneously hypertensive, rat arterioles. Am J Physiol Heart Circ Physiol, 286: 1681-1687. 193870

Johnson FK; Johnson RA (2003). Carbon monoxide promotes endothelium-dependent constriction of isolated gracilis muscle arterioles. Am J Physiol, 285: R536-R541. 053611

Johnson FK; Johnson RA; Durante W; Jackson KE; Stevenson BK; Peyton KJ (2006). Metabolic syndrome increases endogenous carbon monoxide production to promote hypertension and endothelial dysfunction in obese Zucker rats. Am J Physiol Regul Integr Comp Physiol, 290: 601-608. 193874

Katoue MG; Khan I; Oriowo MA (2005). Increased expression and activity of heme oxygenase-2 in pregnant rat aorta is not involved in attenuated vasopressin-induced contraction. Naunyn Schmiedebergs Arch Pharmacol, 372: 220-7. 193896

Katoue MG; Khan I; Oriowo MA (2006). Pregnancy-induced modulation of calcium mobilization and down-regulation of Rho-kinase expression contribute to attenuated vassopressin-induced contraction of the rat aorta. Vascul Pharmacol, 44: 170-176. 193954

Khan AA; Wang Y; Sun Y; Mao XO; Xie L; Miles E; Graboski J; Chen S; Ellerby LM; Jin K; Greenberg DA (2006). Neuroglobin-overexpressing transgenic mice are resistant to cerebral and myocardial ischemia. PNAS, 103: 17944-17948. 193955

Kim HP; Wang X; Nakao A; Kim SI; Murase N; Choi ME; Ryter SW; Choi AM (2005). Caveolin-1 expression by means of p38beta mitogen-activated protein kinase mediates the antiproliferative effect of carbon monoxide. PNAS, 102: 11319-11324. 193959

Kim HS; Loughran PA; Rao J; Billar TR; Zuckerbraun BS (2008). Carbon monoxide activates NF-kappaB via ROS generation and Akt pathways to protect against cell death of hepatocytes. Am J Physiol Gastrointest Liver Physiol, 295: G146-G152. 193961

Kinobe R; Vlahakis J; Soong J; Szarek W; Brien J; Longo L; Nakatsu K (2006). Heme oxygenase activity in fetal and adult sheep is not altered by acclimatization to high altitude hypoxia. Can J Physiol Pharmacol, 84: 893 - 901. 188447

Knuckles TL; Lund AK; Lucas SN; Campen MJ (2008). Diesel exhaust exposure enhances venoconstriction via uncoupling of eNOS. Toxicol Appl Pharmacol, 230: 346-351. 191987

Korres S; Riga M; Balatsouras D; Papadakis C; Kanellos P; Ferekidis E (2007). Influence of smoking on developing cochlea: Does smoking during pregnancy affect the amplitudes of transient evoked otoacoustic emissions in newborns? Int J Pediatr Otorhinolaryngol, 71: 781-786. 190908

Kreiser D; Baum M; Seidman DS; Fanaroff A; Shah D; Hendler I; Stevenson DK; Schiff E; Druzin ML (2004). End tidal carbon monoxide levels are lower in women with gestational hypertension and pre-eclampsia. J Perinatol, 24: 213-217. 193948

Lash GE; McLaughlin BE; MacDonald-Goodfellow SK; Smith GN; Brien JF; Marks GS; Nakatsu K; Graham CH (2003). Relationship between tissue damage and heme oxygenase expression in chorionic villi of term human placenta. Am J Physiol Heart Circ Physiol, 284: H160-H167. 193849

Li X; Zhang C; Wang S; Ji Y; Wang H; Zhao L; Xu D (2008). Maternally administered lipopolysaccharide (LPS) upregulates the expression of heme oxygenase-1 in fetal liver: The role of reactive oxygen species. Toxicol Lett, 176: 169-177. 187003

Liu Y; Fechter LD (1995). MK-801 protects against carbon monoxide-induced hearing loss. Toxicol Appl Pharmacol, 132: 196-202. 076524

Loennechen JP; Beisvag V; Arbo I; Waldum HL; Sandvik AK; Knardahl S; Ellingsen O (1999). Chronic carbon monoxide exposure in vivo induces myocardial endothelin-1 expression and hypertrophy in rat. Pharmacol Toxicol, 85: 192-197. 011549

Longo M; Jain V; Vedernikov YP; Saade GR; Goodrum L; Facchinetti F; Garfield RE (1999). Effect of nitric oxide and carbon monoxide on uterine contractility during human and rat pregnancy. Am J Obstet Gynecol, 181: 981-988. 011548

Lopez I; Acuna D; Webber DS; Korsak RA; Edmond J (2003). Mild carbon monoxide exposure diminishes selectively the integrity of the cochlea of the developing rat. J Neurosci Res, 74: 666-75. 193901

Lopez IA; Acuna D; Beltran-Parrazal L; Espinosa-Jeffrey A; Edmond J (2008). Oxidative stress and the deleterious consequences to the rat cochlea after prenatal chronic mild exposure to carbon monoxide in air. Neuroscience, 151: 854-867. 097343

Lund AK; Knuckles TL; Obot Akata C; Shohet R; McDonald JD; Gigliotti A; Seagrave JC; Campen MJ (2007). Gasoline exhaust emissions induce vascular remodeling pathways involved in atherosclerosis. Toxicol Sci, 95: 485-94. 125741

Lund AK; Lucero J; Lucas S; Madden MC; McDonald JD; Seagrave JC; Knuckles TL; Campen MJ (2009). Vehicular emissions induce vascular MMP-9 expression and activity associated with endothelin-1 mediated pathways. Arterioscler Thromb Vasc Biol, 29: 511-517. 180257

Lyall F; Barber A; Myatt L; Bulmer JN; Robson SC (2000). Hemeoxygenase expression in human placenta and placental bed implies a role in regulation of trophoblast invasion and placental function. FASEB J, 14: 208-19. 193902

Lyall F; Myatt L (2002). The role of the placenta in pre-eclampsia -- a workshop report. Placenta, 23: S142-145. 193971

Mactutus CF; Fechter LD (1984). Prenatal exposure to carbon monoxide: learning and memory deficits. Science, 223: 409-411. 011355

McGregor HP; Westcott K; Walker DW (1998). The effect of prenatal exposure to carbon monoxide on breathing and growth of the newborn guinea pig. Pediatr Res, 43: 126-131. 085342

McLaughlin BE; Hutchinson JM; Graham CH; Smith GN; Marks GS; Nakatsu K; Brien JF (2000). Heme oxygenase activity in term human placenta. Placenta, 21: 870-873. 015815

McLaughlin BE; Lash GE; Graham CH; Smith GN; Vreman HJ; Stevenson DK; Marks GS; Nakatsu K; Brien JF (2001). Endogenous carbon monoxide formation by chorionic villi of term human placenta. Placenta, 22: 886-888. 193823

McLaughlin BE; Lash GE; Smith GN; Marks GS; Nakatsu K; Graham CH; Brien JF (2003). Heme oxygenase expression in selected regions of term human placenta. Exp Biol Med, 228: 564-567. 193827

McLean M; Bowman M; Clifton V; Smith R; Grossman AB (2000). Expression of the heme oxygenase - carbon monoxide signalling system in human placenta. J Clin Endocrinol Metab, 85: 2345-2349. 016269

Melin A; Bonnet P; Eder V; Antier D; Obert P; Fauchier L (2005). Direct implication of carbon monoxide in the development of heart failure in rats with cardiac hypertrophy subjected to air pollution. Cardiovasc Toxicol, 5: 311-320. 193833

Melin A; Obert P; Rebocho M; Bonnet P (2002). Cardiac morphology and function following long-term exposure to carbon monoxide at high altitude in rats. J Toxicol Environ Health A Curr Iss, 65: 1981-1998. 037502

Mereu G; Cammalleri M; Fà M; Francesconi W; Saba P; Tattoli M; Trabace L; Vaccari A; Cuomo V (2000). Prenatal exposure to a low concentration of carbon monoxide disrupts hippocampal long-term potentiation in rat offspring. J Pharmacol Exp Ther, 294: 728-734. 193838

Middendorff R; Kumm M; Davidoff MS; Holstein AF; Muller D (2000). Generation of cyclic guanosine monophosphate by heme oxygenases in the human testis--a regulatory role for carbon monoxide in Sertoli cells? Biol Reprod, 63: 651-657. 015842

Montagnani M; Serio M; Potenza MA; Mansi G; De Salvia MA; Cagiano R; Cuomo V; Mitolo-Chieppa D (1996). Prenatal exposure to carbon monoxide and vascular responsiveness of rat resistance vessels. Life Sci, 59: 1553-1561. 080902

Naik JS; Walker BR (2003). Heme oxygenase-mediated vasodilation involves vascular smooth muscle cell hyperpolarization. Am J Physiol Heart Circ Physiol, 285: 220-228. 193852

Ndisang JF; Tabien HE; Wang R (2004). Carbon monoxide and hypertension. Am J Hypertens, 22: 1057-1074. 180425

Neggers YH; Singh J (2006). Zinc supplementation to protein-deficient diet in CO-exposed mice decreased fetal mortality and malformation. Biol Trace Elem Res, 114: 269-279. 193964

Newby D; Cousins F; Myatt L; Lyall F (2005). Heme oxygenase expression in cultured human trophoblast cells during in vitro differentiation: Effects of hypoxia. Placenta, 26: 201-209. 193966

Odrcich MJ; Graham CH; Kimura KA; McLaughlin BE; Marks GS; Nakatsu K; Brien JF (1998). Heme oxygenase and nitric oxide synthase in the placenta of the guinea-pig during gestation. Placenta, 19: 509-516. 193958

Ozawa N; Goda N; Makino N; Yamaguchi T; Yoshimura Y; Suematsu M (2002). Leydig cell-derived heme oxygenase-1 regulates apoptosis of premeiotic germ cells in response to stress. J Clin Invest, 109: 457-467. 193841

Patel AP; Moody JA; Handy RD; Sneyd JR (2003). Carbon monoxide exposure in rat heart: glutathione depletion is prevented by antioxidants. Biochem Biophys Res Commun, 302: 392-396. 043155

Penney DG; Baylerian MS; Thill JE; Fanning CM; Yedavally S (1982). Postnatal carbon monoxide exposure: immediate and lasting effects in the rat. Am J Physiol, 243: H328-H339. 011387

Penney DG; Baylerian MS; Thill JE; Yedavally S; Fanning CM (1983). Cardiac response of the fetal rat to carbon monoxide exposure. Am J Physiol, 244: H289-H297. 011385

Piantadosi CA (2002). Biological chemistry of carbon monoxide. Antioxid Redox Signal, 4: 259-270. 037463

Piantadosi CA (2008). Carbon monoxide, reactive oxygen signaling, and oxidative stress. Free Radic Biol Med, 45: 562-569. 180423

Piantadosi CA; Carraway MS; Suliman HB (2006). Carbon monoxide, oxidative stress, and mitochondrial permeability pore transition. Free Radic Biol Med, 40: 1332-1339. 180424

Prigge E; Hochrainer D (1977). Effects of carbon monoxide inhalation on erythropoiesis and cardiac hypertrophy in fetal rats. Toxicol Appl Pharmacol, 42: 225-228. 012326

Raub JA; Benignus VA (2002). Carbon monoxide and the nervous system. Neurosci Biobehav Rev, 26: 925-940. 041616

Richardson RS; Noyszewski EA; Saltin B; Gonzalez-Alonso J (2002). Effect of mild carboxy-hemoglobin on exercising skeletal muscle: Intravascular and intracellular evidence. Am J Physiol, 283: R1131-R1139. 037513

Ryter SW; Alam J; Choi AMK (2006). Heme oxygenase-1/carbon monoxide: From basic science to therapeutic applications. Physiol Rev, 86: 583-650. 193765

Sartiani L; Cerbai E; Lonardo G; DePaoli P; Tattoli M; Cagiano R; Carratu M; Cuomo V; Mugelli A (2004). Prenatal exposure to carbon monoxide affects postnatal cellular electrophysiological maturation of the rat heart: a potential substrate for arrhythmogenesis in infancy. Circulation, 109-: 419-423. 190898

Schwetz BA; Smith FA; Leong BKJ; Staples RE (1979). Teratogenic potential of inhaled carbon monoxide in mice and rabbits. Teratology, 19: 385-391. 011855

Shaoqing Y; Ruxin Z; Yinjian C; Jianqiu C; Chunsheng Z; Jiangfeng T; Genhong L (2008). Possible contribution of endogenous carbon monoxide to the development of allergic rhinitis in guinea pigs. J Inflamm, 5: 23. 192384

Singh J (1986). Early behavioral alterations in mice following prenatal carbon monoxide exposure. Neurotoxicology, 7: 475-481. 012827

Singh J (2003). Gastroschisis is caused by the combination of carbon monoxide and protein-zinc deficiencies in mice. Birth Defects Res B Dev Reprod Toxicol, 68: 355-362. 053624

Singh J (2006). Interaction of maternal protein and carbon monoxide on pup mortality in mice: implications for global infant mortality. Birth Defects Res B Dev Reprod Toxicol, 77: 216-26. 190512

Singh J; Aggison L Jr; Moore-Cheatum L (1993). Teratogenicity and developmental toxicity of carbon monoxide in protein-deficient mice. Teratology, 48: 149-159. 013892

Singh J; Scott LH (1984). Threshold for carbon monoxide induced fetotoxicity. Teratology, 30: 253-257. 011409

Singh J; Smith CB; Moore-Cheatum L (1992). Additivity of protein deficiency and carbon monoxide on placental carboxyhemoglobin in mice. Am J Obstet Gynecol, 167: 843-846. 013759

Sitdikova GF; Islamov RR; Mukhamedyarov MA; Permyakova VV; Zefirov AL; Palotas A (2007). Modulation of neurotransmitter release by carbon monoxide at the frog neuro-muscular junction. Curr Drug Metab, 8: 177-184. 180417

Song R; Mahidhara RS; Liu F; Ning W; Otterbein LE; Choi AMK (2002). Carbon monoxide inhibits human airway smooth muscle cell proliferation via mitogen-activated protein kinase pathway. Am J Respir Cell Mol Biol, 27: 603-610. 037531

Sorhaug S; Steinshamn S; Nilsen OG; Waldum HL (2006). Chronic inhalation of carbon monoxide: Effects on the respiratory and cardiovascular system at doses corresponding to tobacco smoking. Toxicology, 228: 280-290. 180414

Stevens CF; Wang Y (1993). Reversal of long-term potentiation by inhibitors of haem oxygenase. Nature, 364: 147-149. 188458

Stockard-Sullivan JE; Korsak RA; Webber DS; Edmond J (2003). Mild carbon monoxide exposure and auditory function in the developing rat. J Neurosci Res, 74: 644-654. 190947

Storm JE; Fechter LD (1985). Alteration in the postnatal ontogeny of cerebellar norepinephrine content following chronic prenatal carbon monoxide. J Neurochem, 45: 965-969. 011653

Storm JE; Fechter LD (1985). Prenatal carbon monoxide exposure differentially affects postnatal weight and monoamine concentration of rat brain regions. Toxicol Appl Pharmacol, 81: 139-146. 011652

Storm JE; Valdes JJ; Fechter LD (1986). Postnatal alterations in cerebellar GABA content, GABA uptake and morphology following exposure to carbon monoxide early in development. Dev Neurosci, 8: 251-261. 012136

Styka PE; Penney DG (1978). Regression of carbon monoxide-induced cardiomegaly. Am J Physiol, 235: H516-H522. 011166

Suliman HB; Carraway MS; Tatro LG; Piantadosi CA (2007). A new activating role for CO in cardiac mitochondrial biogenesis. J Cell Sci, 120: 299-308. 193768

Sun Y; Jin K; Mao XO; Zhu Y; Greenberg DA (2001). Neuroglobin is up-regulated by and protects neurons from hypoxic-ischemic injury. PNAS, 98: 15,306-15,311. 026022

Tattoli M; Carratu MR; Cassano T; Cortese I; Di Giovanni V; Elia G; Renna G; Cagiano R (1999). Effects of early postnatal exposure to low concentrations of carbon monoxide on cognitive functions in rats. Pharmacol Res, 40: 271-274. 011557

Telfer JF; Itoh H; Thomson AJ; Norman JE; Nakao K; Campa JS; Poston L; Tribe RM; Magness RR (2001). Activity and expression of soluble and particulate guanylate cyclases in myometrium from nonpregnant and pregnant women: down-regulation of soluble guanylate cyclase at term. J Clin Endocrinol Metab, 86: 5934-5943. 193769

Teran FJ; Johnson RA; Stevenson BK; Peyton KJ; Jackson KE; Appleton SD; Durante W; Johnson FK (2005). Heme oxygenase-derived carbon monoxide promotes arteriolar endothelial dysfunction and contributes to salt-induced hypertension in Dahl salt-sensitive rats. Am J Physiol Regul Integr Comp Physiol, 288: 615-622. 193770

Thom SR; Bhopale VM; Han ST; Clark JM; Hardy KR (2006). Intravascular neutrophil activation due to carbon monoxide poisoning. Am J Respir Crit Care Med, 174: 1239-1248. 098418

Thom SR; Fisher D; Manevich Y (2001). Roles for platelet-activating factor and NO-derived oxidants causing neutrophil adherence after CO poisoning. Am J Physiol Heart Circ Physiol, 281: H923-H930. 193779

Thom SR; Fisher D; Xu YA; Garner S; Ischiropoulos H (1999). Role of nitric oxide-derived oxidants in vascular injury from carbon monoxide in the rat. Am J Physiol, 276: H984-H992. 016753

Thom SR; Fisher D; Xu YA; Notarfrancesco K; Ischiropoulos H (2000). Adaptive responses and apoptosis in endothelial cells exposed to carbon monoxide. PNAS, 97: 1305-1310. 011574

Thom SR; Ischiropoulos H (1997). Mechanism of oxidative stress from low levels of carbon monoxide. Health Effects Institute. Boston, MA. 085644

Thom SR; Ohnishi ST; Fisher D; Xu YA; Ischiropoulos H (1999). Pulmonary vascular stress from carbon monoxide. Toxicol Appl Pharmacol, 154: 12-19. 016757

Thom SR; Ohnishi ST; Ischiropoulos H (1994). Nitric oxide released by platelets inhibits neutrophil B2 integrin function following acute carbon monoxide poisoning. Toxicol Appl Pharmacol, 128: 105-110. 076459

Thom SR; Xu YA; Ischiropoulos H (1997). Vascular endothelial cells generate peroxynitrite in response to carbon monoxide exposure. Chem Res Toxicol, 10: 1023-1031. 084337

Thorup C; Jones CL; Gross SS; Moore LC; Goligorsky MS (1999). Carbon monoxide induces vasodilation and nitric oxide release but suppresses endothelial NOS. Am J Physiol, 277: F882-F889. 193782

Tolcos M; Mallard C; McGregor H; Walker D; Rees S (2000). Exposure to prenatal carbon monoxide and postnatal hyperthermia: short and long-term effects on neurochemicals and neuroglia in the developing brain. Exp Neurol, 162: 235-246. 010468

Tolcos M; McGregor H; Walker D; Rees S (2000). Chronic prenatal exposure to carbon monoxide results in a reduction in tyrosine hydroxylase-immunoreactivity and an increase in choline acetyltransferase-immunoreactivity in the fetal medulla: implications for sudden infant death syndrome. J Neuropathol Exp Neurol, 59: 218-228. 015997

Toyoda M; Saito H; Matsuki N (1996). Nitric oxide but not carbon monoxide is involved in spatial learning of mice. J Pharmacol Sci, 71: 205-211. 079945

Tschugguel W; Stonek F; Zhegu Z; Dietrich W; Schneeberger C; Stimpfl T; Waldhoer T; Vycudilik W; Huber JC (2001). Estrogen increases endothelial carbon monoxide, heme oxygenase 2, and carbon monoxide-derived cGMP by a receptor-mediated system. J Clin Endocrinol Metab, 86: 3833-3839. 193785

Vallone B; Nienhaus K; Matthes A; Brunori M; Nienhaus GU (2004). The structure of carbonmonoxy neuroglobin reveals a heme-sliding mechanism for control of ligand affinity. PNAS, 101: 17351-17356. 193993

Villamor E; Perez-Vizcaino F; Cogolludo AL; Conde-Oviedo J; Zaragoza-Arnaez F; Lopez-Lopez JG; Tamargo J (2000). Relaxant effects of carbon monoxide compared with nitric oxide in pulmonary and systemic vessels of newborn piglets. Pediatr Res, 48: 546-553. 015838

Vreman HJ; Wong RJ; Kadotani T; Stevenson DK (2005). Determination of carbon monoxide (CO) in rodent tissue: effect of heme administration and environmental CO exposure. Anal Biochem, 341: 280-289. 193786

Vreman HJ; Wong RJ; Kim EC; Nabseth DC; Marks GS; Stevenson DK (2000). Haem oxygenase activity in human umbilical cord and rat vascular tissues. Placenta, 21: 337-44. 096915

Weaver LK; Valentine KJ; Hopkins RO (2007). Carbon monoxide poisoning: risk factors for cognitive sequelae and the role of hyperbaric oxygen. Am J Respir Crit Care Med, 176: 491 - 497. 193939

Webber D; Lopez I; Korsak R; Hirota S; Acuna D; Edmond J (2005). Limiting iron availability confers neuroprotection from chronic mild carbon monoxide exposure in the developing auditory system of the rat. J Neurosci Res, 80: 620-633. 190514

Webber DS; Korsak RA; Sininger LK; Sampogna SL; Edmond J (2003). Mild carbon monoxide exposure impairs the developing auditory system of the rat. J Neurosci Res, 74: 655-665. 190515

Wellenius GA; Batalha JRF; Diaz EA; Lawrence J; Coull BA; Katz T; Verrier RL; Godleski JJ (2004). Cardiac effects of carbon monoxide and ambient particles in a rat model of myocardial infarction. Toxicol Sci, 80: 367-376. 087874

Wellenius GA; Coull BA; Batalha JRF; Diaz EA; Lawrence J; Godleski JJ (2006). Effects of ambient particles and carbon monoxide on supraventricular arrhythmias in a rat model of myocardial infarction. Inhal Toxicol, 18: 1077-1082. 156152

Yoshiki N; Kubota T; Aso T (2001). Identification of heme oxygenase in human endometrium. J Clin Endocrinol Metab, 86: 5033-5038. 193790

Zamudio S; Palmer SK; Dahms TE; Berman JC; Young DA; Moore LG (1995). Alterations in uteroplacental blood flow precede hypertension in preeclampsia at high altitude. J Appl Physiol, 79: 15-22. 193908

Zenclussen ML; Anegon I; Bertoja AZ; Chauveau C; Vogt K; Gerlof K; Sollwedel A; Volk HD; Ritter T; Zenclussen AC (2006). Over-expression of heme oxygenase-1 by adenoviral gene transfer improves pregnancy outcome in a murine model of abortion. Am J Reprod Immunol, 69: 35-52. 193873

Zhang C; Li XY; Zhao L; Wang H; Xu DX (2007). Lipopolysaccharide (LPS) up-regulates the expression of haem oxygenase-1 in mouse placenta. Placenta, 28: 951-957. 193879

Zhang X; Shan P; Alam J; Fu XY; Lee PJ (2005). Carbon monoxide differentially modulates STAT1 and STAT3 and inhibits apoptosis via a phosphatidylinositol 3-kinase/akt and p38 kinase-dependent STAT3 pathway during anoxia-reoxygenation injury. J Biol Chem, 280: 8714-8721. 184460

Zhao H; Wong RJ; Doyle TC; Nayak N; Vreman HJ; Contag CH; Stevenson DK (2008). Regulation of maternal and fetal hemodynamics by heme oxygenase in mice. Biol Reprod, 78: 744-751. 193883

Zhuo M; Small SA; Kandel ER; Hawkins RD (1993). Nitric oxide and carbon monoxide produce activity-dependent long-term synaptic enhancement in hippocampus. Science, 260: 1946-1950. 013905

Zuckerbraun BS; Chin BY; Bilban M; d'Avila JC; Rao J; Billiar TR; Otterbein LE (2007). Carbon monoxide signals via inhibition of cytochrome c oxidase and generation of mitochondrial reactive oxygen species. FASEB J, 21: 1099-1106. 193884