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TRABAJO DE PASANTÍA:

ESTIMACIÓN CUANTITATIVA DE RIESGO ATRIBUIBLE A SO_2 EN ZONAS VULNERABLES DE CHILE

MACARENA VALDÉS SALGADO

Programa de Doctorado en Salud Pública

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Departamento de Normas

División de Calidad del Aire y Cambio Climático

Ministerio del Medio Ambiente

Carmen Gloria Conteras, Jefe del Departamento de Normas

Cristián Ibarra, responsable revisión de la norma calidad de SO_2

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RESUMEN

El dióxido de azufre impacta sobre la calidad del aire y subsecuentemente sobre la salud de las personas, especialmente en áreas de zona industrial donde la combustión de energía fósil es común. Efectos a corto plazo del dióxido de azufre provenientes de estudios toxicológicos, reunidos en el estudio AHW, proveen extensa y sólida evidencia sobre el efecto de concentraciones mínimas sobre la salud[1]. En humanos este daño, implica cambios en la función pulmonar que llegan a ser irreversibles en poblaciones vulnerables tales como los asmáticos. Efectos a largo plazo se han asociado a eventos como aumento de la mortalidad general, enfermedad respiratoria y enfermedad cardiovascular.

Una forma de estimar o evaluar los eventos adversos que ocurren en determinados escenarios, se realiza a través del análisis de riesgo. El análisis de riesgo o evaluación de riesgo permite cuantificar los eventos de salud atribuibles a la polución y que pueden ser evitados en la medida que se establezcan normativas orientadas a la disminución de los contaminantes. Dicho lo anterior, las normas primaria de calidad de aire son instrumentos que utilizan los países para proteger la salud de las personas. Normas sustentadas en la evidencia científica que incorporan elementos como el análisis de riesgo, son consistentes con una gobernanza sustentable.

El objetivo de este informe es aportar en el proceso de revisión de la norma primaria de la calidad del aire para dióxido de azufre (SO_2) que lleva a cabo el Ministerio del Medio Ambiente. Su contribución es estimar cuantitativamente el riesgo en salud asociado a la exposición a dióxido de azufre, en cuanto a cuatro eventos de salud: mortalidad general, mortalidad infantil, asma en niños y consultas de urgencia por eventos respiratorios en niños, en 10 zonas vulnerables de Chile. Esto permitirá conocer el número de casos atribuibles a la polución por dióxido de azufre así como el riesgo relativo asociado a distintos escenarios de normas.

[1] Health Effects Associated with Short-term Exposure to Low Levels of Sulphur Dioxide (SO2) – A Technical Review. Alberta Health and Wellness, Health Surveillance, Edmonton, Alberta. Canadá (2006). ISBN 0-7785-3480-4. www.health.gov.ab.ca

INTRODUCCIÓN

La contaminación del ecosistema afecta el desarrollo de la comunidad así como su salud, aumentado la morbilidad y mortalidad asociada a polución. Lo anterior involucra la gestión de políticas públicas orientadas a resguardar el derecho a un ambiente saludable y próspero, lo cual es consistente con el discurso de la Organización Panamericana de Salud, la prevención de riesgos modernos y el desarrollo de una gobernanza sustentable (1, 2).

El dióxido de azufre (SO_2) es un gas incoloro, de olor penetrante generado en la combustión de fósiles como carbón o petróleo y en la fundición de menas que contienen azufre. La fuente principal de SO_2 antropogénico, se debe a la combustión de fósiles que contienen azufre usados principalmente para la calefacción doméstica, la generación de electricidad y los vehículos a motor (3), actividades comunes y necesarias en el mundo de hoy. En Chile, la actividad industrial de fundiciones de cobre (Cu) y termoeléctricas, se asocian a la contaminación por SO_2.

Existe evidencia científica sobre los efectos en salud que tiene SO_2, tanto agudos como crónicos. El SO_2, afecta el sistema respiratorio a nivel de epitelio, lo que se traduce en cambios en la función pulmonar debido a la cascada inflamatoria producida por este contaminante. Una concentración ambiental alta en el aire respirable de este compuesto, tiene efectos agudos evidentes como irritación de ojos, tos, secreción mucosa y agravamiento del asma en el caso de individuos aquejados por esta afección; esto genera un aumento en la propensión de la población general a contraer infecciones del sistema respiratorio así como un agravamiento de la condición de base de pacientes aquejados por asma y otras afecciones respiratorias (4). Los ingresos hospitalarios aumentan en los días en que los niveles de SO_2 son más elevados. Efectos crónicos del SO_2 se han asociados a eventos respiratorios, cardiovasculares y aumento de la mortalidad general (5). En el ecosistema, el SO_2 en combinación con el agua, se convierte en ácido sulfúrico, que es el principal componente de la lluvia ácida causante causante de acidificación de los suelos y de la deforestación (6).

Agencias y organismos reguladores como la Agencia de Protección Ambiental de Estados Unidos (US-EPA) o la Organización Mundial de la Salud (OMS), recomiendan valores de referencia que eviten los efectos adversos de la exposición a SO_2 (75 ppb, equivalente a 196,5 ug/m^3 de exposición a SO_2 a nivel horario es lo señalado por US-EPA; 125 ug/m^3 de exposición a SO_2 por 24 horas es lo señalado por la OMS). Sin embargo estos valores representan un desafío para países como el nuestro, donde actividades económicas relevantes, tales como la generación de electricidad por termoeléctricas y la producción de cobre fino a través de las fundiciones, genera SO_2 al ambiente.

Por lo tanto las regulaciones y normas de calidad de aire representan conjuntamente instrumentos de prevención de eventos en salud tanto crónicos como agudos. En Chile, la norma primaria referente al SO_2 en aire indica valores de 80 ug/m^3 de exposición promedio anual, y de 250 ug/m^3 de exposición promedio de 24 horas. Los registros nacionales, indican que estos valores varían dependiendo de las fuentes de contaminación asociadas a las zonas de monitoreo. Dicho lo anterior, es necesario estimar el riesgo atribuible a SO_2 en zonas vulnerables mediante un análisis de riesgo de modo de conocer la distribución de estos eventos de salud a nivel comunal y no tan sólo a nivel nacional. Por lo tanto, el objetivo general de este informe es aportar en el proceso de revisión de la norma primaria para dióxido de azufre (SO_2) estimando cuantitativamente el riesgo en salud asociado a la exposición a dióxido de azufre, considerando para ello cuatro eventos de salud: mortalidad general, mortalidad infantil, asma en niños y consultas de urgencia por eventos respiratorios. Esto se realizara en 10 zonas consideradas como vulnerables y de interés para el Ministerio del Medio Ambiente, debido a su cercanía a importantes núcleos industriales que son fuentes emisoras de este contaminante (principalmente termoeléctricas y fundiciones). Para la cuantifiación de casos atribuibles a la contaminación se usaron las funciones de dosis respuesta reportadas en la revisión de literatura científica realizada por el Centro Nacional de Medio Ambiente[2] (7), paro los 4 efectos estudiados: mortalidad general, mortalidad infantil y asma en niños como eventos crónicos y visitas a urgencia por asma en niños como evento agudo.

[2] Centro Nacional del Medio Ambiente. Informe preparado para el Ministerio de Medio Ambiente “Análisis de Antecedentes y Evaluación Técnica-Económica para Revisar la Norma Primaria de Calidad del Aire de Dióxido de Azufre (SO2).Diciembre, 2014; Capítulo 3.

OBJETIVOS

Objetivo General

-Estimar el riesgo atribuible a dióxido de azufre (SO_2) en zonas consideradas vulnerables y de interés pare el Ministerio del Medio Ambiente, mediante análisis de riesgo

Objetivos específicos

- Analizar la revisión de literatura científica en documentos asociados a la norma primaria de SO_2 y seleccionar evidencia científica para cuantificación de casos atribuibles.

- Estimar casos atribuibles a polución en efectos agudos y crónicos a través de una medida de impacto de salud pública.

- Identificar variables confusoras y modificadoras de efecto relacionadas con los efectos estudiados.

- Comparar la estimación de casos atribuibles en distintas comunas.

CAPITULO 1. Evaluación de Riesgo

Para la evaluación de riesgo, se escogieron 3 eventos crónicos: Mortalidad General, Mortalidad Infantil, y Asma en niños; y 1 evento agudo: Visitas diarias a urgencia por asma en niños. Se usaron estos efectos en salud dada la disponibilidad de datos para la estimación de casos atribuibles a la polución. Otros efectos mencionados en la revisión de la literatura realizada en el informe realizado por el CENMA[2], tales como hipertensión en el embarazo, polimorfismo y resistencia a la insulina, malformaciones congénitas, implante de desfibrilador cardiaco o arritmias por mencionar algunos, no fueron estudiados ya que no hay disponibilidad de registros centralizados e institucionales a nivel nacional, regional o comunal sobre tasa de basal o prevalencia de estos eventos ni tampoco existe casuística de corto, mediano o largo plazo, para la estimación de eventos atribuibles.

Para el cálculo de los eventos evitables, se utilizaron los siguientes datos y sus respectivas fuentes (Tabla 1):

Tabla 1. Datos usados para la estimación de casos atribuibles a la polución y fuente de referencia.

Dato	Fuente
Población total por comuna, 2011	Departamento de Estadística e Información en Salud (DEIS)[3]. Se considera este año dado que se cuenta con información completa
Nacidos vivos inscritos según peso al nacer, por Región y Comuna de residencia de la madre. Chile, 2011	Departamento de Estadística e Información en Salud (DEIS). Se considera este año dado que se cuenta con información completa
Población menor a 15 años	Estimación propia. Se aplica la prevalencia de niños entre 0 y 14 años por región estimada por el Instituto Nacional de estadística para calcular la cantidad de niños por comuna.
Tasa de mortalidad general por región	Documento de Indicadores. Proyección de Población 2014 (Actualización). Instituto Nacional de Estadísticas[4]
Tasa de mortalidad infantil por región	Documento de Indicadores. Proyección de Población 2014 (Actualización). Instituto Nacional de Estadísticas
Tasa de Asma por región en niños	Encuesta Nacional de Salud 2009. Información reportada en Informe de Centro Nacional de Medio Ambiente[5]

Visitas diarias a sala de urgencia por asma en niños (Considerado en el CIE 10 como los códigos :J40-J46.	Egresos hospitalarios del año 2011 (base de datos completa y más actualizada de uso público). Departamento de Estadística e Información en Salud (DEIS)

Fuente: Elaborado por Macarena Valdés, Doctorante Programa Doctorado Salud Pública.

En el caso de las funciones de dosis-respuesta reportadas en cada evento de salud estimado en este informe, se utilizó los datos de la revisión de la literatura realizada en el informe del Centro Nacional de Medio Ambiente para el Ministerio(8). En cada evento se seleccionó el artículo que se especifica a continuación y luego se cálculo el estimador de dosis respuesta conocido como "Beta" (ver Tabla 2).

a) Mortalidad General (5) : Carey IM, Atkinson RW, Kent AJ, van Staa T, Cook DG, Anderson HR. Mortality associations with long-term exposure to outdoor air pollution in a national English cohort. Am J Respir Crit Care Med. 2013;187(11):1226-33.

b) Mortalidad Infantil (9): Hajat S, Armstrong B, Wilkinson P, Busby A, Dolk H. Outdoor air pollution and infant mortality: analysis of daily time-series data in 10 English cities. J Epidemiol Community Health. 2007;61(8):719-22.

c) Asma en niños (10): Pan G, Zhang S, Feng Y, Takahashi K, Kagawa J, Yu L, et al. Air pollution and children's respiratory symptoms in six cities of Northern China. Respir Med. 2010;104(12):1903-11.

d) Visitas a urgencia por asma (11): Ito K, Thurston GD, Silverman RA. Characterization of PM2.5, gaseous pollutants, and meteorological interactions in the context of time-series health effects models. J Expo Sci Environ Epidemiol. 2007;17 Suppl 2:S45-60.

[3] Departamento de Estadística e Información en Salud (DEIS). Acápite "Descargar bases de datos" http://www.deis.cl/.

[4] Instituto Nacional de Estadísticas (INE). Acapité: Productos Estadísticos. Demógraficos y Vitales y INE Regiones. http://www.ine.cl

[5] Centro Nacional del Medio Ambiente. Informe preparado para el Ministerio de Medio Ambiente "Análisis de Antecedentes y Evaluación Técnica-Económica para Revisar la Norma Primaria de Calidad del Aire de Dióxido de Azufre (SO2).Diciembre, 2014; pp 179.

Tabla 2. Estimadores de dosis-respuesta (conocidos como "Beta") según evento estudiado.

Evento en salud	Artículo científico	Concentración de SO_2 reportada en el artículo ($\mu g/m^3$)	Dosis respuesta reportada en el artículo	Beta Calculado*
Mortalidad General	Carey et al. 2013. Am. J. Resp Crit Car Med.	2,2	RR:1,03 IC95%(1,01-1,05)	0,0134
Mortalidad Infantil	Hajat el at. 2007.JECH	10	RR:1,02 IC95%(1,01-1,04)	0,0020
Asma en niños	Pan et al 2010. RM.Ashtma Chronic	69	RR:1,52 IC95%(1,21-1,92)	0,0061
Visitas urgencias por Asma	Ito et al.2007.JESEE.Timeseries	15,708 (6ppb)	RR: 1,2 IC95%(1,13-1,28)	0,0116

***Beta Calculado = ln(RR)/concentración reportada $\mu g/m^3$**

Fuente: Elaborado por Macarena Valdés, Doctorante Programa Doctorado Salud Pública.

Las zonas estudiadas fueron aquellas consideraras de interés por el Ministerio del Medio Ambiente debido a su proximidad a fuentes de emisión de SO_2.

Tabla 3. Número de habitantes considerada por zona vulnerable estudiada.

REGIÓN	COMUNA	POBLACIÓN	ZONAS VULNERABLES	POBLACION TOTAL*	CONCENTRACION PROMEDIO SO_2 $\mu g/m^3$ **
Antofagasta	Tocopilla	21.328	Tocopilla	21.328	64,4
Antofagasta	Calama	148.784	Calama	148.784	4,1
Antofagasta	Mejillones	11.096	Mejillones	11.096	8,9
Antofagasta	Antofagasta	372.973	Antofagasta – La Negra Coviefi	372.973	0,8
Atacama	Copiapó	163.866	Copiapó-Paipote-Tierra Amarilla*	177.771	32,9
	Paipote	No se considera como comuna			
	Tierra Amarilla	13.905			

Atacama	Huasco	8.000	Huasco - SM9 Escuela JJ Carrera	8.000	18,1
Valparaiso	Catemu	13.303	Catemu – LlayLlay*	36902	68
	LlayLlay	23.599			
Valparaiso	Puchuncavi	16.268	Quintero – Puchuncavi*	42.086	80,6
	Quintero	25.818			
O'Higgins	Machali	35.942	Machali - Coya	35.942	29,5
	Coya	No se considera como comuna			
Bio-Bio	Coronel	109.625	Coronel - Lota-Hualpen-Talcahuano*	413.901	17,7
	Lota	47.542			
	Hualpén	85.110			
	Talcahuano	171.624			

*** El número de personas considerado en zonas compuestas por más de una comuna, correspondió a la suma de personas de cada comuna cuando el dato estaba disponible.**

**** Las concentraciones de SO_2 reportadas corresponden a los Promedio anuales de concentraciones de SO2 por zona y estación, periodo 2011-2013. Fuente: Centro Nacional del Medio Ambiente. Informe preparado para el Ministerio de Medio Ambiente "Análisis de Antecedentes y Evaluación Técnica-Económica para Revisar la Norma Primaria de Calidad del Aire de Dióxido de Azufre (SO2).Diciembre, 2014; pp 327.**

Adicionalmente se consideraron 3 zonas controles de la Región Metropolitana, para comparar lo sucedido en las zonas vulnerables respecto de lo ocurrido en RM.

Tabla 4. Número de habitantes proyectado para el 2011 y concentración promedio de SO_2 durante el año 2011.

COMUNA	POBLACION TOTAL	CONCENTRACIÓN PROMEDIO µg/m^3
Independencia	51.277	4,585
El Bosque	168.302	4,11
Puente Alto	735.415	4,66

Eventos de salud

Para cuatro eventos en salud considerados: mortalidad general, mortalidad infantil, asma en niños y visitas diarias a urgencia por asma, existen otras variables que pueden influir en la cuantificación de eventos.

A) CONFUSORES: Son aquellas variables que tienen relación con la exposición y con el evento en salud. A nivel comunal, la cantidad de centros de salud disponible así como la actividad económica predominante de la comuna podrían representar confusores que para los fines de este estudio no serán medidos.

B) MODIFICADORES DE EFECTO: Son aquellas variables que como su nombre lo indica generan distintos niveles del efecto esperado. A nivel comunal el índice de adultos mayores, o el porcentaje de migración podría representar un modificador de efecto.

1. Mortalidad General

En este caso se puede calcular el número de eventos evitables (si la concentración del contaminante fuera cero) de la siguiente forma:

Casos Evitados = Población * Tasa Basal de evento estudiado* Beta* Concentración contaminante

Sin embargo el SO_2 es parte de la composición de la atmósfera, por lo que es más útil calcular los casos atribuibles a una concentración determinada. Por lo mismo en este caso se calculó el RR asociado a las concentraciones promedios en cada zona y la fracción atribuible poblacional (%FAP). La fracción atribuible poblacional corresponderá al número de casos atribuibles a la polución, del total de eventos en salud. Por ejemplo si esperamos que hayan 100 casos de un evento como hospitalizaciones y el %FAP= 40%, los casos atribuibles a polución serán 40.

Tabla 5. Número de casos atribuibles a la concentración de SO_2 según zona.

Zonas		Población	Tasa basal	Casos esperados según tasa base (1)	RR (2)	PAF (3)	Casos atribuibles al delta de concentracion(4)
Tocopilla	Mortalidad general	21328	0,00474	101,1	2,382	0,580	58,7
	Límite inferior	21328	0,00474	101,1	1,339	0,253	25,6

	Límite superior	21328	0,00474	101,1	4,190	0,761	77,0
Calama	Mortalidad general	148784	0,00474	705,2	1,057	0,054	37,8
	Límite inferior	148784	0,00474	705,2	1,019	0,018	13,0
	Límite superior	148784	0,00474	705,2	1,095	0,087	61,3
Mejillones	Mortalidad general	11096	0,00474	52,6	1,127	0,113	5,9
	Límite inferior	11096	0,00474	52,6	1,041	0,039	2,1
	Límite superior	11096	0,00474	52,6	1,218	0,179	9,4
Antofagasta - La Negra Coviefi	Mortalidad general	372973	0,00474	1767,9	1,011	0,011	18,9
	Límite inferior	372973	0,00474	1767,9	1,004	0,004	6,4
	Límite superior	372973	0,00474	1767,9	1,018	0,018	31,1
Copiapó-Paipote-Tierra Amarilla	Mortalidad general	177771	0,00483	858,6	1,556	0,357	306,8
	Límite inferior	177771	0,00483	858,6	1,160	0,138	118,7
	Límite superior	177771	0,00483	858,6	2,074	0,518	444,7
Huasco	Mortalidad general	8000	0,00483	38,6	1,275	0,216	8,3
	Límite inferior	8000	0,00483	38,6	1,085	0,079	3,0
	Límite superior	8000	0,00483	38,6	1,494	0,331	12,8
Catemu - LlayLlay	Mortalidad general	36902	0,00659	243,2	2,493	0,599	145,7
	Límite inferior	36902	0,00659	243,2	1,360	0,265	64,4
	Límite superior	36902	0,00659	243,2	4,518	0,779	189,4
Quintero - Puchuncavi	Mortalidad general	42086	0,00659	277,3	2,953	0,661	183,4
	Límite inferior	42086	0,00659	277,3	1,440	0,305	84,7
	Límite superior	42086	0,00659	277,3	5,974	0,833	230,9
Machali - Coya	Mortalidad general	35942	0,00591	212,4	1,486	0,327	69,5
	Límite inferior	35942	0,00591	212,4	1,143	0,125	26,5
	Límite superior	35942	0,00591	212,4	1,924	0,480	102,0
Coronel - Lota-Hualpen-Talcahuano	Mortalidad general	413901	0,00583	2413,0	1,268	0,212	510,7

	Límite inferior	413901	0,00583	2413,0	1,083	0,077	185,6
	Límite superior	413901	0,00583	2413,0	1,481	0,325	783,4
Independencia	Mortalidad general	51277	0,00537	275,4	1,064	0,060	16,5
	Límite inferior	51277	0,00537	275,4	1,021	0,021	5,7
	Límite superior	51277	0,00537	275,4	1,107	0,097	26,6
El Bosque	Mortalidad general	168302	0,00537	903,8	1,057	0,054	48,6
	Límite inferior	168302	0,00537	903,8	1,019	0,018	16,7
	Límite superior	168302	0,00537	903,8	1,096	0,087	78,8
Puente Alto	Mortalidad general	735415	0,00537	3949,2	1,065	0,061	239,9
	Límite inferior	735415	0,00537	3949,2	1,021	0,021	82,4
	Límite superior	735415	0,00537	3949,2	1,109	0,098	388,0

Para el cálculo de eventos esperados tenemos

(1) Casos Esperados= Población * Tasa Basal Regional de evento estudiado (se usa la tasa regional en lugar de la comunal por su estabilidad)

(2) Riesgo Relativo (RR)= exp $^{\text{(Función dosis-resp * Concentración Contaminante)}}$

(3) Fracción atribuible poblacional (PAF) = (RR -1)/RR

(4) Casos atribuibles = Casos Esperados * PAF

2. Mortalidad Infantil.

Para el calculo de los casos atribuibles a mortalidad infantil se considera como población el número de nacidos vivos por comuna y la tasa de mortalidad infantil regional, por ser más estable que la comunal.

Tabla 6. Número de casos atribuibles a la concentración de SO_2 según zona.

Zonas		Población (nacidos vivos)	Tasa basal	Casos esperados según tasa base (1)	RR (2)	PAF (3)	Casos atribuibles al delta de concentracion(4)

Tocopilla	Mortalidad infantil	436	0,00845	3,7	1,136	0,120	0,4
	Límite inferior	436	0,00845	3,7	1,066	0,062	0,2
	Límite superior	436	0,00845	3,7	1,288	0,224	0,8
Calama	Mortalidad infantil	2893	0,00845	24,4	1,008	0,008	0,2
	Límite inferior	2893	0,00845	24,4	1,004	0,004	0,1
	Límite superior	2893	0,00845	24,4	1,016	0,016	0,4
Mejillones	Mortalidad infantil	159	0,00845	1,3	1,018	0,017	0,0
	Límite inferior	159	0,00845	1,3	1,009	0,009	0,0
	Límite superior	159	0,00845	1,3	1,036	0,034	0,0
Antofagasta - La Negra - Coviefi	Mortalidad infantil	6128	0,00845	51,8	1,002	0,002	0,1
	Límite inferior	6128	0,00845	51,8	1,001	0,001	0,0
	Límite superior	6128	0,00845	51,8	1,003	0,003	0,2
Copiapó-Paipote-Tierra Amarilla	Mortalidad infantil	3096	0,00909	28,1	1,067	0,063	1,8
	Límite inferior	3096	0,00909	28,1	1,033	0,032	0,9
	Límite superior	3096	0,00909	28,1	1,138	0,121	3,4
Huasco	Mortalidad infantil	163	0,00909	1,5	1,036	0,035	0,1
	Límite inferior	163	0,00909	1,5	1,018	0,018	0,0
	Límite superior	163	0,00909	1,5	1,074	0,069	0,1
Catemu - LlayLlay	Mortalidad infantil	564	0,00756	4,3	1,144	0,126	0,5
	Límite inferior	564	0,00756	4,3	1,070	0,065	0,3

	Límite superior	564	0,00756	4,3	1,306	0,234	1,0
Quintero - Puchuncavi	Mortalidad infantil	583	0,00756	4,4	1,173	0,148	0,7
	Límite inferior	583	0,00756	4,4	1,084	0,077	0,3
	Límite superior	583	0,00756	4,4	1,372	0,271	1,2
Machali - Coya	Mortalidad infantil	692	0,00771	5,3	1,060	0,057	0,3
	Límite inferior	692	0,00771	5,3	1,030	0,029	0,2
	Límite superior	692	0,00771	5,3	1,123	0,109	0,6
Coronel - Lota-Hualpen-Talcahuano	Mortalidad infantil	5829	0,00719	41,9	1,036	0,034	1,4
	Límite inferior	5829	0,00719	41,9	1,018	0,017	0,7
	Límite superior	5829	0,00719	41,9	1,072	0,067	2,8
Independencia	Mortalidad infantil	1139	0,00707	8,1	1,064	0,060	0,5
	Límite inferior	1139	0,00707	8,1	1,021	0,021	0,2
	Límite superior	1139	0,00707	8,1	1,107	0,097	0,8
El Bosque	Mortalidad infantil	2498	0,00707	17,7	1,057	0,054	0,9
	Límite inferior	2498	0,00707	17,7	1,019	0,018	0,3
	Límite superior	2498	0,00707	17,7	1,096	0,087	1,5
Puente Alto	Mortalidad infantil	8519	0,00707	60,2	1,065	0,061	3,7
	Límite inferior	8519	0,00707	60,2	1,021	0,021	1,3
	Límite superior	8519	0,00707	60,2	1,109	0,098	5,9

3. Asma en niños.

Para el calculo de los casos atribuibles de asma en niños se usó la proyección de niños menores de 15 años del Instituto Nacional de Estadística para el 2011. Y se aplicó la prevalencia regional de uso de tratamiento en asmáticos de la Encuesta Nacional de Salud del año 2009.

Tabla 7. Número de casos atribuibles a la concentración de SO_2 según zona.

Zonas		Población (niños de 15 o menos años)	Tasa basal	Casos esperados según tasa base (1)	RR (2)	PAF (3)	Casos atribuibles al delta de concentracion(4)
Tocopilla	Valor estimado	5183	0,062	321,3	1,480	0,324	104,2
	Límite inferior	5183	0,062	321,3	1,195	0,163	52,5
	Límite superior	5183	0,062	321,3	1,842	0,457	146,9
Calama	Valor estimado	36155	0,062	2241,6	1,025	0,025	55,1
	Límite inferior	36155	0,062	2241,6	1,011	0,011	25,2
	Límite superior	36155	0,062	2241,6	1,040	0,038	85,2
Mejillones	Valor estimado	2696	0,062	167,2	1,055	0,053	8,8
	Límite inferior	2696	0,062	167,2	1,025	0,024	4,1
	Límite superior	2696	0,062	167,2	1,088	0,081	13,5
Antofagasta - La Negra Coviefi	Valor estimado	90632	0,062	5619,2	1,005	0,005	27,2
	Límite inferior	90632	0,062	5619,2	1,002	0,002	12,4
	Límite superior	90632	0,062	5619,2	1,008	0,008	42,3
Copiapó-Paipote-Tierra Amarilla	Valor estimado	43376	0,055	2385,7	1,221	0,181	431,8
	Límite inferior	43376	0,055	2385,7	1,095	0,087	207,3
	Límite superior	43376	0,055	2385,7	1,365	0,267	637,7
Huasco	Valor estimado	1952	0,055	107,4	1,116	0,104	11,2
	Límite inferior	1952	0,055	107,4	1,051	0,049	5,2
	Límite superior	1952	0,055	107,4	1,187	0,157	16,9
Catemu -	Valor	7786	0,044	342,6	1,511	0,338	115,8

LlayLlay	estimado						
	Límite inferior	7786	0,044	342,6	1,207	0,171	58,7
	Límite superior	7786	0,044	342,6	1,902	0,474	162,5
Quintero - Puchuncavi	Valor estimado	8880	0,044	390,7	1,631	0,387	151,1
	Límite inferior	8880	0,044	390,7	1,249	0,200	78,0
	Límite superior	8880	0,044	390,7	2,143	0,533	208,4
Machali - Coya	Valor estimado	8123	0,049	398,0	1,196	0,164	65,2
	Límite inferior	8123	0,049	398,0	1,085	0,078	31,2
	Límite superior	8123	0,049	398,0	1,322	0,243	96,9
Coronel - Lota-Hualpen-Talcahuano	Valor estimado	91472	0,08	7317,8	1,113	0,102	745,2
	Límite inferior	91472	0,08	7317,8	1,050	0,048	349,2
	Límite superior	91472	0,08	7317,8	1,182	0,154	1127,6
Independencia	Valor estimado	11281	0,0066	74,5	1,064	0,060	4,4
	Límite inferior	11281	0,0066	74,5	1,021	0,021	1,5
	Límite superior	11281	0,0066	74,5	1,107	0,097	7,2
El Bosque	Valor estimado	37026	0,0066	244,4	1,057	0,054	13,1
	Límite inferior	37026	0,0066	244,4	1,019	0,018	4,5
	Límite superior	37026	0,0066	244,4	1,096	0,087	21,3
Puente Alto	Valor estimado	161791	0,0066	1067,8	1,065	0,061	64,9
	Límite inferior	161791	0,0066	1067,8	1,021	0,021	22,3
	Límite superior	161791	0,0066	1067,8	1,109	0,098	104,9

4. Visitas diarias a urgencia por problemas de asma

Para el calculo de los casos atribuibles de asma en niños se usó el registro de egresos hospitalarios diarios del DEIS año 2011 (egresos por causas según CIE 10 J40-46) y la proyección de niños menores de 15 años del Instituto Nacional de Estadística para el 2011. Este es el único evento agudo que se estudió.

Tabla 8. Número de casos atribuibles a la concentración de SO_2 según zona.

Zonas		Población (niños de 15 o menos años)	Tasa basal	Casos esperados según tasa base (1)	RR (2)	PAF (3)	Casos atribuibles al delta de concentracion(4)
Tocopilla	Valor estimado	5183	0,0465	241,0	2,117	0,528	127,1
	Límite inferior	5183	0,0465	241,0	1,653	0,395	95,2
	Límite superior	5183	0,0465	241,0	2,760	0,638	153,7
Calama	Valor estimado	36155	0,0465	1681,3	1,049	0,046	78,1
	Límite inferior	36155	0,0465	1681,3	1,032	0,031	52,8
	Límite superior	36155	0,0465	1681,3	1,067	0,062	104,9
Mejillones	Valor estimado	2696	0,0465	125,4	1,109	0,098	12,3
	Límite inferior	2696	0,0465	125,4	1,072	0,067	8,4
	Límite superior	2696	0,0465	125,4	1,150	0,131	16,4
Antofagasta - La Negra Coviefi	Valor estimado	90632	0,0465	4214,6	1,009	0,009	39
	Límite inferior	90632	0,0465	4214,6	1,006	0,006	26,2
	Límite superior	90632	0,0465	4214,6	1,013	0,012	52,7
Copiapó-Paipote-Tierra Amarilla	Valor estimado	43376	0,1012	4390,9	1,465	0,317	1393,7
	Límite inferior	43376	0,0675	2926,8	1,292	0,226	661,0
	Límite superior	43376	0,0675	2926,8	1,677	0,404	1181,6
Huasco	Valor estimado	1952	0,0675	131,7	1,234	0,189	25,0
	Límite inferior	1952	0,0675	131,7	1,151	0,131	17,3
	Límite superior	1952	0,1012	197,6	1,329	0,248	48,9
Catemu - LlayLlay	Valor estimado	7786	0,1012	788,2	2,202	0,546	430,2
	Límite inferior	7812	0,1012	790,8	1,697	0,411	324,9
	Límite superior	7812	0,1012	790,8	2,911	0,657	519,2
Quintero - Puchuncavi	Valor estimado	8880	0,1092	970,1	2,549	0,608	589,4

	Límite inferior	8880	0,1092	970,1	1,872	0,466	451,9
	Límite superior	8880	0,1092	970,1	3,549	0,718	696,7
Machali - Coya	Valor estimado	8123	0,1319	1071,6	1,408	0,290	310,7
	Límite inferior	8123	0,1319	1071,6	1,258	0,205	219,8
	Límite superior	8123	0,1319	1071,6	1,590	0,371	397,5
Coronel - Lota-Hualpen-Talcahuano	Valor estimado	91472	0,1468	13426,8	1,228	0,186	2493,5
	Límite inferior	91472	0,1468	13426,8	1,148	0,129	1727,4
	Límite superior	91472	0,1468	13426,8	1,321	0,243	3260,4
Independencia	Valor estimado	11281	0,0921	1039,2	1,064	0,060	62,1
	Límite inferior	11281	0,0921	1039,2	1,021	0,021	21,3
	Límite superior	11281	0,0921	1039,2	1,107	0,097	100,5
El Bosque	Valor estimado	37026	0,0921	3410,8	1,057	0,054	183,4
	Límite inferior	37026	0,0921	3410,8	1,019	0,018	62,9
	Límite superior	37026	0,0921	3410,8	1,096	0,087	297,4
Puente Alto	Valor estimado	161791	0,0921	14903,7	1,065	0,061	905,2
	Límite inferior	161791	0,0921	14903,7	1,021	0,021	311,1
	Límite superior	161791	0,0921	14903,7	1,109	0,098	1464,4

CAPITULO 2. Evaluación de Riesgo en distintos escenarios de norma primaria de calidad del aire de SO_2.

Considerando que el cálculo de eventos atribuibles de un determinado evento en salud asociado a la contaminación por SO_2, depende del riesgo relativo reportado en el paper de referencia y subsecuentemente de la concentración de SO_2 utilizada en dicha evidencia, la siguiente tabla ejemplifica el cambio en el riesgo relativo y en la fracción atribuible poblacional de la mortalidad general (Tabla 8) y mortalidad infantil (Tabla 9), según la concentración de referencia que se esté usando.

Tabla 9. de Riesgos Relativos (RR) y Fracción Atribuible Poblacional (PAF) asociados a valor de concentración anual de SO_2: 80 µg/Nm^3 y 60 µg/Nm^3, en Mortalidad General

		Normativa anual 80 ug/m^3			Normativa anual 60 ug/m^3		
Zonas		**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**
Tocopilla	Mortalidad general	2,9	0,66	66,6	2,2	0,55	55,9
	Límite inferior	1,4	0,30	30,7	1,3	0,24	24,0
	Límite superior	5,9	0,83	83,9	3,8	0,74	74,4
Calama	Mortalidad general	2,9	0,66	464,5	2,2	0,55	390,3
	Límite inferior	1,4	0,30	214,1	1,3	0,24	167,6
	Límite superior	5,9	0,83	585,6	3,8	0,74	518,8
Mejillones	Mortalidad general	2,9	0,66	34,6	2,2	0,55	29,1
	Límite inferior	1,4	0,30	16,0	1,3	0,24	12,5
	Límite superior	5,9	0,83	43,7	3,8	0,74	38,7
Antofagasta - La Negra Coviefi	Mortalidad general	2,9	0,66	1164,4	2,2	0,55	978,4
	Límite inferior	1,4	0,30	536,7	1,3	0,24	420,2
	Límite superior	5,9	0,83	1468,0	3,8	0,74	1300,6
Copiapó-Paipote-Tierra Amarilla	Mortalidad general	2,9	0,66	565,5	2,2	0,55	475,2
	Límite inferior	1,4	0,30	260,7	1,3	0,24	204,1

	Límite superior	5,9	0,83	713,0	3,8	0,74	631,7
Huasco	Mortalidad general	2,9	0,66	25,5	2,2	0,55	21,4
	Límite inferior	1,4	0,30	11,7	1,3	0,24	9,2
	Límite superior	5,9	0,83	32,1	3,8	0,74	28,4
Catemu - LlayLlay	Mortalidad general	2,9	0,66	160,2	2,2	0,55	134,6
	Límite inferior	1,4	0,30	73,8	1,3	0,24	57,8
	Límite superior	5,9	0,83	201,9	3,8	0,74	178,9
Quintero - Puchuncavi	Mortalidad general	2,9	0,66	182,7	2,2	0,55	153,5
	Límite inferior	1,4	0,30	84,2	1,3	0,24	65,9
	Límite superior	5,9	0,83	230,3	3,8	0,74	204,0
Machali - Coya	Mortalidad general	2,9	0,66	139,9	2,2	0,55	117,6
	Límite inferior	1,4	0,30	64,5	1,3	0,24	50,5
	Límite superior	5,9	0,83	176,4	3,8	0,74	156,3
Coronel - Lota- Hualpen- Talcahuano	Mortalidad general	2,9	0,66	1589,4	2,2	0,55	1335,4
	Límite inferior	1,4	0,30	732,6	1,3	0,24	573,5
	Límite superior	5,9	0,83	2003,7	3,8	0,74	1775,3
Independencia	Mortalidad general	2,9	0,66	181,4	2,2	0,55	152,4
	Límite inferior	1,4	0,30	83,6	1,3	0,24	65,4
	Límite superior	5,9	0,83	228,7	3,8	0,74	202,6
El Bosque	Mortalidad general	2,9	0,66	595,3	2,2	0,55	500,2
	Límite inferior	1,4	0,30	274,4	1,3	0,24	214,8
	Límite superior	5,9	0,83	750,5	3,8	0,74	664,9
Puente Alto	Mortalidad general	2,9	0,66	2601,2	2,2	0,55	2185,6
	Límite inferior	1,4	0,30	1199,0	1,3	0,24	938,6
	Límite superior	5,9	0,83	3279,3	3,8	0,74	2905,4

Tabla 10. de Riesgos Relativos (RR) y Fracción Atribuible Poblacional (PAF) asociados a valor de concentración anual de SO_2: 80 µg/Nm^3 y 60 µg/Nm^3, en Mortalidad Infantil.

		Normativa anual 80 ug/mm3			Normativa anual 60 ug/mm3		
Zonas		**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**
Tocopilla	Mortalidad infantil	1,17	0,15	0,54	1,13	0,11	0,41
	Límite inferior	1,08	0,08	0,28	1,06	0,06	0,21
	Límite superior	1,37	0,27	0,99	1,27	0,21	0,77
Calama	Mortalidad infantil	1,17	0,15	3,58	1,13	0,11	2,74
	Límite inferior	1,08	0,08	1,87	1,06	0,06	1,42
	Límite superior	1,37	0,27	6,58	1,27	0,21	5,13
Mejillones	Mortalidad infantil	1,17	0,15	0,20	1,13	0,11	0,15
	Límite inferior	1,08	0,08	0,10	1,06	0,06	0,08
	Límite superior	1,37	0,27	0,36	1,27	0,21	0,28
Antofagasta - La Negra Coviefi	Mortalidad infantil	1,17	0,15	7,59	1,13	0,11	5,80
	Límite inferior	1,08	0,08	3,96	1,06	0,06	3,00
	Límite superior	1,37	0,27	13,95	1,27	0,21	10,86
Copiapó-Paipote-Tierra Amarilla	Mortalidad infantil	1,17	0,15	4,12	1,13	0,11	3,15
	Límite inferior	1,08	0,08	2,15	1,06	0,06	1,63
	Límite superior	1,37	0,27	7,58	1,27	0,21	5,90
Huasco	Mortalidad infantil	1,17	0,15	0,22	1,13	0,11	0,17
	Límite inferior	1,08	0,08	0,11	1,06	0,06	0,09

	Límite superior	1,37	0,27	0,40	1,27	0,21	0,31
Catemu - LlayLlay	Mortalidad infantil	1,17	0,15	0,62	1,13	0,11	0,48
	Límite inferior	1,08	0,08	0,33	1,06	0,06	0,25
	Límite superior	1,37	0,27	1,15	1,27	0,21	0,89
Quintero - Puchuncavi	Mortalidad infantil	1,17	0,15	0,65	1,13	0,11	0,49
	Límite inferior	1,08	0,08	0,34	1,06	0,06	0,26
	Límite superior	1,37	0,27	1,19	1,27	0,21	0,92
Machali - Coya	Mortalidad infantil	1,17	0,15	0,78	1,13	0,11	0,60
	Límite inferior	1,08	0,08	0,41	1,06	0,06	0,31
	Límite superior	1,37	0,27	1,44	1,27	0,21	1,12
Coronel - Lota- Hualpen- Talcahuano	Mortalidad infantil	1,17	0,15	6,14	1,13	0,11	4,70
	Límite inferior	1,08	0,08	3,21	1,06	0,06	2,43
	Límite superior	1,37	0,27	11,29	1,27	0,21	8,79
Independencia	Mortalidad infantil	2,93	0,66	5,30	2,24	0,55	4,46
	Límite inferior	1,44	0,30	2,44	1,31	0,24	1,91
	Límite superior	5,90	0,83	6,69	3,78	0,74	5,92
El Bosque	Mortalidad infantil	2,93	0,66	11,63	2,24	0,55	9,77
	Límite inferior	1,44	0,30	5,36	1,31	0,24	4,20
	Límite superior	5,90	0,83	14,67	3,78	0,74	12,99
Puente Alto	Mortalidad infantil	2,93	0,66	39,67	2,24	0,55	33,33
	Límite inferior	1,44	0,30	18,29	1,31	0,24	14,31
	Límite superior	5,90	0,83	50,01	3,78	0,74	44,31

Para el cálculo de eventos asociados a escenarios de norma diaria (Tabla 10) y horaria (Tabla 11) se usará únicamente el evento de visitas diarias a urgencia en niños que es el único evento agudo considerado.

Tabla 11. Riesgos Relativos (RR) y Fracción Atribuible Poblacional (PAF) asociados a valor de concentración diaria de SO_2: 250 µg/Nm^3,150 µg/Nm^3 y 125 µg/Nm^{3}en visitas a urgencia diarias por consulta respiratorio en niños.

			Normativa diaria 250 ug/m3			Normativa diaria 150 ug/m3			Normativa diaria 125 ug/m3		
Zonas		**Casos esperados en un año según tasa base**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**
Tocopilla	Valor estimado	241,01	18,21	0,95	227,77	5,70	0,82	198,75	4,27	0,77	184,52
	Límite inferior	241,01	6,99	0,86	95,21	3,21	0,69	165,99	2,64	0,62	149,88
	Límite superior	241,01	50,85	0,98	153,69	10,56	0,91	218,19	7,13	0,86	207,21
Calama	Valor estimado	1681,27	18,21	0,95	78,13	5,70	0,82	1386,48	4,27	0,77	1287,23
	Límite inferior	1681,27	6,99	0,86	52,79	3,21	0,69	1157,94	2,64	0,62	1045,57
	Límite superior	1681,27	50,85	0,98	104,91	10,56	0,91	1522,10	7,13	0,86	1445,50
Mejillones	Valor estimado	125,39	18,21	0,95	12,31	5,70	0,82	103,40	4,27	0,77	96,00
	Límite inferior	125,39	6,99	0,86	8,39	3,21	0,69	86,36	2,64	0,62	77,98
	Límite superior	125,39	50,85	0,98	16,37	10,56	0,91	113,51	7,13	0,86	107,80
Antofagasta - La Negra Coviefi	Valor estimado	4214,62	18,21	0,95	2615,61	5,70	0,82	3475,63	4,27	0,77	3226,85
	Límite inferior	4214,62	6,99	0,86	2013,69	3,21	0,69	2902,73	2,64	0,62	2621,04
	Límite superior	4214,62	50,85	0,98	3079,98	10,56	0,91	3815,61	7,13	0,86	3623,59
Copiapó-Paipote-Tierra Amarilla	Valor estimado	4390,88	18,21	0,95	1393,73	5,70	0,82	3620,99	4,27	0,77	3361,80
	Límite inferior	2926,84	6,99	0,86	661,01	3,21	0,69	2015,80	2,64	0,62	1820,18
	Límite superior	2926,84	50,85	0,98	1181,62	10,56	0,91	2649,75	7,13	0,86	2516,40
Huasco	Valor estimado	131,71	18,21	0,95	24,96	5,70	0,82	108,62	4,27	0,77	100,84
	Límite inferior	131,71	6,99	0,86	17,30	3,21	0,69	90,71	2,64	0,62	81,91

	Límite superior	197,60	50,85	0,98	48,92	10,56	0,91	178,89	7,13	0,86	169,89
Catemu - LlayLlay	Valor estimado	788,19	18,21	0,95	430,22	5,70	0,82	649,99	4,27	0,77	603,47
	Límite inferior	790,80	6,99	0,86	324,90	3,21	0,69	544,65	2,64	0,62	491,79
	Límite superior	790,80	50,85	0,98	519,18	10,56	0,91	715,93	7,13	0,86	679,90
Quintero - Puchuncavi	Valor estimado	970,07	18,21	0,95	589,43	5,70	0,82	799,98	4,27	0,77	742,72
	Límite inferior	970,07	6,99	0,86	451,93	3,21	0,69	668,11	2,64	0,62	603,28
	Límite superior	970,07	50,85	0,98	696,73	10,56	0,91	878,23	7,13	0,86	834,03
Machali - Coya	Valor estimado	1071,59	18,21	0,95	310,69	5,70	0,82	883,70	4,27	0,77	820,44
	Límite inferior	1071,59	6,99	0,86	219,77	3,21	0,69	738,03	2,64	0,62	666,41
	Límite superior	1071,59	50,85	0,98	397,55	10,56	0,91	970,14	7,13	0,86	921,31
Coronel - Lota-Hualpen-Talcahuano	Valor estimado	13426,85	18,21	0,95	2493,54	5,70	0,82	11072,61	4,27	0,77	10280,03
	Límite inferior	13426,85	6,99	0,86	1727,42	3,21	0,69	9247,45	2,64	0,62	8350,05
	Límite superior	13426,85	50,85	0,98	3260,42	10,56	0,91	12155,70	7,13	0,86	11543,95
Independencia	Valor estimado	1039,16	28,76	0,97	62,08	7,50	0,87	900,67	5,36	0,81	845,39
	Límite inferior	1039,16	3,10	0,68	21,33	1,97	0,49	511,88	1,76	0,43	448,76
	Límite superior	1039,16	255,78	1,00	100,47	27,84	0,96	1001,84	15,99	0,94	974,19
El Bosque	Valor estimado	3410,75	28,76	0,97	183,39	7,50	0,87	2956,20	5,36	0,81	2774,74
	Límite inferior	3410,75	3,10	0,68	62,87	1,97	0,49	1680,09	1,76	0,43	1472,91
	Límite superior	3410,75	255,78	1,00	297,37	27,84	0,96	3288,25	15,99	0,94	3197,49
Puente Alto	Valor estimado	14903,67	28,76	0,97	905,20	7,50	0,87	12917,44	5,36	0,81	12124,56
	Límite inferior	14903,67	3,10	0,68	311,07	1,97	0,49	7341,36	1,76	0,43	6436,06
	Límite superior	14903,67	255,78	1,00	1464,40	27,84	0,96	14368,40	15,99	0,94	13971,80

Tabla 12. Riesgos Relativos (RR) y Fracción Atribuible Poblacional (PAF) asociados a valores de concentración horaria de SO_2: 500 µg/Nm^3, 350 µg/Nm^3 y 197 µg/Nm^3 en visitas a urgencia diarias por consulta respiratorio en niños.

			Normativa horaria 500 ug/m3			Normativa horaria 350 ug/m3			Normativa horaria 197 ug/m3		
Zonas		**Casos esperados en un año según tasa base**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**	**RR**	**PAF**	**Casos atribuibles al delta de concentracion**
Tocopilla	Valor estimado	241,01	331,44	1,00	240,28	58,11	0,98	236,86	9,84	0,90	216,52
	Límite inferior	241,01	48,93	0,98	95,21	15,23	0,93	225,18	4,63	0,78	188,97
	Límite superior	241,01	2585,78	1,00	153,69	244,80	1,00	240,02	22,11	0,95	230,11
Calama	Valor estimado	1681,27	331,44	1,00	78,13	58,11	0,98	1652,34	9,84	0,90	1510,43
	Límite inferior	1681,27	48,93	0,98	52,79	15,23	0,93	1570,87	4,63	0,78	1318,22
	Límite superior	1681,27	2585,78	1,00	104,91	244,80	1,00	1674,40	22,11	0,95	1605,22
Mejillones	Valor estimado	125,39	331,44	1,00	12,31	58,11	0,98	123,23	9,84	0,90	112,64
	Límite inferior	125,39	48,93	0,98	8,39	15,23	0,93	117,15	4,63	0,78	98,31
	Límite superior	125,39	2585,78	1,00	16,37	244,80	1,00	124,87	22,11	0,95	119,71
Antofagasta - La Negra Coviefi	Valor estimado	4214,62	331,44	1,00	2615,61	58,11	0,98	4142,10	9,84	0,90	3786,35
	Límite inferior	4214,62	48,93	0,98	2013,69	15,23	0,93	3937,87	4,63	0,78	3304,53
	Límite superior	4214,62	2585,78	1,00	3079,98	244,80	1,00	4197,40	22,11	0,95	4023,99

Copiapó-Paipote-Tierra Amarilla	Valor estimado	4390,88	331,44	1,00	1393,73	58,11	0,98	4315,32	9,84	0,90	3944,70
	Límite inferior	2926,84	48,93	0,98	661,01	15,23	0,93	2734,65	4,63	0,78	2294,83
	Límite superior	2926,84	2585,78	1,00	1181,62	244,80	1,00	2914,88	22,11	0,95	2794,46
Huasco	Valor estimado	131,71	331,44	1,00	24,96	58,11	0,98	129,45	9,84	0,90	118,33
	Límite inferior	131,71	48,93	0,98	17,30	15,23	0,93	123,06	4,63	0,78	103,27
	Límite superior	197,60	2585,78	1,00	48,92	244,80	1,00	196,79	22,11	0,95	188,66
Catemu - LlayLlay	Valor estimado	788,19	331,44	1,00	430,22	58,11	0,98	774,63	9,84	0,90	708,10
	Límite inferior	790,80	48,93	0,98	324,90	15,23	0,93	738,87	4,63	0,78	620,04
	Límite superior	790,80	2585,78	1,00	519,18	244,80	1,00	787,57	22,11	0,95	755,03
Quintero - Puchuncavi	Valor estimado	970,07	331,44	1,00	589,43	58,11	0,98	953,38	9,84	0,90	871,49
	Límite inferior	970,07	48,93	0,98	451,93	15,23	0,93	906,37	4,63	0,78	760,60
	Límite superior	970,07	2585,78	1,00	696,73	244,80	1,00	966,10	22,11	0,95	926,19
Machali - Coya	Valor estimado	1071,59	331,44	1,00	310,69	58,11	0,98	1053,15	9,84	0,90	962,70
	Límite inferior	1071,59	48,93	0,98	219,77	15,23	0,93	1001,22	4,63	0,78	840,19
	Límite superior	1071,59	2585,78	1,00	397,55	244,80	1,00	1067,21	22,11	0,95	1023,12
Coronel - Lota-Hualpen-Talcahuano	Valor estimado	13426,85	331,44	1,00	2493,54	58,11	0,98	13195,81	9,84	0,90	12062,48
	Límite inferior	13426,85	48,93	0,98	1727,42	15,23	0,93	12545,19	4,63	0,78	10527,52
	Límite superior	13426,85	2585,78	1,00	3260,42	244,80	1,00	13372,00	22,11	0,95	12819,54
Independencia	Valor	1039,16	827,09	1,00	62,08	110,23	0,99	1029,73	14,11	0,93	965,51

	estimado										
	Límite inferior	1039,16	9,60	0,90	21,33	4,87	0,79	825,76	2,44	0,59	612,85
	Límite superior	1039,16	65425,91	1,00	100,47	2349,77	1,00	1038,72	78,96	0,99	1026,00
El Bosque	Valor estimado	3410,75	827,09	1,00	183,39	110,23	0,99	3379,81	14,11	0,93	3169,02
	Límite inferior	3410,75	9,60	0,90	62,87	4,87	0,79	2710,33	2,44	0,59	2011,52
	Límite superior	3410,75	65425,91	1,00	297,37	2349,77	1,00	3409,30	78,96	0,99	3367,55
Puente Alto	Valor estimado	14903,67	827,09	1,00	905,20	110,23	0,99	14768,46	14,11	0,93	13847,39
	Límite inferior	14903,67	9,60	0,90	311,07	4,87	0,79	11843,10	2,44	0,59	8789,55
	Límite superior	14903,67	65425,91	1,00	1464,40	2349,77	1,00	14897,32	78,96	0,99	14714,92

***Notese que este evento está consignado diariamente en las bases de egresos hospitalarios.**

CAPITULO 3. Comunicación de Riesgo

Los resultados de estudios de investigación deben ser preparados con precisión, especificidad y con lenguaje objetivo y científico. Sin embargo dependiendo de la audiencia, es necesario simplificar los reportes de modo de transmitir el mensaje clave del estudio sin caer en tecnicismos que entorpezcan la comunicación de riesgo y que puedan ocasionar una malinterpretación. Científicos y epidemiólogos deben colaborar en la comunicación y apoyar a los tomadores de decisiones en la administración de riesgo (12).

National Research Council (1989) define la comunicación de riesgos como “un proceso interactivo de intercambio de información y opiniones entre individuos, grupos e instituciones” y si este proceso cumple con su propósito, entonces “eleva el nivel de comprensión de temas o acciones relevantes para aquellos involucrados y los satisface porque están adecuadamente informados dentro de los límites del conocimiento disponible” (13). Dicho lo anterior, el objetivo fundamental de la comunicación de riesgo es fomentar el conocimiento y comprensión de los distintos miembros de la sociedad, fortaleciendo la confianza, credibilidad, cooperación y diálogo constructivo.

En el proceso de comunicación de riesgo es relevante destacar el concepto de riesgo percibido en la población. Como indica Peter Sandmand (14), riesgo implica el conocimiento objetivo del peligro asociado a un determinado compuesto o sustancia y a esto se suma la emoción evocada por la situación en debate, lo cual se conoce como agravio. Esto último, hará que una audiencia adopte una posición más o menos reactiva a la comunicación que brinden las autoridades sobre un tema de interés público, y primará en la medida que exista menos información o conocimiento objetivo.

En el caso de los efectos del dióxido de azufre, existen diversos factores de agravio que pueden sensibilizar a los involucrados y que deben considerarse en el proceso de comunicación de riesgo, en especial aquellos vinculados a la distribución geográfica del contaminante. Por ejemplo, contar con una norma ejerce un efecto positivo en la población fomentando una sensación de seguridad generalizada. Por otro lado, en las zonas vulnerables mencionadas en este informe, elementos como justicia, incertidumbre, efectos retardados, efectos en niños y efectos en generaciones futuras, generan un ambiente adverso que el tomador de decisión debe manejar y contrarrestar con una comunicación que logre aumentar la confianza y comprensión y disminuir el temor por parte de los implicados (13).

Es por ello que en esta situación es recomendable cuantificar el riesgo a través de una medida relativa y una medida absoluta. En el caso de comunas que tengan una gran desidad poblacional es preferible acompañar el riesgo relativo con el numero de casos atribuibles el cual se obtiene luego de aplicar la fracción atribuible poblacional

(FAP) a la tasa de casos esperados. Por ejemplo si en una población de 100000 personas tengo un RR=2,2 asociado a un contaminante, es relevante contar con el numero de casos atribuibles a la contaminación para darle contexto a ese RR. Por otro lado si la población es pequeña, por ejemplo 30 personas, debo acompañar mi RR con el %FAP, pero sin entregar un número de casos atribuibles ya que en algunos casos el numero de casos en poblaciones pequeñas no llega a ser un numero entero. Como corolario de esto, una medida relativa debe ser acompañada de una medida absoluta que le otorgue contexto; comunicar medidas relativas como el riesgo relativo (RR), demanda cautela dado que el RR depende de la concentración de exposición de la población. Asimismo, reportar medidas absolutas en comunas con pocos habitantes también puede prestarse para malinterpretaciones, dado que en algunos casos a pesar de que existe una medida relativa de riesgo, la medida absoluta puede involucrar pocos o ningún casos, subestimando el riesgo en esa comunidad. Según la definición de Instituto Nacional de Estadísticas del 2005, caseríos y aldeas definidos por un número de habitantes de menos de 301 y entre 301 y 1000 habitantes respectivamente, corresponderían a poblaciones menores, y por otro lado ciudades mayores se definen por poblaciones entre 100.001 y 500.000 habitantes y grandes áreas urbanas se definen por 500.000 hasta 1.000.000 de habitantes (15). En ambos casos se deben tener las consideraciones de comunicación de riesgo anteriormente mencionadas.

Reportar medidas de impacto absolutas y relativas, permite cumplir con los principios de la comunicación de riesgo, otorgando veracidad, legitimidad y satisfaciendo la necesidad de información de los involucrados, los medios de comunicación y la población en general, estableciendo un contexto mediante el uso de una medida absoluta y permitiendo la comparación con otros escenarios a través de una medida relativa.

LIMITACIONES DE LA METODOLOGÍA

Como se ha menicionado anteriormente, la realización de este informe se basa en el reporte de estadísticas e indicadores provistos por distintas fuentes de información. Por lo mismo, es necesario declarar las limitaciones e incertidumbres asociadas a dichos registros así como la reproducibilidad y validez de los estudios epidemiológicos utilizados.

1. En el caso de los eventos crónicos atribuibles al SO_2 y que son reportados en este informe, existe evidencia y datos disponibles para su estimación. En el caso del asma en niños, la aproximación realizada se basa en la Encuesta Nacional de Salud (ENS) reportada en el informe del CENMA como se mencionó anteriormente. La utilización de ENS genera imprecisiones en la estimación dado que se utiliza la prevalencia de haber recibido tratamiento de asma alguna vez como tasa basal de asma. A pesar de que no es el mejor *proxy* de asma en niños, es una forma de aproximarse a los niños con asma que se encuentran en tratamiento y que por ende se encuentran en una etapa crónica, aunque controlada de su patología.

En esta situación la Encuesta Nacional de Salud es la mejor información disponible respecto de algunos estudios clínicos, principalemente por el diseño de muestreo que busca ser representativo y aleatorio. La evidencia reportada por estudios locales pareciera ser menos relevante dado que usan principalmente muestras por conveniencia reclutadas directamente en los centros de atención.

Contar con un registro centralizado nacional que de cuenta de todos los pacientes que son atendidos tanto en la red pública como privada, precisando variables como diagnóstico, inicio de la patología y seguimiento y que además esté disponible para todos, es la mejor forma de aproximarnos a la tasa basal de cada uno de los eventos en salud. Sin embargo, a la actualidad carecemos de la institucionalidad y recursos para llevar a cabo esta tarea.

2. En el caso de eventos agudos, la estimación de eventos atribuibles es compleja. En la actualización de las guías sobre calidad de aire de la Organización Mundial de la Salud del año 2005, se destaca el cambio en el Volumen Espiratorio Forzado en población vulnerable, los asmáticos. Sin embargo este evento no puede ser calculado en población como la nuestra dado que no existen registro ad hoc. Adicionalmente, las fuentes de información sobre otros eventos agudos, no están disponibles a nivel comunal, por lo cual los eventos tanto crónicos como agudos seleccionados, se basan en la disponibilidad de datos.

3. Otra limitación de este informe está dada por las altas concentraciones de SO_2 reportadas en algunas zonas vulnerables; esto hace que el cálculo de eventos

atribuibles a la contaminación sea estimado de mejor forma con la fracción atribuible que con la ecuación que utiliza el número de habitantes, el beta de dosis-respuesta, la concentración de SO_2 y la tasa basal. El riesgo relativo no es una función lineal y por lo mismo en la medida que aumentan las concentraciones de exposición al contaminante es necesario estimarlo considerando las concentraciones de exposición del escenario de análisis.

CONCLUSIONES

La evaluación de riesgo es un proceso que permite identificar y conocer los eventos adversos asociados a contaminantes ambientales, estableciendo un marco de antecedente que combina información toxicológica, epidemiológica, e información propia del escenario que se está evaluando.

En ocasiones esta evaluación puede ser cualitativa estableciendo escenarios más riesgosos en presencia de mayores dosis de un contaminante específico en el ambiente. A pesar de que esta apreciaciones son útiles, los métodos cuantitativos son particularmente ventajosos para los tomadores de decisiones, quienes deben considerar los costos asociados a determinadas políticas publicas orientadas a disminuir el riesgo en la población.

En el presente informe, se han usado métodos de salud pública para cuantificar el riesgo atribuible a la concentración de SO_2 presente en el aire de 10 zonas consideradas como vulnerables, debido a su proximidad con termoeléctricas y fundiciones. Los casos cuantificados se basan en información provista por la evidencia epidemiológica, los registros nacionales de eventos de salud y las estimaciones poblacionales de Instituto Nacional de Estadística. Asímismo se entrega información de tres comunas de la región metropolitana que sirven como control de las zonas en análisis.

Lo anterior permite concluir que los valores utilizados como referencia, conllevan a distintos escenarios de riesgo relativo que se traducen en una fracción atribuible a contaminación distinta para cada evento estudiado. A pesar de que exista una referencia nacional, es necesario contar con información a nivel comunal dadas las distintas realidades de producción de polución asi como de acceso a salud a nivel de comuna.

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Consultas pasantía "Estimación cuantitativa de riesgo atribuible a SO_2 en zonas vulnerables de Chile". Autora: Macarena Valdés.

Fecha: marzo de 2015.

Pregunta 1: ¿Los *papers* elegidos son avalados como representativos? ¿Hay consistencia de los resultados entre los estudios que analizan la misma causa?

R. Los *papers* fueron elegidos según el criterio de validez externa principalmente en cuanto a fuentes de datos y operatividad de la variable de exposición, co-variables y registro del evento en estudio, en el contexto chileno. En algunos casos a pesar de que el paper incluido no cuenta con una muestra totalmente idéntica a la nuestra, fueron considerados modelos ajustados por co-variables del nivel individual.

Lamentablemente los registros chilenos de eventos en salud adolecen de desarrollo y no contamos con registros de eventos como: registro nacional de asmático por edades, o con registro específicos como consultas a urgencia por daño cromosómico en trabajadores. Por lo mismo la elección de estos papers estuvo en concordancia con la disponibilidad de registros similares a los del estudio incluido, para la realización de los cálculos posteriores.

Adicionalmente se trataron de incluir únicamente papers incluidos en el informe solicitado por el MMA al CENMA, aprovechando el recurso disponible, y tratando de mantener una consistencia con el trabajo realizado anteriormente. La revisión incluida en este informe indica que los eventos estudiados están asociados a la exposición estudiada, a pesar de no contar con un meta análisis en todos los casos. Aunque la revisión de la literatura detallada en el informe es exhaustiva, no todos los papers fueron útiles para la estimación de riesgo.

Sobre el estudio "*Air pollution and children's respiratory symptoms in six cities of Northern China":*

Pregunta 2: En relación a la tabla 5, el modelo conjunto para tres parámetros involucrados genera que el SO2 pierda significancia estadística. Esto suele suceder, por ejemplo, cuando se analiza PM10 y PM2.5, donde este último acapara toda la significancia dado que ambos parámetros están correlacionados. La opción elegida en los cálculo de casos fue el modelo econométrico con un solo parámetro (SO2) ¿Es válido técnicamente utilizar este valor siendo que hay correlación entre ellos?

R. Es válido dependiendo de la pregunta de investigación. La construcción de un modelo simple o múltiple, estadísticamente implica varios supuestos estadísticos. El supuesto de independencia es uno de ello, y elegir el modelo ajustado implica contestar una pregunta que aunque tiene ribetes multicausal, al integrar varios contaminantes pierde independencia y podría generar errores en la estimación debido a un sobreajuste del modelo, induciendo co-linealidad. La elección del modelo crudo en este caso respondía a nuestra pregunta de investigación efecto del SO_2 sobre un evento en salud, considerando que en condiciones reales

se está expuesto a una mezcla de contaminantes y no sólo a uno (múltiples exposiciones correlacionadas).

Sobre el estudio "Mortality Associations with Long-Term Exposure to Outdoor Air Pollution in a National English Cohort":

Pregunta 3: Se menciona que los pacientes estudiados corresponden a un rango de edad entre 40 y 89 años. ¿No debería considerarse el mismo rango de edad en las poblaciones consideradas en el análisis?

R. Efectivamente como ustedes indican, deberíamos haber tenido un paper que midiera mortalidad general, en toda la población que es como se calcula esta tasa. Sin embargo, existe escaza literatura donde se mida este outcome en una serie de tiempo integrando exposición a largo plazo. Como en el punto anterior, se considera a esta como la mejor evidencia disponible de acuerdo al objetivo planteado en calculo de riesgo. Debo añadir que la función utilizada es aquella ajustada por el efecto de las características de los sujetos de estudios, y en este caso se incluyó en el modelo la edad, de modo que *hazard ratio* usado es aplicable a cualquier edad.

Pregunta 4: las conclusiones del paper mencionan que "*However, the stronger associations with respiratory mortality are not consistent with most US studies in which associations with cardiovascular causes of death tend to predominate*". Considerando esto ¿Es válido igualmente utilizar estos resultados?

R. En este artículo se consignó el dato sobre mortalidad general y no por causa especifica correspondiente a la exposición a SO_2. Como los autores expresan, los datos sobre mortalidad general fortalecen la evidencia ya existente, no mencionan datos discordantes.

En el caso de la exposición a PM2.5 se encontraron los resultados controversiales que tu mencionas. De todos modos que existan diferencias en cuanto a otros estudios o similitudes, es normal dependiendo de la población incluida y como ellos puntualizan en el articulo, la población que ellos consideraron en los registros consumía otros medicamentos debido a las comorbilidades. Probablemente las diferencias encontradas no fueron tan fuertes dado a que los pacientes crónicos de atención primaria, están mas controlados. Hubiese sido interesante estimar el efecto de polifarmacia en los modelos. Por otro lado eventos agudos de estancias por urgencia podrían ayudar a estimar el efecto agudo del contaminante en un paciente que generalmente no se cuida y donde el efecto del tratamiento de comorbilidades no está presente.

Pregunta 5: ¿Por qué el valor elegido corresponde al ajustado por "age, sex, smoking, BMI, education†" y no, por ejemplo, por el de ingreso u otro?

R. Los 3 modelos ajustados finales que se presentan en la tabla 3 "Hazard Ratios For All-Cause Mortality In 2003–2007 For An Interquartile Range Change In 2002 Pollutant Concentrations" difieren únicamente en el proxy de la posición socioeconómica. Personalmente me incliné por educación dada la forma de recolección de datos. Como lo indican los papers de Galobardes, según tu momento de la vida podríamos utilizar una variable distinta para aproximarnos a posición socioeconómica. Según Galobardes, la educación presenta ventajas comparativas con respecto al ingreso, en especial en condiciones donde las personas pueden tender a reportar menos ingresos. En este grupo tenemos una mezcla de cohorte de nacimiento distintas donde la educación, o el ingreso podría ser más o menos útil. Por tratarse de una cohorte cuyas variables son reportadas por el sujeto en estudio en condiciones de atención primaria, se elige educación de modo de evitar el sesgo de clasificación.

Sobre el estudio "Outdoor air pollution and infant mortality: analysis of daily time-series data in 10 English cities":

Pregunta 6: se señala que el rango de población es de 3 a 12 años, sin embargo en el documento de pasantía se considera la población menor a 15 años.

R. Creo que acá hay un error porque este paper habla de mortalidad infantil y como se detalla en la metodología se incluyeron los registro de mortalidad infantil "Data on all-cause infant deaths (death within the first year of life) recorded between 1990 and 2000 were obtained from the Office for National Statistics for the following 10 major cities in England: Birmingham, Bristol, Leeds, Liverpool, London, Manchester, Middlesbrough, Newcastle, Nottingham and Sheffield. For each city, data were collapsed by date of death to generate a time series of daily infant death counts between 1990 and 2000".

Para el calculo de la tasa de mortalidad infantil siempre se consideran los menores de 1 año muertos divido por los nacidos vivos. En este informe se consignó información sobre los nacidos vivos y tasa de mortalidad infantil según la información del DEIS.

Sobre el estudio "Characterization of PM2.5, gaseous pollutants, and meteorological interactions in the context of time-series health effects models":

Pregunta 7: En relación a la figura 8, el paper menciona que "C*O and SO2's associations with asthma ED visits (RR=1.15 (95% CI: 1.07, 1.25) per 1.3 p.p.m. increase and 1.20 (95% CI: 1.13, 1.28) per 6 p.p.b. increase, respectively) were "eliminated*" *once NO2 was included in the model, which is consistent with the result of monitor-to-monitor correlations, suggesting that NO2 has less exposure error than CO or SO2 in this data set.*". ¿Es válido utilizar el valor elegido si el efecto pierde significancia al incorporar un parámetro adicional?

R. La elección de un modelo no se realiza únicamente con criterios de significancia estadística. La elección de un modelo simple o múltiple está en consonancia con la pregunta de investigación que se busca contestar. La utilización de pruebas paramétricas en la fase de análisis obliga a resguardar los supuestos estadísticos tras estas pruebas. En este caso ellos utilizan modelos que dejan al NO_2 fuera debido a las pruebas de concurvidad prefiriendo un modelo más parsimonioso, a pesar de reportarlo como un fuerte confusor. En la figura 7 de este mismo paper se reportan los RR para cada contaminante y podemos ver que las diferencias de los efectos entre los contaminantes son marginales y que el efecto confusor es despreciable o insignificante.

Anexo I: Referencias del trabajo de pasantía en salud pública, revisión de la norma primaria de calidad del aire para dióxido de azufre (SO_2).

A continuación se listan las referencias de la información utilizada para confeccionar el trabajo de pasantía en salud pública para la revisión de la norma primaria de calidad de aire para dióxido de azufre:

1. Health Effects Associated with Short-term Exposure to Low Levels of Sulphur Dioxide (SO_2) – A Technical Review. Alberta Health and Wellness, Health Surveillance, Edmonton, Alberta. Canadá (2006). ISBN 0-7785-3480-4. www.health.gov.ab.ca

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REPORT

Health Effects Associated with Short-term Exposure to Low Levels of Sulphur Dioxide (SO_2) - A Technical Review

Alberta Health and Wellness

2006

Health Surveillance

Alberta Health & Wellness
Health Surveillance
Health Strategies Division
24th floor, 10025 Jasper Avenue
Edmonton, Alberta T5J 2N3
Phone: (780) 427-4518
Fax: (780) 427-1470

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HEALTH EFFECTS ASSOCIATED WITH SHORT-TERM EXPOSURE TO LOW LEVELS OF SULPHUR DIOXIDE (SO_2) -A TECHNICAL REVIEW-

Alberta Health and Wellness
Health Surveillance
Health Strategies Division

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Expert panel

Dr. Randy Angle	Alberta Environment
Justin Balko	Alberta Health and Wellness
Dr. Nicholas Bayliss	Alberta Health and Wellness
Dr. Donald Davies	Cantox Environmental Inc.
Dr. Stephan Gabos	Alberta Health and Wellness
Geoff Granville	Shell Canada
Alex MacKenzie	Alberta Health and Wellness
Dr. Ingrid Vicas	Calgary Health Region

Review Panel

James Andruchow
Lorelei Betke
Michael Lam
Norah Lee
Rabindra Mahabeer
Christine Teixeira
Corinna Watt

Health Surveillance Staff

Dr. Karina Bodo
Ada Chan
Nancy Hlady
Leigh Li

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EXECUTIVE SUMMARY

In response to Recommendations 9 and 59 of the final report of the Provincial Advisory Committee on Public Safety and Sour Gas released in December 2000, Alberta Health and Wellness commissioned reports on the health effects of low-level exposure to hydrogen sulphide (H_2S) and sulphur dioxide (SO_2). The H_2S report on short-term exposure was released in July 2002 (Cantox Environmental, 2002). The present report on SO_2 is the second of four reports. The goal of these reports was to provide a comprehensive review of the available primary scientific literature in order to develop a quantitative understanding of the current state of knowledge with respect to the dose-response relationship between exposure to these contaminants (H_2S and SO_2) and health effects based on the weight of evidence in the peer-reviewed scientific literature. The focus of the third and fourth reports will be on the health effects of chronic exposure to H_2S and SO_2.

The development of the Terms of Reference of the H_2S report was undertaken by an expert panel over a six-month period. The format and goal of this SO_2 report was much the same as the previously completed H_2S report. In addition the Terms of Reference for this report were adopted directly from the H_2S report with few changes. The Terms of Reference state that the focus of this scientific review is to be on the health effects of short-term exposure to SO_2.

The eligibility criteria for the selection of literature were also adopted directly from the H_2S report. The criteria were developed from the Terms of Reference. Only primary studies published in peer-reviewed publications were included in this review. Articles that were not primary scientific studies but were reviews themselves were not included, the primary goal of this review being an unbiased assessment of the scientific literature, not a re-reporting of previously published reviews. Studies reviewed included human clinical studies (clinical), animal toxicology studies (non-clinical), and population studies and case reports (epidemiology). 347 studies satisfied the final eligibility criteria for inclusion in this report, substantially more than for the H_2S report (45 studies) due in part to the inclusion of epidemiology studies.

Each study was critically assessed in terms of technical quality, including experimental design, conduct, and reporting. A level of confidence was assigned to each study based on the technical quality as judged by the reviewing team. The reviewing team consisted of seven members, all with scientific and/or epidemiologic backgrounds and extensive experience critically reviewing scientific literature. Each study was reviewed independently by three members of the reviewing team. The team members followed a pre-defined set of criteria for judging study quality. Of the 347 eligible studies reviewed, 184 (53%) were judged to be of low quality, 150 (43%) were of moderate quality, and only 15 (4%) were of high quality with no major weaknesses in study design or reporting.

The quality ranking of the studies was based on weaknesses or limitations identified by the reviewers. Some of the

more common limitations identified included: too few study subjects, too few exposure concentrations (inability to determine dose-response relationship), failure to follow Good Laboratory Practice guidelines, failure to follow conventional testing protocols, critical information missing on experimental protocols, and unmeasured, poorly measured or unreported exposure concentrations and/or times. In drawing conclusions from this review, emphasis was placed on those studies ranked "high" or "moderate". These studies were judged to have the fewest limitations and therefore provided the strongest and most reliable evidence of association. For some health effects, few moderate or high quality studies were identified.

Results of animal and human studies were evaluated separately. No attempt was made to extrapolate from the animal testing evidence to human effects. It must also be emphasized that this report is a scientific review and as such the interpretations of the science do not represent policy or suggest public health implications.

The greatest number of studies, as well as the greatest number of high and moderate quality studies were those investigating respiratory effects as a result of SO_2 exposure. The strength-of-evidence for respiratory effects provided by these studies confirms that SO_2 exposure under certain conditions (exposure concentration, duration, and breathing method) can adversely affect the respiratory system. Human studies evaluating subjects with bronchopulmonary disease were included as well as those evaluating healthy subjects.

A. Evidence from Human Studies

Two types of studies were evaluated for evidence of effects on humans.

- Clinical studies involved controlled experiments on human volunteers.
- Epidemiology studies investigated short-term changes in health effects in populations with short-term changes in ambient concentration.

Both healthy subjects and those with respiratory illness (asthma or chronic obstructive pulmonary disease) were included in the studies.

Clinical studies covered a broad range of exposure durations. Therefore, the summaries of the findings are broken down by exposure time to facilitate comparison.

The weight of evidence for exposures up to 30 minutes suggests that healthy humans can experience exposures to SO_2 up to 10 ppm with transitory effects[1] on pulmonary function[2], even under challenging conditions involving hyperventilation, mouth-only exposure, and heavy exercise. Transitory effects may be observed at concentrations as low as 0.75 ppm.

[1] Transitory effects: these effects were observed generally, but not always, for the duration of exposure with functioning returning to normal levels within minutes of hours of cessation of exposure.

[2] Pulmonary function or pulmonary effects: this refers primarily to spirometric changes (e.g. specific airways resistance, forced expiratory volume, etc.) that are measured in a clinical setting. In some cases, pulmonary effects may include clinical symptoms such as bronchoconstriction or throat irritation.

For exposures up to 30 minutes, asthmatics appear to demonstrate pulmonary effects at lower thresholds compared to healthy humans (0.1 ppm). However, even in this population subgroup the clinical effects are transient and may or may not require transient pharmacologic intervention.

The weight of evidence suggests that for single exposures up to 4 hours and repeated exposures between 3 days and 3 weeks, transitory pulmonary effects might occur for asthmatics at exposure concentrations between 0.5 and 1 ppm with exercise and for healthy humans between 0.75 and 25 ppm with exercise, with some evidence for a concentration-dependent response in healthy subjects.

Epidemiology studies were divided into two types based on presentation of exposure concentration. One set of studies calculated exposures as increases in ambient concentration above a baseline or average concentration. The other set of studies reported exposure as discrete concentrations, either as average concentrations or a concentration range.

A weight of evidence evaluation is difficult for the epidemiology studies. This is because the majority of the epidemiology studies (107 of 147) were ranked low quality. For those that ranked moderate quality, there were an equal number of studies that found insignificant or no associations between ambient SO_2 concentration and health outcomes as there were that reported an association.

Deriving causal associations from environmental epidemiologic studies is difficult for a number of reasons. No high quality epidemiology studies were identified. All of the epidemiology studies were subject to substantial limitations due to misclassification of either or both exposure and outcome. The majority of these studies are ecological in nature with outcomes determined on an individual level and exposure determined at a population level. The exposure data collected was generally for ambient levels. Since humans spend a large portion of their time indoors and travel through various microclimates during various activities, ambient levels will likely not provide a good measure of exposure at the individual level. Subsequently, the major weakness observed in these epidemiology studies is the potential for exposure misclassification as a result of the exposure assessment methods. Much of the exposure and outcome data used in these studies is retrospective and from public records, which increases the probability of misclassification due to inconsistent diagnosis of disease status or incorrect assessment of exposure. In addition, many confounding factors cannot be accounted for when using these types of data.

The epidemiology studies also present challenges for interpretation. The different exposure metrics used in the studies makes for difficulty in interpretation. For those studies looking at increases above a baseline, it should be noted that the baseline concentrations differ for each study. The time-averaging or time over which exposure was calculated is different between studies, making comparisons difficult. The populations used tended to be small and relatively undefined. For those studies that did report statistically significant results, the lower confidence intervals

were often very close to one and there were few or no associations where the OR>2.

In addition, SO_2 is just one element in a mixture of pollutants found in "air pollution". It is difficult to isolate the effects of SO_2 from those of other single pollutants or combinations of pollutants. Because of these substantial limitations, the confidence in the results and conclusions from these epidemiology studies could not be judged to be higher than moderate and in most cases the confidence was judged to be low.

There is little reliable evidence in the peer-reviewed scientific literature that meets the terms of reference for this review of human health effects involving the eye, kidney and liver, or the cardiovascular, gastrointestinal, metabolic, immunological, reproductive, or nervous systems. It should be noted that SO_2 is generally considered an eye irritant. However, the conclusion in this report stems from the paucity of good-quality peer-reviewed scientific literature reporting specific effects on the eye. Much of the literature on reproductive effects on humans involves exposures longer than 30 days, which were not covered in this report, but will be covered in subsequent reports.

B. Evidence from animal studies

Much of the animal evidence for respiratory effects concentrates on the mechanisms of action of health effects from SO_2 exposure. Animal studies are also referred to as "**non-clinical**" studies.

As in the human clinical studies, the non-clinical animal studies covered a broad range of exposure durations. Therefore, the summaries of the findings are broken down by exposure time to facilitate comparison.

The concentrations in studies of animals exposed for up to 2 hours ranged between 0.5 ppm and 1000 ppm. For concentrations up to 100 ppm, effects reported were predominantly very mild respiratory effects and changes at the cellular or ciliary level. Above 100 ppm, greater pulmonary effects were in evidence, with indications of changes to the lung. There is evidence of increasing severity of effect with increasing concentration suggesting a possible dose response relationship.

In studies employing exposures between 2 and 24 hours, mild respiratory effects and delayed airway reactivity were reported with concentrations up to 40 ppm. Damage to the lungs was reported at concentrations of 800 ppm and 1225 ppm.

With exposures between 1 and 7 days, slight changes were observed in lung function and in response to virus challenges at concentrations of 0.1 ppm to 34.5 ppm. At the higher concentrations of 100 ppm and 600 ppm, changes to lung structure were reported.

Only five studies investigated exposures between 7 and 30 days. One study reported changes in response to virus challenges with exposures up to 0.1 ppm for 4 weeks. The other four studies reported changes in lung biochemistry and some decrease in pulmonary function at concentrations between 10 and 600 ppm.

Only a few animal studies looked at the effect of SO_2 exposure on the liver or

kidneys. However, there is some evidence of decreased levels of liver lipids and triglycerides and decreased enzyme activity in liver and kidney following continuous SO_2 exposure at 10 ppm for 15 days.
There is some evidence that exposure to SO_2 can affect the metabolic system, in particular lipid metabolism, at exposure times of several days. This effect seems to differ depending on which organ of the body is investigated.

There is some evidence from animal studies that SO_2 exposure both as an adult and prenatally can affect behaviour in adult mice subjected to challenging conditions. There is also some evidence that exposure to SO_2 can affect the lipid content of the brain. The outcomes of both these studies are of unknown clinical significance and the number of studies is limited, although the quality of the studies suggests the results are reliable. It has been established in several species that bronchial restriction upon SO_2 exposure is a reflex reaction; however, the mechanism of this reflex has not been conclusively determined.

In conclusion, there is limited animal evidence with respect to signs and symptoms, or effects on the eye, and reproductive, gastrointestinal, or cardiovascular systems found in the studies reviewed for this report.

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Sí Se Puede: Using Participatory Research to Promote Environmental Justice in a Latino Community in San Diego, California

Meredith Minkler, Analilia P. Garcia, Joy Williams, Tony LoPresti, and Jane Lilly

ABSTRACT *Community-based participatory research (CBPR) increasingly is seen as a potent tool for studying and addressing urban environmental health problems by linking place-based work with efforts to help effect policy-level change. This paper explores a successful CBPR and organizing effort, the Toxic Free Neighborhoods Campaign, in Old Town National City (OTNC), CA, United States, and its contributions to both local policy outcomes and changes in the broader policy environment, laying the groundwork for a Specific Plan to address a host of interlocking community concerns. After briefly describing the broader research of which the OTNC case study was a part, we provide background on the Environmental Health Coalition (EHC) partnership and the setting in which it took place, including the problems posed for residents in this light industrial/residential neighborhood. EHC's strong in-house research, and its training and active engagement of* promotoras de salud *(lay health promoters) as co-researchers and policy change advocates, are described. We explore in particular the translation of research findings as part of a policy advocacy campaign, interweaving challenges faced and success factors and multi-level outcomes to which these efforts contributed. The EHC partnership's experience then is compared with that of other policy-focused CBPR efforts in urban environmental health, emphasizing common success factors and challenges faced, as these may assist other partnerships wishing to pursue CBPR in urban communities.*

KEYWORDS *Community-based particatory research, Environmental justice policy, Promotoras, Latinos*

INTRODUCTION

Visitors to the historic "Old Town" district of San Diego, CA, United States rarely venture beyond this chic tourist destination to the 6×15 block neighborhood 10 miles to the south, known as Old Town National City (OTNC). However, this formerly residential community, which "has for decades been treated by planners as a dumping ground for polluting industry and warehouses,"[1] provides researchers and environmental health advocates with a textbook example of the potential of community-based participatory research (CBPR), organizing and advocacy for studying urban environmental health problems, and working on the policy level to help effect change.

CBPR is concisely defined as "systematic inquiry, with the participation of those affected by the issue, for the purposes of education and action or effecting change."[2]

Minkler, Garcia, and LoPresti are with the UC Berkeley, Berkeley, CA, USA; Williams and Lilly are with the Environmental Health Coalition, Old Town National City, CA, USA.

Correspondence: Meredith Minkler, UC Berkeley, Berkeley, CA, USA. (E-mail: mink@berkeley.edu)

With its emphasis on empowerment, co-learning, community capacity building, and balancing research and action,[3] this orientation to research has shown particular promise in the areas of urban health and environmental justice.[4–8]

This paper explores a successful CBPR and organizing effort, the Toxic Free Neighborhoods Campaign, in OTNC, and its contributions to both local policy outcomes and changes in the broader policy environment laying the groundwork for a Specific Plan to address a host of interlocking community concerns. After briefly describing the broader research of which the OTNC case study was a part, we provide background on the Environmental Health Coalition (EHC) partnership and the setting in which it took place, including the problems posed for residents in this light industrial/residential neighborhood. The EHC's strong in-house research and its training and active engagement of *promotoras de salud* (lay health promoters) as co-researchers and policy change advocates are described. We explore in particular the translation of research findings as part of a policy advocacy campaign, interweaving challenges and success factors and multi-level outcomes to which these efforts contributed. The EHC partnership's experience then is compared with that of other policy-focused CBPR efforts in urban environmental health, emphasizing common success factors and challenges faced, as these may assist other partnerships wishing to pursue a CBPR approach in urban communities.

STUDY PURPOSE AND METHODS

The EHC partnership was one of six policy-focused CBPR partnerships in California included in a broader study, funded by The California Endowment, to explore the role of CBPR as a strategy for linking place-based work and policy to promote healthier communities. Following Yin's[9] case study protocol, two members of the research team visited OTNC in 2008, conducting key source interviews with the lead community and academic partners and a focus group with four *promotoras*, each of whom signed a consent form approved by our university's Institutional Review Board. Phone interviews with three local policy makers and observation at a hearing also were undertaken, along with a guided tour of the neighborhood, and archival review and analysis of relevant internal documents and media coverage.

Data analysis followed a procedure developed and successfully used in an earlier, cross-site case study analysis of ten CBPR partnerships undertaking policy-focused work across the United States.[10,11] A coding template developed for the national study included key domains that were also of interest in the present study (e.g., partnership genesis, research methods, policy goals, activities and outcomes, contextual factors, capacity building, and sustainability). In addition, and based on subsequent literature,[12,13] new coding categories were added, including changes in the policy environment and what needs to be in place for successful work to occur at the policy level. Audiotapes of the interviews and focus group were professionally transcribed, and an initial round of coding was independently conducted by two of the authors, who identified key themes and codes, compared their findings, and returned to the data to reconcile any discrepancies.[14] The qualitative software package, ATLAS.ti ™ (version 5.5) was then used to group all key domains by site and generate reports. A second round of coding was conducted using the reports, and a similar reconciliation process was undertaken. Consistent with CBPR principles, a

preliminary case study report based on the findings was shared with partners at EHC for member checking to help ensure the accuracy of data interpretation.

BACKGROUND

The Environmental Health Coalition was founded in 1980 as a non-profit organization, to study and address environmental and social justice issues by building community capacity and providing an organizational base for neighborhood engagement in political decision making.[15] The nonprofit's staff includes both professionally trained researchers and organizers and three to five community residents hired for their expert knowledge of the region and their skills in community building, organizing, and advocacy.

Central to EHC's modus operandi has been its *Salud Ambiental, Lideres Tomando Accion* program (SALTA, or Environmental Health, Leaders Taking Action) through which lay health promoters have been trained since 1995. The SALTA trainings' dual components focus on (1) skill building in community organizing and advocacy, media, and the political process, and (2) specific issues, such as land use, air quality, and energy. Each *promotora* goes through the skill-based SALTA program, and a separate SALTA program focused on the issue set most relevant in her neighborhood. Although EHC has undertaken campaigns in a variety of topical areas in both San Diego and the border regions of Tijuana, Mexico, we focus here on its Toxic Free Neighborhoods Campaign in OTNC, and subsequent efforts to help enact a Specific Plan that would help address this and other concerns of the area's approximately 1,600 residents.[16] Founded in 1887 and known historically as the center of the area's large Latino community, Old Town National City lost many of its residential property rights in the 1950s and 1960s, when an all-white City Council passed measures that encouraged industries to move into the neighborhood.[1] During this same era, Interstate 5 was constructed, demolishing homes, cutting through the original neighborhood, and becoming the western boundary of the neighborhood. As a result of these developments, OTNC suffers from a disproportionate burden of toxic air contaminants. According to a 2006 audit, just eight of 133 businesses in this community had all necessary operating permits, and EHC's own research suggested that well over two thirds of the toxic pollutants in this community come from its many, often noncompliant autobody and paint shops.[1] A truck-driving school situated across the street from an elementary school and other stationary and mobile polluting facilities also contributed to the fact that OTNC had asthma rates significantly higher than those of San Diego at large, or the state. Fourteen percent of children under 18 in OTNC were reported by their parents to have been diagnosed with asthma in EHC's 2005 community survey.[1] In contrast, Behavioral Risk Factor Surveillance Survey data from 2005 found that 11% of boys and 6% of girls aged 0–17 in California had this condition.[17] Numerous studies have shown strong associations between high levels of diesel exhaust and elevated rates of respiratory ailments and asthma.[18,19] Similarly, many of the chemical emissions from autobody and paint shops have been shown to cause or exacerbate asthma, key among them diisocyanates, the major cause of occupational asthma in the United States.[20]

Although as noted above, OTNC suffers disproportionately from environmental hazards and related adverse health outcomes, it also has many assets, particularly in the area of civic engagement. An active neighborhood council and church organizing ministry, a local school with substantial parental involvement, and the EHC itself are

among key building blocks that have enabled the community to stand up for its rights and work to effect change. Finally, the very small size of the community, which occupies just 0.036 square miles, means that "everybody knows everybody," and city council members and other community leaders are easily accessible to residents.

THE PARTNERSHIP

Although the EHC had not historically targeted particular health issues, the high level of community concern over asthma and its potential links to industry in the neighborhood made this an important focus of attention. With support from The California Endowment, the James Irvine Foundation, and two environmental justice grants from the National Institute of Environmental Health Sciences (2000–2004 and 2004–2008) focused on land use, air quality, and children's health, EHC formed a partnership with the Southern California Environmental Health Sciences Center at the University of Southern California (USC) to help address these concerns. Later, during the policy phase of the work in 2005–2006, a partnership with the University of San Diego's (USD) Environmental Law Clinic was formed as well.

RESEARCH METHODS, ROLES, AND FINDINGS

EHC's Toxic Free Neighborhoods Campaign involved a range of research approaches from secondary data analysis to Geographic Information Systems (GIS) mapping, survey research, air sampling using ultra-fine particulate (P-trak) counters, and legal and policy analysis. Children's Health Study researchers at USC made available to the Coalition their own work on air quality and children's health, as well as on the links between proximity of sources of diesel pollution and children's respiratory health.[21,22] The burden of disease analyses conducted by these researchers indicated estimates of excess respiratory illnesses attributable to nitrogen dioxide, ozone, and particulate matter in local communities.[21,22] These outside academic colleagues' successful efforts to quantify excess cases of asthma symptoms (manifested in school absenteeism, etc.) that could be attributed to excess particulate matter exposures "did apply specifically to National City" and provided important context for the current study.

Coalition members also did their own air quality measurements, using P-trak counters to measure the smallest and most dangerous particles, both near the Momax truck-driving school (located opposite an elementary school) and at a control site (City Hall). This simple comparison showed a dramatic difference in air quality, from 25,000 particles per cubic centimeter at City Hall to 150,000 near a moving Momax truck.[23]

EHC's in-house academic researcher then conducted GIS mapping to quantify toxic emissions exposures on a larger scale (see Figure 1). Data on local air toxics "hot spots" were collected from the California Air Resources Board's inventories of toxic emissions by facility (http://www.arb.ca.gov/app/emsinv/facinfo/facinfo.php) and the San Diego County Air Pollution Control District. Using the ESRI mapping program ArcView TM, boundaries of OTNC were used to create a "footprint" of the neighborhood and three other similarly sized (0.036 square miles) footprints adjacent to OTNC, in order to compare the annual number of pounds of toxic emissions to which residents were exposed. As indicated in Figure 1, the "footprint" around

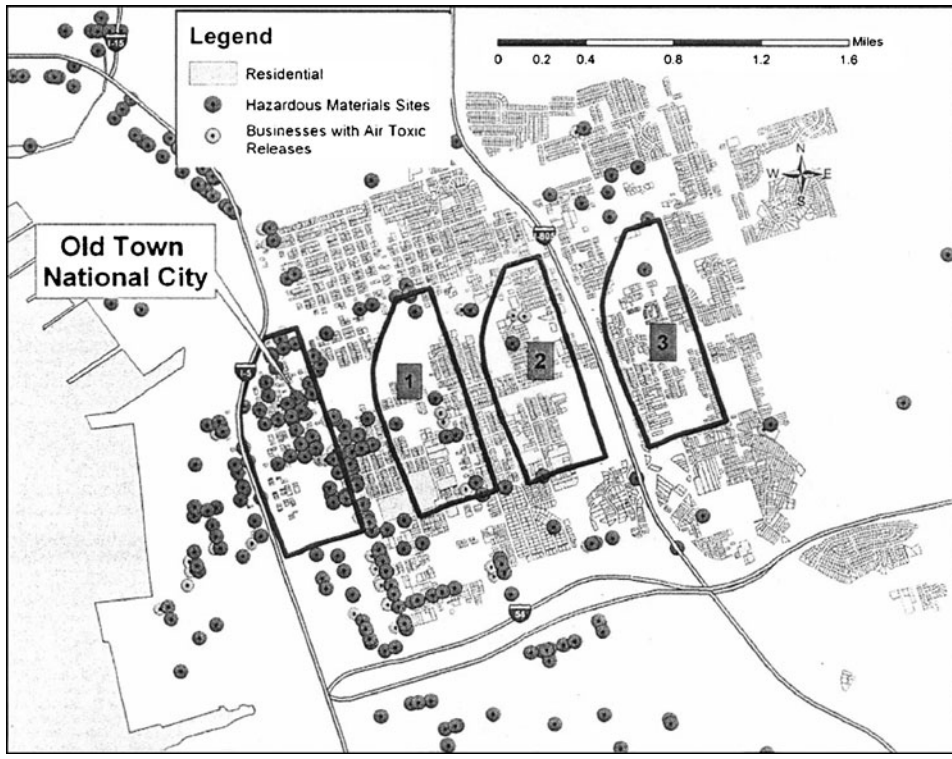

FIGURE 1. Comparing emissions: Old Town National City and three adjacent footprints.

Toxic Air Contaminant Emissions (lbs. per yr.)

Old Town	**23,114**
Footprint 1	**5,963**
Footprint 2	**3,674**
Footprint 3	**0**

Source: J. Williams, in EHC Report, *Reclaiming Old Town National City, 2005.* Based on data from County Department of Environmental Health and California Air Resources Board, available through Right to Know legislation.

Note: Does not include acetone and other gases and particulates that are not regulated as "toxic air contaminants" in California

OTNC is far more densely packed with hazardous materials sites and businesses with toxic air releases, with over 23,000 lbs of toxic air contaminants released in OTNC in 2005, with comparison figures of 6,000, 3500, and zero lbs, respectively, in the three adjacent footprints.[1] The far higher rates of air toxics in the OTNC footprint were attributed largely to the more than 20 autobody shops in this area, which together account for 70% of the reported toxics in this area.[1]

Complementing the academic partners' studies was a third prong of the research: a 56-item survey of 119 adult residents of OTNC conducted by bilingual

teams of trained *promotoras* with guidance from EHC staff. Seventeen *promotoras* completed the full, six-session training, which included sessions on topics including land use and environmental health and on how to conduct surveys and minimize bias. Six of the *promotoras* then conducted the survey with a nonrandom convenience sample obtained primarily through door-to-door canvassing, with additional parents contacted in front of the local school and invited to participate. An estimated 66% response rate was achieved, with 110 of the 119 surveys having all questions answered. Following survey data collection, two EHC members with formal research training conducted preliminary data analysis creating simple frequencies, breaking the data down, where appropriate, by categories (e.g., renter versus homeowner), and putting the findings into graphs and pie charts to facilitate the *promotoras*' involvement in the interpretation process. In the words of one staff member, "We pasted the entire large conference room with those pie charts," and the promotoras engaged in lively discussions of their meaning and resultant recommendations for action. Community meetings were then held to further disseminate the study findings and elicit additional input.

Survey results indicated that 14% of the respondents' children had been diagnosed with asthma and that 32% of children and 51% of adults lacked health insurance. Survey respondents reported a high level of support for a proposed Specific Plan, which would end the neighborhood's designation as a "light manufacturing/residential" area, and they had strong feelings about what the Plan should include. Over 90% of respondents, for example, supported a Plan that would involve relocating industry to a new industrial park outside the neighborhood. Finally, and despite widespread concern with addressing air pollution, the number one priority item turned out to be affordable housing—a finding that helped broaden the action agenda of EHC.

The findings of the survey, along with the principles developed by the *promotoras*, other community members and EHC staff, were published in August, 2005 as part of a widely publicized report entitled, *Reclaiming Old Town National City: A Community Survey*.[1] Although the town's mayor occasionally made comments like, "Anyone can conduct a survey and get any result," an EHC leader reported that few accusations of bias were made. In contrast, as noted below, a number of newspaper articles and editorials, and even the draft Specific Plan itself, cited the study in positive ways, and the report's principles or recommendations were used to develop the formal land use map that in turn helped shape the final Specific Plan.

From Research to Policy Action

Although the action component of CBPR can take many forms, policy- or systems-level change frequently is critical for affecting the lives of large numbers of people.[24] For EHC, policy level advocacy, drawing on the research findings and related recommendations, has been a particularly important avenue for working to address environmental injustice and quality of life in OTNC. Following publication of the report and its "Principles for Revitalization in Old Town," EHC and its partners undertook a number of policy related steps and activities to help effect change. Although the nonlinear nature of policymaking process was clearly evidenced in EHC's experience in this regard, key policy steps and activities identified by Kingdon[25] and others[26,27] were in evidence. Briefly, Kingdon discusses the three "policy streams" that need to converge for successful policy-making efforts: a *problem stream*, in which issues are identified as problems and included in the policy

agenda; a *policy stream*, in which different policy solutions are considered; and a *political stream*, in which policy makers provide their support in favor of a particular solution. He and other policy analysts[26,27] also discuss the steps in the policy process as including problem definition, setting an agenda and creating awareness, considering policy alternatives and deciding on which to pursue, policy enactment, implementation, and modification.

Problem Definition/Identification Studies by USC researcher Jerrett and his colleagues[21] had shown an association between traffic-related pollution and the onset of asthma, while the work of Guaderman et al.[22] suggested that current levels of air pollution had chronic, adverse effects on lung development of children ages 10–18, leading to significant deficits in lung functioning in adulthood. This academic research, coupled with EHC's survey findings of children's asthma rates well above the state average and residents' shared personal experiences, helped shine a spotlight on asthma and its likely relationship to poor land use planning. Together with the Coalition's powerful GIS data (see Figure 1), the research further helped demonstrate a broader problem: environmental injustice in the location of autobody shops and other toxic release facilities, with OTNC bearing the brunt of resultant pollution and other adverse human and environmental costs of the neighborhood's designation as a "light manufacturing/residential" area.[1] Together, this research played an important role in providing credible evidence during the problem identification/problem-stream phase of the policy process.

Setting an Agenda and Creating Awareness As part of the problem stream, agenda setting takes place when a problem is recognized as an issue that calls out for government attention and potential action.[25] Using both quantitative data and residents' stories regarding poor land use planning and its consequences, including high rates of asthma linked in part to toxic releases from autoboby shops, EHC and its partners initiated a broad-based and multi-faceted public and policy maker awareness campaign. Effective use of media advocacy, with articles in the *San Diego Union Tribune*[28] and on popular city blogs[29] as well as stories in EHC's newsletter *Toxinformer*, published in English and Spanish, were among the strategies used to create awareness. A *Union Tribune* article thus reported the survey's finding that 14% of local children had diagnosed asthma but also cited EHC's belief that poor access to care probably meant that this was a very conservative figure. The article further quoted a USC academic partner's findings regarding the relationship between proximity to diesel sources and adverse childhood health outcomes, including both asthma and stunted lung development.[22,28]

Door knocking by EHC volunteers, passing out flyers, and urging attendance at hearings and community and house meetings also were employed, as was residents' and staff members' testimony at public meetings, and briefing of elected officials.

EHC's success in creating awareness and organizing OTNC was greatly aided by its relationships with key institutions in the neighborhood, chief among these the local elementary school (one of whose teachers chaired EHC's board), the church-based Saint Anthony's Organizing Ministry, and the Old Town Neighborhood Council. The *promotoras*' frequent involvement with the school and church, and their bridge building with such institutions, helped EHC reach local families effectively and efficiently.

Although the academically trained research partners frequently played key roles in providing testimony and in other ways helping get on the policy makers' agenda,

a special effort was made by EHC to enable the "front and center" participation of *promotoras* and other residents, who described in detail having been taught "how to look at the TV cameras, speak to reporters… reach a wider audience with our message."

Constructing Policy Alternatives and Deciding on a Policy to Pursue As Themba et al.[30] point out, developing good policy requires a careful exploration of the larger context in which an issue is embedded. In a process similar to what policy makers themselves go through as part of the policy stream in the policymaking process, EHC used strategic planning and other means to help community members think through their priorities, and the policy strategies most likely to be effective in helping achieve them. With respect to the signature goal of reducing neighborhood pollution, EHC leaders thus helped residents review the pros and cons of a variety of policy alternatives, among them eminent domain (state power to take private property for public use, compensating the owner), code compliance, re-zoning, relying on market forces, and amortization. The latter approach sets a reasonable time period for an individual whose business is inconsistent with current zoning to "recoup" his or her investment before that use is terminated. Since residents trusted neither the government (regarding eminent domain and code enforcement) nor market forces, and believed re-zoning was necessary but not sufficient to bring about change, working for an amortization ordinance was deemed the best immediate policy option for which to work. This effort in turn led EHC and its community residents and partners to focus on a larger policy goal: getting a Specific Plan for OTNC, which would address not only the toxic emissions issue but also other hot-button concerns of residents, among them limiting gentrification pressures and increasing access to housing which is affordable to the mostly low-income residents of OTNC.

Policy Advocacy EHC staff, *promotoras*, and other partners and allies engaged in a variety of activities to help achieve their policy objectives and impact on the political stream of the policymaking process. Using "power mapping"[31] (a process in which groups select the specific policy objective they seek and identify policy targets and other key players, their strength and stance on the issue, etc.), they literally mapped out on butcher block paper key allies and opponents and their policy targets, e.g., the City Council and other organizations and individuals with the power to make desired changes. EHC then worked with the USD Environmental Law Clinic to develop the legal grounds for the amortization ordinance and help advocate for its adoption.

Presentations at City Council meetings were described by policy makers and others as particularly effective, and included the *promotoras*' sharing of "statistics and stories" (e.g., their survey findings and their lived experience as residents and mothers), EHC staff and researchers' presentations of visually compelling GIS and other data, and the *promotoras*' then giving Council members a handout or "leave behind" summarizing the problem, the evidence, and their proposed solutions. A "great relationship with the local media" and strong alliances with advocates well beyond OTNC further contributed to the successful passage of an amortization ordinance in August 2006. Maintenance of strong lines of communication with key policy makers was also described as a key strategy, as was mobilizing the community to be present at hearings and other events and show their support on this and related issues. Although one policy maker interviewed commented that amortization had

already been under consideration by the City Council when the EHC became involved, two others who were intimately involved in the process, as well as mass media accounts, stressed the important role which the partnership played during the convergence of the three policy streams resulting in an actual policy change. One policy maker remarked that:

> "They [EHC] played a major role because as policymakers when we see a community of 15–30 fill up a meeting room, and 30 different leaders come from the community at large, we see that it is a concern. We as policymakers see that we really need to look into [it] before we can make decisions."

Another City Council member commented that EHC "influenced the policy environment" largely because of its effectiveness in "bringing all of the parties together to resolve whatever issues were at stake. Without that approach… usually change does not happen."

Similarly, policy advocacy through these and related channels was used to help make the case for a Specific Plan. In the words of a City Council member we interviewed, "They [EHC] brief me, share concerns… one-on-one, through phone calls…" and by inviting her to be part of relevant community events. This policymaker also noted the value of EHC's data in policy advocacy, commenting that "numbers and statistics make or break an argument."

POLICY IMPLEMENTATION AND OUTCOMES

Credible research and follow-up actions by EHC and its allies were described by policy makers and others as having had a substantial impact on several policy-related outcomes. As one EHC leader commented with respect to the coalition's footprints graphic, for example, (Figure 1), the map was "the scientific articulation" of what the residents and the local church and school "had been calling out [and] when politicians saw that, they went, 'Oh wow. This is actually an issue for us and we really need to deal with it. We're going to look real bad if we don't." Passage of the amortization ordinance in August 2006 would allow Council members to phase out polluters. EHC's data on the extremely high rates of ultra fine particulate matter in diesel exhaust from Momax trucks near the local elementary school, together with effective advocacy by EHC and its allies at the school and a nearby church, also were credited with helping limit the operation of the truck-driving school.

EHC was further described by key informants we interviewed as "a major force" in getting a $180,000, City-funded feasibility study on the creation of an industrial park outside the city limits where polluting industries could relocate. Furthermore, and in response to the *promotoras*' survey finding that affordable housing was the number one concern of residents, EHC and its allies were successful in getting an agreement from the City to convert a 10-acre brownfield in the middle of Old Town into a 250-unit affordable housing project, which would include five acres of restored marshland and recreational space. The City's hiring of an architect in September 2008 to conduct a community outreach process for site development, and inclusion of the site plans in the bidding process to select a developer in December 2008, also were described as stemming in substantial measure from the work of EHC and its allies on this issue.

In October 2009, the OTNC City Council voted to include a Health and Environmental Justice Element in its General Plan to better address the way land use

practices affect community health. In so doing, National City became the first municipal area in California to include environmental justice as a full element of its general plan. Following additional community meetings and a City Council meeting in which EHC members, residents, teachers, scientists, and other supporters offered testimony, the Council unanimously adopted the Westside (Old Town) Specific Plan in March 2010. The Specific Plan will slowly relocate industrial businesses out of the neighborhood while allowing businesses that provide residents with "goods and services, recreation and public transit."[32] Several policy makers we interviewed described the EHC partnership as a major contributor to both the form and content of the Plan and its eventual passage. EHC's survey findings on community preferences regarding building heights (e.g., two or three versus five stories), density, and provisions for affordable housing thus provided some of the data needed to ensure that the Plan reflected resident concerns and desires. As a city councilmember commented:

> "EHC [kept] the City Council informed on key changes identified by the community to be included in the Specific Plan. They get residents to be involved [and] bring up issues that without their participation or input, we as the City Council would not have thought about. EHC and its partners bring to the forefront key examples of changes we can make to create and design a better, more inclusive plan."

An op ed piece by the current mayor and a long-time resident announcing passage of the Specific Plan further both cited EHC's GIS data and emphasized the role of community involvement in achieving this historic victory.[33]

Not all of the outcomes of this project have been positive, however: while expressing her support for the amortization ordinance, for example, another policy maker commented that this tool "has a negative association" [and] "when we talked to gross polluters and specific businesses, they accused us of being anti-business." Furthermore, without the needed zoning changes, actual enforcement of the amortization ordinance proved impossible. As a Council member remarked, the presence of just two code enforcers for the entire city precluded enforcement of even the existing codes—a particular problem given that the vast majority of the businesses operating in OTNC are not in compliance.

Of even greater concern to an EHC leader was the worry that with its emphasis on new housing with recreational spaces and other desirable features, as well as offering a profit-making opportunity for developers, it may have an undesirable consequence, since "You're creating an atmosphere that's ripe for gentrification." He added that it was critical, therefore, that the Specific Plan be developed and implemented in such a way that "the folks who have been suffering these injustices for decades and fighting for change are the ones who benefit from it, and that they're not just simply displaced."

ADDITIONAL OUTCOMES: BUILDING COMMUNITY CAPACITY FOR SUSTAINABLE CHANGE

Although this paper has focused primarily on environmental justice research and policy advocacy and its outcomes, EHC's contributions to individual community capacity building also should be underscored, as this too is a key goal of CBPR.[3,24,30] As noted earlier, integral to the Coalition's work has been the training and continued

mentoring of *promotoras* who received small stipends, meals, and childcare and have been actively engaged in EHC's community outreach and organizing work. Describing the intensive training in which she had participated as part of her preparation for participation in the Toxic Free Neighborhoods Campaign, one promotora remarked that participants learned not only about EHC's history and mission but also "how to educate ourselves, how to keep our homes healthy… how to talk to [people], how to get them involved." Another *promotora* described how they learned to design and conduct credible surveys based on community-identified concerns, how to approach potential participants and later, "how to express yourself within City Council." In the latter regard, an important part of the training involved preparation for participation in Council meetings and similar public venues and debriefings, which were held immediately afterwards. In conducting such sessions, however, EHC staff had to walk a difficult tightrope. As one staff member remarked,

> "I think there's a tension between helping people structure and organize their presentation and making sure that folks don't get so caught up in the technical side of it that they lose the emotion in what they're saying. It's the emotion behind the stories that carries the potential to impact the decision makers. I think that we had to pull back at certain times when it came off like over-preparation, and just tell them to let it fly."

As assessed by both staff members and the *promotoras* themselves, however, the trainings were successful in helping participants feel more empowered and capable of helping make a difference. As one *promotora* reflected, "One of the things I learned from the training is that we, as a community, have the *power* to make changes… that if the entire community is united and we are all in agreement and want that change, we have the power to have *them* [city officials] change their minds."

The *promotoras* also faced challenges, however, among them frustrations caused by slowness of change, particularly with respect to long term goals and objectives. Reflecting on this problem, an EHC staff member commented that, in retrospect,

> "I would have liked to have worked with them on smaller, practical, get-it-done-quickly projects during the course of the Specific Plan. We knew it would be long, but we didn't know it would be over five years from start to finish. You can use every organizing trick in the book, but after that much time, it gets very difficult to sustain interest."

Although some shorter term projects were undertaken, e.g., the amortization ordinance and efforts to close the trucking school across the street from the local elementary school, "more small, hands-on stuff that energized people, such as community gardens, neighborhood watch [and] alley restorations" could have helped them achieve smaller victories along the way.

The *promotoras* also noted personal problems, including being labeled *chismosas* (gossips) by some other women in the community, facing distrust and resentment from their husbands and sometimes incurring bad feelings from their children for being out of the house. Although none of the *promotoras* quit because of family pressures, according to EHC staff, "there were definitely some very rough patches, and a lot of tearful office conversations where that decision was contemplated." To help address these challenges, one of EHC's most successful strategies was to recruit and involve husbands. As a staff member noted,

"Those that got up close to it realized that it was noble, respectful, important work, and had pride. I also think that inviting the guys to the celebrations and graduations helped." This male staff member also mentioned the importance of just meeting and hanging out with the husbands, "in part because it defused any sort of suspicion they had about their wives working with a guy." Emphasizing that men were involved in the work, too, also helped dispel stereotypic notions some of the men had that their wives were simply "gossiping."

Most of the women interviewed reported that, with time, their family members became not only accepting of their roles but proud of them and sometimes actively engaged in the campaign themselves. As one *promotora* commented,

> "Every time we go to a City Council meeting and see the reports on TV, my kids will say, 'Mom, that is not true what the City Council members are saying.' Because they are also educating themselves alongside us and that is something very beautiful."

Finally, and of particular importance from the perspective of sustainability, five trained *promotoras* have been hired onto EHC staff as community organizers. Furthermore, one of the community residents who had worked closely with the EHC and its allies at the local church subsequently was elected to the City Council and now serves as Vice Mayor of OTNC. In helping to groom current and future civic leaders, EHC and its partners have further helped improve the prospects for policy-level changes that can in turn promote health and environmental justice.

DISCUSSION

Fleishman[34] has noted that "Meaningful community engagement in urban health research is an aspirational goal that deserves the attention of the research community and the public at large." As illustrated in this and other case studies,[6–8,35–37] the form of engagement known as CBPR also merits, and is receiving, increased attention from policy makers. The EHC partnership is an example of a CBPR effort that appears to have both produced credible science and helped bring about environmental health policy change. EHC's in-house research, including toxic release footprints of OTNC and adjacent areas, provided visually powerful data on the toll that disproportionate exposure was taking on this community. Similarly, both quantitative data from university-based colleagues and a *promotora*-led survey of residents received good media coverage and frequently were cited in testimony before the City Council and other bodies to help capture the key concerns and priorities of residents and in turn help shape the Specific Plan.

From a policy perspective, passage of the amortization ordinance, the passing of a law to limit the operation a truck-driving school adjacent to the local elementary school, and the securing of funds for a feasibility study for an industrial park outside the city limits all were described by local media and relevant policy makers and other stakeholders as having been substantially related to the work of EHC and its partnership.[23,28] These incremental changes, moreover, were important in helping achieve the longer term goal of putting into place a Specific Plan, whose content and passage were described as reflecting substantially the contributions of EHC and its allies.

Although the findings of the case study presented in this article are, by definition, not generalizable, they reinforce those of a number of other studies involving policy-focused CBPR in environmental justice. The Trade, Health and Environment (THE) Impact Project, for example, a regional coalition comprised of community-based organizations (CBOs) and academic partners in Los Angeles, Long Beach, and the Inland Valleys, trained community members to serve on neighborhood assessment teams and gather data through traffic counts and the measurement of particle concentration.[37] Their collaboration, with academic partners at USC, contributed to the passing of the Clean Truck Plan and to a successful delay of the expansion of a major freeway to allow more public participation and consideration of its community and health impacts.[37] In Northern Manhattan, NY, United States, impressive CBPR by a partnership between West Harlem Environmental Action (WE ACT) and epidemiologists at the Mailman School of Public Health at Columbia University[38] was described by EPA policy makers as having played a key role in helping to secure tighter air-quality standards, as well as the placement, by the EPA, of permanent air monitors in Harlem and other "hot spots" around the country.[10,35] Furthermore, several of these efforts have been credited with helping change the broader policy environment. THE Impact Project has been described as having helped "change the debate" on neighborhood contamination through increased community participation.[37] Similarly, the Southern California Environmental Justice Collaborative was given substantial credit for the fact that the state EPA and other decision-making bodies increasingly think in terms of *cumulative* rather than individual risk in their policy deliberations.[7,10,39] Although National City represents a much smaller geographic area, the work of the EHC partnership likewise was described by policy makers and others interviewed as having helped change the policy environment, with the organization and its active community base identified as an important force influencing governmental planning efforts.

Several of the factors that appeared critical to the success of the EHC partnership also have been observed with respect to other environmental health CBPR partnerships. The need for strong alliances and a solid community base has been widely cited,[6,7,10,30,39,40] as has the importance of credible science that can "stand up to careful scrutiny."[7,10,24,35,36,41] The powerful combination of research, community organizing and policy advocacy in this work also frequently has been emphasized. As Morello-Frosch and her colleagues[7] argue:

> [Strong CBPR partnerships] "promote not only good science, but science that is focused on important problems that affect the lives of real people, and they do so while enhancing community capacity and participation in research and advocacy—all of which can ultimately improve the regulatory and policymaking process"

The combining of several kinds of data collection, and of balancing "statistics and stories," similarly has been highlighted as enhancing efforts to move policy.[7,10,24,30,42,43] Indeed, EHC and each of the other abovementioned projects both undertook quantitative data collection and provided training for community members in public speaking and in other ways communicating their personal stories and messages as a key component of the work.

The importance of making the time to engage in substantial background work, including strategic planning, power mapping, and researching policy options and alternatives as a prelude to policy action, has been widely discussed in the literature[6,24,30,35–37,40,43] and was well-demonstrated in the EHC partnership.

Relatedly, effective use of the mass media has proven an important feature of policy-oriented CBPR in environmental justice and related areas.[6,7,10,30,40]

Although attention to and skills in the above areas served the EHC partnership well, a number of challenges and barriers were uncovered in this case study, many of which also have been reported in other policy-focused CBPR partnerships working to promote environmental justice in low income urban areas.

In both OTNC and West Oakland, CA, United States, for example, a policy win (OTNC's amortization ordinance and West Oakland's 2006 truck ordinance) proved difficult to enforce due to either zoning that precluded enforcement or inadequate staff for providing oversight.[44] In New York City, the WE ACT partnership's successful efforts to help close a bus depot in Northern Manhattan (which was home to seven of the City's eight depots) similarly was described as involving a shell game, with the City soon opening another depot in a different part of this community.

Time and role constraints and complications, particularly for community partners, also have been widely reported[10,34,42–47] and were a particular issue for EHC *promotoras* in the early stages of the work. Resentment from husbands and children, and being labeled as "gossips" by some community women not involved in the work, were of particular concern and are a reminder of the need to address the fact that training and hiring community members as team members may make them "outsiders within" or as Freire[48] remarks, "strangers in their own community." Substantial time for trust building,[34,45,47] special training, and mentoring of community partners with respect to these and other challenging aspects of their roles, and, in the case of communities like the heavily Latino OTNC, outreach to participants' husbands, are an important part of individual and community capacity building. Provision of meals and childcare, as well as a modest stipend also can be important in helping to lessen some of the burdens that community partners often face in this work. Finally, training for academic and other outside partners is needed so that they can better understand, and where possible avoid or ameliorate, such problematic aspects of participation for their community partners.[10,45–47]

Interestingly, one widely cited limitation faced by many CBPR partnerships, namely, inadequate financial support, particularly for community partners,[10,34,45–47] appeared not to have presented a major obstacle to the EHC partnership. EHC's earlier noted ability to bring in substantial funding from The California Endowment and The James Irvine Foundation, as well as eight years of NIH funding in support of its work, was a major contributor to its fiscal viability and its consequent ability to foster sustainability. The EHC partnership's experience, like that of WE ACT and the Southern California Environmental Justice Collaborative highlighted above, underscores the importance of foundation and federal funding that makes "long term investment in change,"[7] including support for developing the internal capacity of CBO partners to bring in and administer large federal or foundation grants over a long time period. The value of having strong, in-house researchers who can both help design rigorous research and write competitive grant proposals also was pointed out.

Policy-focused CBPR is labor and time intensive and, as indicated above, may face numerous barriers and obstacles at each step of the process. At the same time, however, partnerships like that of the EHC in OTNC remain important examples of the potential of CBPR for producing sound research and at the same time helping to amplify community voice toward the end of helping to promote policies that can improve the prospects for environmental justice in urban communities.

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Air Pollution, Aeroallergens, and Emergency Room Visits for Acute Respiratory Diseases and Gastroenteric Disorders among Young Children in Six Italian Cities

Flavia Orazzo,[1] Luigi Nespoli,[2] Kazuhiko Ito,[3] Davide Tassinari,[4] Daniela Giardina,[5] Maurizio Funis,[6] Alessandra Cecchi,[7] Chiara Trapani,[7] Gisella Forgeschi,[8] Massimo Vignini,[9] Luana Nosetti,[2] Sabrina Pigna,[10] and Antonella Zanobetti[11]

[1]Pediatric Emergency Room, Santobono's Hospital, Naples, Italy; [2]Pediatric Emergency Room, Pediatric Department, University of Varese, Varese, Italy; [3]Nelson Institute of Environmental Medicine, New York University School of Medicine, New York, New York, USA; [4]Pediatric Emergency Room, Pediatric Department, University of Bologna, Bologna, Italy; [5]Pediatric Emergency Room, Maggiore's Hospital, Bologna, Italy; [6]Pediatric Emergency Room, Pediatric Department, Torre Galli, Florence, Italy; [7]Pediatric Emergency Room, Mayer Hospital, Florence, Italy; [8]Pediatric Emergency Room, Ponte a Niccheri Hospital, Florence, Italy; [9]Pediatric Emergency Room, Pediatric Department, Salesi Hospital, Ancona, Italy; [10]Pediatric Emergency Room, Gallarate Pediatric Hospital, Gallarate, Italy; [11]Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA

Background: Past studies reported evidence of associations between air pollution and respiratory symptoms and morbidity for children. Few studies examined associations between air pollution and emergency room (ER) visits for wheezing, and even fewer for gastroenteric illness. We conducted a multicity analysis of the relationship between air pollution and ER visits for wheezing and gastroenteric disorder in children 0–2 years of age.

Methods: We obtained ER visit records for wheezing and gastroenteric disorder from six Italian cities. A city-specific case–crossover analysis was applied to estimate effects of particulate matter (PM), nitrogen dioxide, sulfur dioxide, ozone, and carbon monoxide, adjusting for immediate and delayed effects of temperature. Lagged effects of air pollutants up to 6 prior days were examined. The city-specific results were combined using a random-effect meta-analysis.

Results: CO and SO_2 were most strongly associated with wheezing, with a 2.7% increase [95% confidence interval (CI), 0.5–4.9] for a 1.04-μg/m^3 increase in 7-day average CO and a 3.4% (95% CI, 1.5–5.3) increase for an 8.0-μg/m^3 increase in SO_2. Positive associations were also found for PM with aerodynamic diameter ≤ 10 μg and NO_2. We found a significant association between the 3-day moving average CO and gastroenteric disorders [3.8% increase (95% CI, 1.0–6.8)]. When data were stratified by season, the associations were stronger in summer for wheezing and in winter for gastroenteric disorders.

Conclusion: Air pollution is associated with triggering of wheezing and gastroenteric disorders in children 0–2 years of age; more work is needed to understand the mechanisms to help prevent wheezing in children.

Key words: air pollution, asthma in children, epidemiology of asthma, children's health. *Environ Health Perspect* 117:1780–1785 (2009). doi:10.1289/ehp.0900599 available via *http://dx.doi.org/* [Online 13 August 2009]

Mounting evidence indicates that air pollution plays an important role on morbidity and mortality in all ages and especially in children. Many studies have focused on the association between pollutants and adverse respiratory health effects in children around the world (Bates 1995; Bedeschi et al. 2007; Dockery et al. 1996; Loomis et al. 1999; Ostro et al. 1999; Romieu et al. 2002; Thurston et al. 1997; Vigotti et al. 2007). In a European review, Valent et al. (2004) reported that among children 0–4 years of age, between 1.8% and 6.4% deaths could be explained by outdoor air pollution, whereas acute lower respiratory tract infections due to indoor air pollution accounted for 4.6% of all deaths and 3.1% of disability-adjusted life-years (DALYs). Recently, epidemiologic studies have also suggested that the effects of air pollution, at current levels, are particularly pronounced in the first years of life (Brauer et al. 2002).

Children are especially susceptible and may be more exposed than adults to ambient air pollution, partly because children have higher ventilation rates than adults and because they tend to spend more time outdoors. Gastroenteritis is an inflammation of the gastrointestinal tract. The inflammation can be caused by infection with certain viruses, bacteria, or toxicants or by adverse reaction to ingested material or medication. Inhaled environmental pollutants in the first ages of life can have profound impacts on the interrelationships between signaling molecules and their targets, thereby upsetting homeostasis in the lung and possibly in the intestine (Kasper et al. 2005).

A few multicity studies have investigated the short-term effects of air pollutants on the development of respiratory infections and wheezing in very young children, using a case–crossover analysis or time-series analysis (Barnett et al. 2005; Bedeschi et al. 2007; Galan et al. 2003; Lin et al. 2003; Luginaah et al. 2005; Romeo et al. 2006; Tobias et al. 2003; Vigotti et al. 2007). However, none has studied gastroenteric diseases, which represent a major fraction of morbidity outcomes in children, including visits to the emergency room (ER).

Air pollution is a concern in Italy, and several studies of mortality and hospital admissions in adults (Katsouyanni et al. 1996) and children (Bedeschi et al. 2007; Romeo et al. 2006; Vigotti et al. 2007) have addressed this issue.

In this study, we examined the association between air pollution and pediatric hospital ER visits for wheeze and gastroenteric disorders among children 0–2 years of age in six Italian cities between 1996 and 2002.

We applied a multicity case–crossover analysis to study the acute effect of particulate matter with aerodynamic diameter ≤ 10 μg (PM_{10}), nitrogen dioxide, sulfur dioxide, ozone, and carbon monoxide, and aeroallergens (Graminaceae and Urticaceae) on the risk of ER visits for wheezing and gastroenteric disorders among children 0–2 years of age, and we examined whether that risk was modified by season.

Data and Methods

Health data. We examined the association between air pollution and daily pediatric hospital ER visits of children 0–2 years of age living in six Italian cities: Ancona (west on the

Address correspondence to A. Zanobetti, Department of Environmental Health, Exposure Epidemiology, and Risk Program, Harvard School of Public Health, 401 Park Drive, Landmark Center, Suite 415 West, P.O. Box 15698, Boston, MA 02215 USA. Telephone: (617) 384-8751. Fax: (617) 384-8745. E-mail: azanobet@hsph.harvard.edu

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sea), Bologna (center), Padua (north), Varese and Gallarate (north), Florence (center), and Naples (south). Varese and Gallarate were analyzed as one because these are two small municipalities near to each other in a zone with several industries in the north of Italy.

We collected information on daily ER visits for wheezing (Castro-Rodriguez et al. 2000) for the years 1996–2000 from the main pediatric hospitals in each city. Pediatric doctors in the ER collected information through questionnaires administered to the family when they were bringing their children to the ER.

We extracted daily counts of wheezing, defined as respiratory disease of lower airways (Martinez 2005). Wheezing resembles a musical sound generated by the high-speed airflow through the lumen that obstructs the airways. The children present rhinitis with coughing, and dyspnea; the chest is enlarged. Soft rantoles and wheezing, especially at the end of inspiration, are detected through auscultation.

We also extracted gastroenteric disorders, defined as acute enteric disease with diarrhea and vomiting (Elliott and Dalby-Payne 2004). In the study, children were excluded if they accidentally ingested poisonous substances, had urinary infection, or had gastroesophageal reflux.

Environmental data. Air pollution data were obtained from the Italian Environmental Protection Agency ARPA (Agenzia Regionale per la Protezione Ambientale) for the six cities during the years 1996–2002.

We analyzed ambient PM_{10} (available in Florence, Bologna, and Naples), total suspended particulates (TSP) (available in Ancona, Varese, Padua), NO_2, SO_2, O_3, and CO.

PM_{10} and TSPs were measured by β attenuation, SO_2 by pulse fluorescence, NO_2 by chemiluminescence, O_3 by ultraviolet absorption, and CO by infrared absorption. Pollutants concentrations were expressed as 24-hr means for TSP, PM_{10}, SO_2, and NO_2 and as the maximum of 8-hr means between 0800 and 1600 hours for CO and O_3. The 24-hr and 8-hr averages were computed if at least 77% of the measures were available for all the pollutants.

We transformed the TSP data in PM_{10} in those cities where only TSP was available using the conversion factor ($PM_{10} = 0.83 \times$ TSP) suggested by the 1999 Council Directive of European Commission (Council Directive EC 1999).

Many of the cities have more than one monitoring location, and we computed local daily mean pollution concentrations as the average of all monitors in the city. We obtained local mean temperature and relative humidity from the same monitoring stations that collected air pollution data. We also obtained data on aeroallergens such as Gramineae and Urticaceae. The levels of these airborne pollens were collected using a volumetric spore trap (VPPS 2000; Lanzoni Co., Bologna, Italy) located on the rooftop of each city's central station. Daily pollen counts were converted into 24-hr average concentrations expressed as grains per cubic meter. During the study period, daily pollen data were available from April to September in each city, and in Naples, Ancona, and Varese-Gallarate for all year. Because pollen data were very sparse during winter, this analysis was performed only in the summer.

Statistical methods. We investigated the association between daily air pollution concentrations and emergency visits for wheezing and acute enteric disease in children using a case–crossover design (Maclure 1991). The case–crossover design samples only case days, and a case subject becomes a control subject on days without event, in this analysis ER admission. By using control days close in time to the event day, there is no confounding by slowly varying personal characteristics, because each subject is the perfect match for himself. Moreover, the case–crossover method controls for long-term trend and seasonality by design. Air pollution has short-term serial correlation, and to ensure that all of our control days were independent, we chose control days matched on day of the week in the same month and year as the event day. In addition, for a sensitivity analysis, we conducted case–crossover analysis by matching on every third day from the case day in the same month and year, which provides more control days. In the every-third-day referent sampling method, day-of-week variable was included in the regression model.

To control for potential impacts of weather, we used same-day mean temperature to control for immediate effects and the average of the lags 1–3 of mean temperature to represent the delayed effects. Because risk may vary nonlinearly with temperature, we used natural cubic spline (with three degrees of freedom) for both the same day and the moving average of the previous 3 days. Both temperature terms (same day and lag 1–3) were included simultaneously in the models. We also included a natural cubic spline with three degrees of freedom to control for relative humidity. Because the relationship between air pollution and wheeze or gastroenteric illness may change across seasons, we also conducted stratified analyses by season, defined as summer for the months of April–September and winter as October–March. Air pollution was modeled linearly. We analyzed the effect from the same day up to 6 prior days; we also computed the moving averages as averages of the exposure lags. For example, the 2-day moving average (lag 0–1) was computed as the mean of the same and previous days; the 3-day moving average (lag 0–2) included lag 0, 1, and 2, and so on, up to the 7-day moving average (lag 0–6), which is the average of lag 0–6 days.

The analysis was conducted in each city separately. To estimate an average effect for all cities, the city-specific results were combined using a random-effect meta-analysis using the method of DerSimonian and Laird (1986). We also report the *p*-values for the test of homogeneity. The results are expressed as percentage increase in each outcome for an interquartile range (IQR) increase in exposure. The IQRs were computed as the average IQR across the cities. The data were analyzed using a conditional logistic regression (PROC PHREG release 8.2; SAS Institute Inc., Cary, NC, USA).

Results

The six cities analyzed in this study span north, central, western, and southern regions of Italy and present differences in terms of weather and population. The largest among the six cities is Naples, with a population of around 1 million. The smallest city, Gallarate (population ~ 50,000), and the second smallest city, Varese (~ 90,000), were combined for the analysis. Thus, Ancona (population ~ 100,000) effectively had the smallest population in our analysis. The population of children 0–2 years of age was about 2% of the total population in these cities.

Table 1 shows the daily mean and SD of ER visits for wheeze and gastroenteric illness for all year and by season. The mean number of emergency visits for total wheezing varies between 18 in Naples, the largest city, and < 1 in Ancona, the smallest city. The daily counts for wheeze are generally larger in cold season

Table 1. Descriptive statistics for daily counts of ER visits in each city, in total and by season (mean ± SD).

	Ancona	Bologna	Florence	Naples	Padua	Varese–Gallarate
Total wheeze						
All	0.7 ± 1.0	3.6 ± 3.4	1.9 ± 2.2	18.3 ± 9.1	4.8 ± 4.9	1.0 ± 1.3
Winter	0.9 ± 1.1	4.7 ± 3.7	2.6 ± 2.6	22.1 ± 10.1	6.6 ± 5.7	1.3 ± 1.4
Summer	0.6 ± 0.9	2.4 ± 2.5	1.1 ± 1.3	14.6 ± 5.8	3.0 ± 2.8	0.7 ± 1.0
No. of admissions	1,337	6,526	4,776	33,501	5,299	1,833
Total gastroenteric disorders						
All	0.4 ± 0.7	1.7 ± 1.6	0.9 ± 1.2	8.0 ± 3.8	2.9 ± 2.4	0.5 ± 0.8
Winter	0.3 ± 0.6	1.9 ± 1.8	1.1 ± 1.4	6.6 ± 3.0	2.9 ± 2.4	0.6 ± 0.9
Summer	0.4 ± 0.7	1.5 ± 1.4	0.8 ± 1.0	9.4 ± 4.0	2.9 ± 2.4	0.5 ± 0.7
No. of admissions	641	3,102	2,372	14,626	3,170	1,003
Years of study	1996–2000	1996–2000	1996–2002	1996–2000	1996–1998	1996–2000

than in warm season, whereas for gastroenteric illness, there is little seasonal pattern.

Table 2 shows the distribution of the weather variables and air pollution. The weather is relatively mild, with the mean temperature ranging from 12.7°C in Varese–Gallarate (north) to 18.6°C in Naples (south). The mean levels of gaseous air pollutants varied by a factor of two across these six cities, with Naples showing the highest levels, whereas the mean levels of PM were less variable. The number of missing values varies by city, with Varese and Gallarate being the city with the highest percentage of missing values (between 1% and 22%). Across the other cities, the percentage of missing values varied between 0 and 8%.

Associations between air pollutants and ER visits for both wheezing and gastroenteric disorders were positive at all single-day lags (result not shown) but consistently less significant than those for moving averages. (For SO_2 only we found significant associations from lag 2 to lag 6.) Therefore, we present the result using moving averages.

Table 3 shows the combined results for total wheezing for all the moving averages. Among the air pollutants, CO was most strongly associated with ER visits for wheezing, followed by SO_2. However, generally positive associations were found for PM_{10} and NO_2 as well, and, although some associations were not statistically significant, for all the pollutants considered the estimated risks increased as the average of longer lags were considered. For CO, the estimated risks were significant for all the moving averages analyzed. For example, the percentage excess risk estimate for the lag 0–6 (i.e., the average of 0- through 6-day lags) was 2.7% [95% confidence interval (CI), 0.5–4.9] in total wheezing for a 1.04-μg/m^3 increase in the average of 0- through 6-day lags of CO. The strongest association between ER visits for wheezing and SO_2 was found for the lag 0–7, with a 3.4% (95% CI, 1.5–5.3) increase for a 8.0-μg/m^3 increase in SO_2. No significant associations were found with O_3.

The associations between air pollution and ER visits for gastroenteric disorders (Table 4) were generally weaker than those for wheezing. CO and SO_2 showed significant associations, but unlike the result for wheezing, the estimated risks for CO were not consistently larger for the moving averages with longer lags. The strongest association for CO was found for the 3-day moving average (i.e., average of 0- through 2-day lags, lag 0–2), with a 3.8% increase (95% CI, 1.0–6.8) per 1.1 μg/m^3 increase in CO. For SO_2, NO_2, and PM_{10}, the estimated risks were larger for the moving averages with longer lags, although significant associations were found only for the lag 0–6 and lag 0–7 of SO_2. No significant associations were found with O_3.

Table 2. Mean ± SD for environmental variables in six cities.

	Ancona	Bologna	Florence	Naples	Padua	Varese–Gallarate
Temperature (°C)						
All	14.6 ± 7.1	16.2 ± 9.1	15.3 ± 7.2	18.6 ± 7.0	15.1 ± 7.4	12.7 ± 7.5
Winter	9.5 ± 4.4	9.7 ± 5.7	9.8 ± 4.7	13.9 ± 4.7	9.4 ± 4.4	6.5 ± 4.5
Summer	19.7 ± 5.4	22.6 ± 7.2	20.7 ± 4.8	23.3 ± 5.7	21.0 ± 4.8	18.4 ± 4.6
Relative humidity (%)						
All	60.8 ± 21.1	69.0 ± 12.0	72.6 ± 15.2	44.0 ± 22.9	83.2 ± 7.3	70.7 ± 18.6
Winter	63.4 ± 21.0	72.5 ± 12.5	76.9 ± 15.8	44.4 ± 23.6	84.6 ± 6.6	73.3 ± 19.6
Summer	58.2 ± 20.8	65.6 ± 10.6	68.1 ± 13.1	43.5 ± 22.3	81.9 ± 7.6	68.3 ± 17.4
PM_{10} (μg/m^3)						
All	43.2 ± 42.1	50.8 ± 26.1	43.8 ± 18.9	44.5 ± 18.3	48.1 ± 13.5	63.2 ± 22.1
Winter	38.1 ± 27.4	61.7 ± 28.4	46.5 ± 20.0	39.4 ± 18.4	46.9 ± 14.6	67.6 ± 25.2
Summer	48.3 ± 52.1	40.1 ± 18.0	41.0 ± 17.2	49.6 ± 16.8	49.4 ± 12.0	59.1 ± 17.7
NO_2 (μg/m^3)						
All	42.5 ± 32.9	64.8 ± 20.3	57.9 ± 17.8	78.6 ± 30.6	48.7 ± 18.2	40.8 ± 17.0
Winter	47.5 ± 35.2	73.3 ± 19.2	63.5 ± 19.1	86.8 ± 35.6	55.2 ± 20.3	49.0 ± 18.1
Summer	37.5 ± 29.5	56.4 ± 17.8	52.3 ± 14.4	70.5 ± 21.9	42.1 ± 12.8	33.1 ± 11.4
SO_2 (μg/m^3)						
All	14.6 ± 9.8	7.2 ± 6.0	5.5 ± 4.3	21.1 ± 25.2	17.3 ± 7.3	7.0 ± 5.9
Winter	14.7 ± 10.8	10.1 ± 6.7	6.9 ± 5.2	18.5 ± 19.3	19.1 ± 8.2	10.9 ± 6.1
Summer	14.5 ± 8.6	4.4 ± 3.3	4.1 ± 2.5	23.6 ± 29.6	15.4 ± 5.6	3.5 ± 2.6
CO (μg/m^3)						
All	2.1 ± 0.9	1.4 ± 0.9	1.5 ± 0.8	2.6 ± 1.3	1.9 ± 0.9	1.3 ± 0.8
Winter	2.3 ± 0.8	1.8 ± 1.0	1.9 ± 0.8	3.0 ± 1.6	2.4 ± 0.9	1.8 ± 0.8
Summer	1.9 ± 0.9	0.9 ± 0.5	1.1 ± 0.4	2.3 ± 1.0	1.4 ± 0.4	0.8 ± 0.3
O_3 (μg/m^3)						
Winter	30.7 ± 30.7	23.9 ± 40.5	22.5 ± 16.7	54.7 ± 18.5	34.6 ± 18.8	23.5 ± 17.9
Summer	41.3 ± 29.6	72.9 ± 40.5	60.7 ± 19.1	86.8 ± 32.4	55.9 ± 20.3	69.0 ± 26.9
Gramineae (grains/m^3)						
Summer	2.6 ± 10.7	25.1 ± 39.2	4.8 ± 12.7	4.2 ± 9.1	4.4 ± 9.8	31.5 ± 113.1
Urticaceae (grains/m^3)						
Summer	37.9 ± 44.4	36.9 ± 65.9	2.7 ± 6.8	59.9 ± 95.0	15.4 ± 32.5	12.1 ± 27.3

Tables 3 and 4 also present the *p*-values for homogeneity; although for total wheeze we found significant (at significance level of 0.05) heterogeneity in PM_{10} and NO_2, not much heterogeneity between the cities was found for gastroenteric disorders.

The results from the sensitivity analyses in which control days were chosen from every third day from the case day in the same month and year show the pattern of associations (the lag structure and relative strength of associations across pollutants) similar to that of the main analysis, but the strength of associations is somewhat weaker in the sensitivity analysis despite larger number control days.

When data were stratified by season (Figure 1), for wheezing, the risk estimates for NO_2, SO_2, and CO were larger in summer than in winter. However, the CIs for these estimates were wide, and therefore these contrasts were not statistically significant. For gastroenteric disorders, the estimated risks for NO_2 and CO were larger in winter than in summer, although, again, these differences were not statistically significant.

The results for aeroallergens during summer are reported in Tables 3 and 4 and in Figure 1. Unlike air pollutants, the extent of lagged associations between the pollen and ER visits were shorter, with the four lag 0–3 being most consistently significant. We found a significant effect at lag 3, with a 0.9% increase (95% CI, 0.1–1.7) in total wheeze for 9.6 grains/m^3 in Graminacee and a 2.6% increase (95% CI, 0.05–5.3) in gastroenteric disorders for 27.7 grains/m^3 in Urticaceae.

The varying widths of CIs seen in Figure 1 are attributable mainly to the difference in distributional characteristics of the exposure variables—those with narrow CIs tend to be the exposure variables with right-skewed distributions, whereas those with wide confidence bands tend to be those with more normally distributed variables.

Discussion

The present study shows a significant association between hospital emergency visits for wheezing and gastroenteric disorders in children 0–2 years of age and air pollution levels in six urban cities in Italy, located in different geographical areas (northern, central and southern Italy, plus seaside localities and hinterland territory) having different climatic conditions.

Very young children represent a population more susceptible to adverse health effects; the immune system in the early ages of life is still underdeveloped, as it must recognize the newly assimilated foods during the weaning period. Furthermore, children having a lesser corporeal surface but a higher respiratory frequency inhale and absorb more pollutants in relation to their weight compared with adults.

However, only a few studies have investigated the respiratory effects of air pollution among very young children to date. A recent study in Copenhagen (Andersen et al. 2008) found an association between incident wheezing symptoms in infants (0–1 years of age) and air pollution (PM_{10}, NO_2, CO) with 3- to 4-day lag, consistent with the delayed associations found in our study. Barnett et al. (2005) analyzed data on respiratory hospital admissions in children for three age groups (< 1, 1–4, 5–14 years) in five cities in Australia and two in New Zealand. They found significant association between air pollution ($PM_{2.5}$, PM_{10}, NO_2, and SO_2) and hospitalizations for pneumonia and acute bronchitis for the age groups < 1 and 1–4 years and all respiratory diseases for the three age groups. Pollution levels in those countries were lower than those observed in Italian cities. Villeneuve et al. (2007) examined associations between air pollution and ER visits for asthma among children (2–4, 5–14 years of age) and adults (e.g., 15–24, 25–44 years of age) and reported that the air pollution associations were strongest among young children, with NO_2 and CO having especially pronounced associations. For the 2- to 4-year-old group, CO showed the strongest associations in the warm season, and the estimated risks increased as longer lags were included in the moving averages, which is also consistent with our finding.

More studies examined either older children or children as defined with wider age ranges. These include two studies from Italian cities. Vigotti and colleagues (2007) investigated associations between air pollution and ER visits for respiratory complaints for children (< 10 years of age) and the elderly (> 65 years of age) in Pisa and found significant increase in the ER visits and with increases in PM_{10} and NO_2 (CO was positive but not significantly associated). Similarly, Bedeschi et al. (2007) found increases in ER visits for respiratory diseases among children < 15 years of age associated with elevated levels of PM_{10} and NO_2, with a magnitude of excess risks comparable with those found in our study. In

Table 3. Percentage increase (95% CI) in risk of total wheeze for an IQR increase in air pollution: combined results across six cities and *p*-value for homogeneity test.

Pollutant	Percent (95% CI)	IQR	*p*-Value for homogeneity
CO lag 0–1	1.7 (0.2 to 3.3)	1.1	0.85
CO lag 0–2	2.2 (0.5 to 3.9)	1.1	0.76
CO lag 0–3	2.3 (0.5 to 4.1)	1.1	0.50
CO lag 0–4	2.1 (0.2 to 4.0)	1.1	0.48
CO lag 0–5	2.4 (0.1 to 4.8)	1.0	0.37
CO lag 0–6	2.7 (0.5 to 4.9)	1.0	0.41
NO_2 lag 0–1	1.4 (–1.6 to 4.4)	26.0	0.02
NO_2 lag 0–2	2.1 (–1.3 to 5.7)	24.9	< 0.001
NO_2 lag 0–3	2.3 (–1.4 to 6.2)	24.0	< 0.001
NO_2 lag 0–4	2.7 (–1.1 to 6.6)	23.2	< 0.001
NO_2 lag 0–5	2.6 (–1.2 to 6.7)	22.8	< 0.001
NO_2 lag 0–6	2.8 (–1.0 to 6.7)	22.2	0.02
PM_{10} lag 0–1	1.8 (–2.0 to 5.7)	21.3	< 0.001
PM_{10} lag 0–2	1.7 (–2.9 to 6.4)	20.7	< 0.001
PM_{10} lag 0–3	2.5 (–2.6 to 7.8)	20.1	< 0.001
PM_{10} lag 0–4	2.9 (–2.9 to 9.0)	19.7	< 0.001
PM_{10} lag 0–5	3.4 (–2.5 to 9.8)	19.3	< 0.001
PM_{10} lag 0–6	3.8 (–2.3 to 10.3)	18.9	< 0.001
SO_2 lag 0–1	0.1 (–1.4 to 1.6)	8.7	0.85
SO_2 lag 0–2	0.9 (–0.7 to 2.5)	8.5	0.90
SO_2 lag 0–3	1.7 (0.0 to 3.4)	8.3	0.82
SO_2 lag 0–4	2.1 (0.4 to 3.9)	8.2	0.54
SO_2 lag 0–5	2.8 (0.9 to 4.6)	8.1	0.52
SO_2 lag 0–6	3.4 (1.5 to 5.3)	8.0	0.61
O_3 lag 0–1	–1.9 (–6.6 to 3.1)	42.1	0.11
O_3 lag 0–2	–3.1 (–8.9 to 3.1)	41.5	0.03
O_3 lag 0–3	–2.9 (–9.5 to 4.1)	41.7	0.02
O_3 lag 0–4	–3.7 (–11.2 to 4.5)	41.5	> 0.001
O_3 lag 0–5	–4.4 (–13.3 to 5.5)	41.5	> 0.001
O_3 lag 0–6	–4.6 (–15.2 to 7.4)	41.6	> 0.001
Summer only Gramineae	0.4 (–0.5 to 1.2)	9.6	0.52
Lag 1	0.4 (–0.4 to 1.2)	9.6	0.61
Lag 2	0.6 (–0.6 to 1.7)	9.6	0.22
Lag 3	0.9 (0.1 to 1.7)	9.6	0.45
Lag 0–1	0.5 (–0.5 to 1.6)	10.2	0.54
Lag 0–2	0.7 (–0.5 to 1.9)	10.4	0.45
Lag 0–3	1.2 (–0.1 to 2.5)	10.7	0.43
Urticaceae	0.3 (–0.3 to 1.0)	27.7	0.54
Lag 1	0.4 (–0.3 to 1.0)	27.7	0.44
Lag 2	0.0 (–0.6 to 0.7)	27.7	0.86
Lag 3	0.4 (–0.2 to 1.1)	27.7	0.70
Lag 0–1	0.5 (–0.3 to 1.3)	28.2	0.52
Lag 0–2	0.5 (–0.5 to 1.4)	29.9	0.53
Lag 0–3	0.7 (–0.4 to 1.8)	30.8	0.71

Table 4. Percentage increase (95% CI) in risk of gastroenteric disorders for an IQR increase in air pollution: combined results across the six cities, and *p*-value for homogeneity.

Pollutant	Percent (95% CI)	IQR	*p*-Value for homogeneity
CO lag 0–1	2.7 (0.1 to 5.4)	1.1	0.71
CO lag 0–2	3.8 (1.0 to 6.8)	1.1	0.85
CO lag 0–3	4.9 (–1.7 to 11.9)	1.1	0.27
CO lag 0–4	4.7 (–7.0 to 17.8)	1.1	0.05
CO lag 0–5	3.5 (–8.5 to 17.0)	1.0	0.05
CO lag 0–6	2.7 (–12.0 to 20.0)	1.0	0.01
NO_2 lag 0–1	–1.1 (–3.2 to 1.1)	26.0	0.57
NO_2 lag 0–2	0.1 (–3.0 to 3.3)	24.9	0.26
NO_2 lag 0–3	1.8 (–2.4 to 6.2)	24.0	0.08
NO_2 lag 0–4	2.9 (–1.6 to 7.6)	23.2	0.07
NO_2 lag 0–5	2.3 (–1.9 to 6.6)	22.8	0.14
NO_2 lag 0–6	2.5 (–1.7 to 6.9)	22.2	0.16
PM_{10} lag 0–1	2.4 (–1.0 to 5.8)	21.3	0.28
PM_{10} lag 0–2	2.4 (–1.4 to 6.3)	20.7	0.21
PM_{10} lag 0–3	2.7 (–1.5 to 7.0)	20.1	0.15
PM_{10} lag 0–4	2.9 (–1.9 to 7.9)	19.7	0.08
PM_{10} lag 0–5	3.2 (–1.6 to 8.3)	19.3	0.09
PM_{10} lag 0–6	3.8 (–1.6 to 9.4)	18.9	0.04
SO_2 lag 0–1	–0.1 (–2.5 to 2.3)	8.7	0.78
SO_2 lag 0–2	0.2 (–2.3 to 2.8)	8.5	0.84
SO_2 lag 0–3	1.0 (–1.6 to 3.7)	8.3	0.50
SO_2 lag 0–4	4.1 (–0.5 to 9.0)	8.2	0.16
SO_2 lag 0–5	7.0 (0.1 to 14.3)	8.1	0.06
SO_2 lag 0–6	8.5 (0.6 to 16.9)	8.0	0.04
O_3 lag 0–1	2.1 (–3.8 to 8.4)	42.1	0.15
O_3 lag 0–2	2.0 (–4.4 to 8.8)	41.5	0.16
O_3 lag 0–3	4.0 (–3.9 to 12.5)	41.7	0.08
O_3 lag 0–4	4.2 (–5.2 to 14.5)	41.5	0.03
O_3 lag 0–5	5.6 (–4.5 to 16.7)	41.5	0.03
O_3 lag 0–6	6.5 (–3.8 to 17.8)	41.6	0.06
Summer only Gramineae	–0.3 (–1.6 to 0.9)	9.6	0.98
Lag 1	0.4 (–0.8 to 1.6)	9.6	0.46
Lag 2	0.8 (–1.2 to 2.9)	9.6	0.05
Lag 3	1.0 (0.0 to 2.1)	9.6	0.66
Lag 0–1	0.1 (–1.5 to 1.6)	10.2	0.74
Lag 0–2	0.7 (–1.7 to 3.0)	10.4	0.18
Lag 0–3	1.2 (–1.2 to 3.7)	10.7	0.21
Urticaceae	0.0 (–1.8 to 1.9)	27.7	0.12
Lag 1	0.7 (–1.3 to 2.8)	27.7	0.07
Lag 2	0.0 (–1.0 to 1.0)	27.7	0.46
Lag 3	2.6 (0.0 to 5.3)	27.7	0.01
Lag 0–1	0.7 (–1.9 to 3.3)	28.2	0.05
Lag 0–2	0.7 (–1.9 to 3.5)	29.9	0.11
Lag 0–3	1.9 (–1.4 to 5.4	30.8	0.06

the study by Bedeschi et al., the associations appeared to increase or persist at longer lags (up to 5 days), which is also consistent with our finding. Thus, the results from the Italian studies that involved older children are consistent with the finding from our study with very young children.

In our study, CO showed the strongest associations with ER visits for wheezing, followed by SO_2. However, PM_{10} and NO_2 also showed consistently positive risk estimates (though not statistically significant) with the lag structure of associations similar to those for CO and SO_2. In the studies that we mentioned above, as well as in other studies that found associations between air pollution and children's respiratory morbidity—such as the analysis by Luginaah et al. (2005) in Windsor, Ontario, Canada, or the study by Lin et al. (2005) in Toronto, Ontario, Canada—researchers found associations with similar groups of air pollutants, generally including two or more from CO, NO_2, SO_2, and some PM indices. These pollutants likely share the same temporal fluctuations due to air stagnation, but they also represent local combustion sources including traffic. Thus, it may be more reasonable to consider these pollutants as surrogate indicator(s) of traffic and local combustions than to attempt to seek independent effects of single pollutants. It is also worth noting that the main source of pollution in five of these urban areas is traffic, whereas one of them is exposed also to industrial sources.

A study conducted by Brauer and coinvestigators (2002) in the Netherlands, though different in the study design, found an association between residing near motorways with intense road traffic and a higher prevalence in respiratory infections with wheezing and asthma in children in the same age group as in our study (0–2 years of age). Studies are needed to investigate connections between short-term associations, incidence, and prevalence of these respiratory outcomes.

Another interesting result of our study is the association between air pollution and gastroenteric emergency visits. This is the first study to report this association in children. Previous studies (Chen et al. 2000; Lipsett et al. 1997), which examined ER visits for gastroenteritis as a control group, did not find association with the gaseous pollutants or PM indices. The mechanisms underlying these effects are not well known. Gastroenteritis is an inflammation of the gastrointestinal tract that could be caused by infection or by adverse reaction to ingested or inhaled material (Kasper et al. 2005). It is possible that particles are involved in the mechanism. Poorly soluble particles deposited in the oral passages may be cleared by coughing and expectoration or by swallowing into the gastrointestinal tract. Soluble particles are likely to be rapidly absorbed after deposition, but deposition depends on the rate of dissolution of the particle and the molecular size of the solute (U.S. Environmental Protection Agency 2004). Our study focused on very young children, who are still developing. Therefore, our findings might reflect the susceptibility of this age group. Clearly, more studied are needed to replicate our finding in this age group and to understand the possible mechanisms.

Public health implication of the impact of air pollution on wheezing at a very young age may be profound. Viral infections determining wheezing are frequent conditions in children < 3 years of age, and in case of an increased individual genetic susceptibility (Martinez 2005), an abnormal reaction may occur because of the immaturity of the immune response, thus facilitating the onset of chronic obstructive pulmonary disease (COPD) in adult ages. Further research is needed to investigate the mechanism(s) contributing to the interactions between viral infections and the exposure to ambient air pollution, to help prevent wheezing in children and the possible onset of COPD in adult ages.

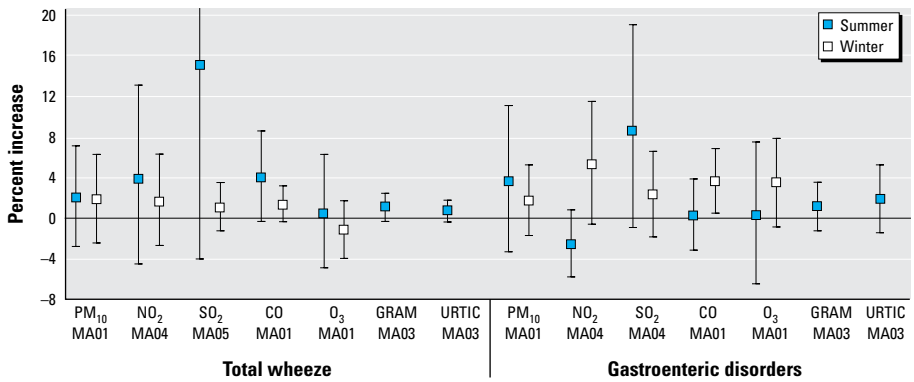

Figure 1. Combined results by season for total wheeze and gastroenteric disorders. Abbreviations: GRAM, Graminaceae; URTIC, Urticaceae. Results are expressed as percent increase (95% CI) in risk of wheeze and gastroenteric disorders for an IQR increase in air pollution. The results by season for selected moving averages (MA) are presented in the *x*-axes for each outcome (total wheeze and gastroenteric disorders) and for each pollutant for lag days 1, 3, 4, and 5.

The limitations of our study include relatively small counts of the outcomes studied, as reflected in the wide CIs—a tradeoff when investigating the outcomes at a very narrow age interval. Also, the particle indices available (TSP and PM_{10}) are somewhat limited in that there were no data available on fine particles or their chemical constituents, which would have allowed a better characterization of the type of air pollution that may be responsible for the observed associations.

In conclusion, we found association between hospital emergency visits for wheezing and gastroenteric disorders in children 0–2 years of age and air pollution levels in urban cities in Italy. Local combustion sources, including traffic, may be responsible for the observed associations. Further research is needed to investigate the impact of air pollution on very young children, as they may also influence their health conditions at a later stage of life.

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Mortality Associations with Long-Term Exposure to Outdoor Air Pollution in a National English Cohort

Iain M. Carey[1], Richard W. Atkinson[1], Andrew J. Kent[2], Tjeerd van Staa[3,4], Derek G. Cook[1], and H. Ross Anderson[1,5]

[1]Division of Population Health Sciences and Education and MRC-PHE Centre for Environment and Health, St George's, University of London, London, United Kingdom; [2]AEA Technology P.L.C., Harwell IBC, Didcot, Oxfordshire, United Kingdom; [3]Clinical Practice Research Datalink, Medicines and Healthcare Products Regulatory Agency, London, United Kingdom; [4]Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands; and [5]MRC-PHE Centre for Environment and Health, King's College London, London, United Kingdom

***Rationale*: Cohort evidence linking long-term exposure to outdoor particulate air pollution and mortality has come largely from the United States. There is relatively little evidence from nationally representative cohorts in other countries.**

***Objectives*: To investigate the relationship between long-term exposure to a range of pollutants and causes of death in a national English cohort.**

***Methods*: A total of 835,607 patients aged 40–89 years registered with 205 general practices were followed from 2003–2007. Annual average concentrations in 2002 for particulate matter with a median aerodynamic diameter less than 10 (PM_{10}) and less than 2.5 μm ($PM_{2.5}$), nitrogen dioxide (NO_2), ozone, and sulfur dioxide (SO_2) at 1 km^2 resolution, estimated from emission-based models, were linked to residential postcode. Deaths (n = 83,103) were ascertained from linkage to death certificates, and hazard ratios (HRs) for all- and cause-specific mortality for pollutants were estimated for interquartile pollutant changes from Cox models adjusting for age, sex, smoking, body mass index, and area-level socioeconomic status markers.**

***Measurements and Main Results*: Residential concentrations of all pollutants except ozone were positively associated with all-cause mortality (HR, 1.02, 1.03, and 1.04 for $PM_{2.5}$, NO_2, and SO_2, respectively). Associations for $PM_{2.5}$, NO_2, and SO_2 were larger for respiratory deaths (HR, 1.09 each) and lung cancer (HR, 1.02, 1.06, and 1.05) but nearer unity for cardiovascular deaths (1.00, 1.00, and 1.04).**

***Conclusions*: These results strengthen the evidence linking long-term ambient air pollution exposure to increased all-cause mortality. However, the stronger associations with respiratory mortality are not consistent with most US studies in which associations with cardiovascular causes of death tend to predominate.**

Keywords: air pollution; mortality; cohort study; respiratory

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Long-term exposure to ambient levels of fine particulate matter has been associated with increased mortality, particularly from cardiovascular disease, in several US population cohorts. There is less cohort evidence available outside the United States on gaseous pollutants and on respiratory outcomes.

What This Study Adds to the Field

Concentrations of particulate matter, nitrogen dioxide, and sulfur dioxide, but not ozone, were associated with increased all-cause mortality in a large national cohort in England. However, unlike US studies we found larger associations for respiratory rather than cardiovascular causes of death. These findings add to the evidence that from an international perspective there is important heterogeneity in the effects of air pollution on cause-specific mortality.

Epidemiologic studies suggest that long-term exposure to ambient air pollution is associated with increased mortality (1, 2). Much of this evidence comes from cohort studies in the United States where the focus has been on associations with fine particles. In particular, the American Cancer Society (ACS) study (3) and the Six-Cities study (4) have been extensively reanalyzed confirming their initial findings (5–9). Associations with the air pollution mixtures experienced by populations in Europe (10–16) and worldwide (17–20) have also been reported.

Where studies have investigated cause-specific mortality, the focus has been on cardiovascular disease (2). By contrast, the evidence for associations with respiratory mortality is less convincing (1) because many studies have lacked statistical power, or used a combined cardiorespiratory outcome because of the smaller number of respiratory deaths (4, 12). A recent report on the global impact of particulate matter with a median aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) on chronic obstructive pulmonary disease (COPD) was reliant on only three studies, all from the United States (21). Few cohort studies have used large, population-based, nationally representative samples to investigate a range of respiratory and cardiovascular causes separately, or considered a range of criteria pollutants.

In this study, we investigate the associations between long-term exposure to a range of outdoor air pollutants and both all-cause and cause-specific mortality using a national cohort of adults registered with family practitioners in England, using linkage to a national mortality register to provide details on date and underlying cause of death.

METHODS

The Clinical Practice Research Datalink is a large, validated, and nationally representative database containing anonymized patient data from UK primary care (22). It includes a full longitudinal medical

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Correspondence and requests for reprints should be addressed to Richard W. Atkinson, Ph.D., Division of Population Health Sciences and Education and MRC-PHE Centre for Environment and Health, St George's, University of London, Cranmer Terrace, London SW17 0RE, UK. E-mail: atkinson@sgul.ac.uk

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record for each patient consulting their family practitioner including information on diagnoses made within the practice. We selected 205 English practices, recording high-quality data according to Clinical Practice Research Datalink internal standards, which had available linked death registrations from the Office for National Statistics. From these, we identified 836,557 patients aged between 40 and 89 years, fully registered for at least 1 year on January 1, 2003 (23).

The following information was extracted from the electronic patient record and used to construct covariates: age; sex; smoking (non-, ex-, and current smoker, with further categories of 1–19, 20–30, and 40+ cigarettes per day); and body mass index (BMI) (<20, ⩾20 and <25, ⩾25 and <30, ⩾30). The last recorded status before January 1, 2003 was used to code the variables, except for nonsmokers, who were reclassified as ex-smokers if they had older historical codes indicating smoking. A "missing" category was assigned for subjects with no recorded value before 2003. Socioeconomic status (SES) was classified using three separate census measures of deprivation (income, employment, and education), measured on a geographic area of approximately 1,500 people (24). A total of 950 patients had no census information and were dropped from the analyses. Deaths were classified according to the underlying cause on the death certificate (ICD-10): circulatory, I00-I99; coronary heart disease (CHD), I20–25; myocardial infarction, I21–23; stroke, I61, I63–64; heart failure, I50; respiratory, J00-J99; pneumonia, J12–18; COPD, J40–44, J47; and lung cancer, C33–34. We performed sensitivity analyses defining circulatory deaths as any mention on the certificate, and respiratory deaths restricted to where there was no mention of circulatory disease on the certificate.

Annual mean concentrations in 2002 of PM_{10} and $PM_{2.5}$, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) for 1-km grid squares covering England were linked anonymously from grid centroid to the nearest residential postcode centroid for each patient (23). The pollutant concentrations were estimated using air dispersion models, developed by AEA Technology (Didcot, Oxfordshire, UK) over the past 10 years (25), for reporting to the UK Government and the European Commission for policy formulation (26). The models for PM_{10}, $PM_{2.5}$, NO_2, and SO_2 were constructed by estimating quantities of emissions by sector (e.g., power generation, domestic combustion, road traffic) with subsequent pollution concentrations calculated by summing estimates for pollutant-specific components, such as point and local area sources. O_3 maps were constructed by interpolating data from rural monitoring stations and adjusting for effects of altitude and nitrogen oxide emissions. Model validation using national air quality monitors and networks (*see* Tables E1 and E2 in the online supplement) was good for NO_2 ($R^2 = 0.57$–0.80) and O_3 ($R^2 = 0.48$–0.71); moderate for PM_{10} ($R^2 = 0.29$–0.46) and $PM_{2.5}$ ($R^2 = 0.23$–0.71); but less successful for SO_2 ($R^2 = 0$–0.39). Further details on the methodology and validation are provided in the online supplement.

We used Cox proportional hazards models (SAS version 9.1.3; SAS Institute, Inc., Cary, NC) to investigate associations between pollution concentrations in 2002 and subsequent mortality in 2003–2007. We adjusted cumulatively for (1) age and sex; (2) smoking and BMI; and (3) in turn, income, employment, and education. Two-pollutant models were considered only when the correlation coefficient between pollutants was below 0.5. We performed stratified analyses to assess effect modification by the covariates. To account for clustering, the modified sandwich estimate of variance was used to produce robust standard errors. As a sensitivity analysis, we investigated the impact of fitting a random effect for practice in a shared frailty model (Stata version 10.1; StataCorp LP, College Station, TX). To allow comparison across pollutants, hazard ratios (HRs) were quantified for an interquartile range change in each pollutant (Table 1).

RESULTS

Of the 835,607 patients with linked census data, successful postcode linkage to all pollutants was made for approximately 99% of patients (Table 1). There was significant variation in modeled pollution concentrations by practice region ($P < 0.001$). Practices in southern England (excluding Greater London) had the lowest annual concentrations of all pollutants except O_3. By contrast, practices within Greater London had the highest concentrations for PM_{10}, $PM_{2.5}$, and NO_2, the latter over 70% higher than other southern practices (33.3 vs. 19.4 $\mu g/m^3$). Areas with a lower SES (higher census deprivation scores of income, employment, and education) were associated with higher concentrations for all pollutants except O_3. Within our cohort, annual concentrations of PM_{10} and $PM_{2.5}$ were both strongly correlated with NO_2 ($r = 0.9$); moderately correlated with SO_2 ($r = 0.5$); and negatively correlated with O_3 ($r = -0.5$).

TABLE 1. SUMMARY OF ASSIGNED POLLUTANT CONCENTRATIONS FOR STUDY COHORT (N = 835,607)

	Assigned Annual Average Concentration in 2002 ($\mu g/m^3$)				
	PM_{10}	$PM_{2.5}$	SO_2	NO_2	O_3
No. of patients with pollution linkage (%)	830,842 (99%)	830,842 (99%)	823,442 (99%)	830,429 (99%)	824,654 (99%)
Mean pollution (SD)	19.7 (2.3)	12.9 (1.4)	3.9 (2.1)	22.5 (7.4)	51.7 (2.4)
Minimum–maximum range	12.6–29.8	8.5–20.2	0.1–24.2	4.5–60.8	44.5–63.0
Interquartile range	3.0	1.9	2.2	10.7	3.0
Practice region means (SD)					
North (81 practices)	19.8 (2.3)	13.0 (1.5)	4.8 (2.1)	23.4 (6.3)	50.9 (2.4)
South (excluding London) (96 practices)	19.1 (2.0)	12.5 (1.2)	3.3 (1.9)	19.4 (6.1)	52.6 (2.2)
London (28 practices)	22.5 (1.2)	14.6 (0.8)	3.8 (1.2)	33.3 (4.5)	50.2 (0.8)
Test for heterogeneity	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$
Correlation with census socioeconomic scores*					
Income deprivation	0.25	0.26	0.11	0.24	−0.11
Employment deprivation	0.15	0.17	0.17	0.16	−0.12
Education deprivation	0.14	0.15	0.20	0.05	−0.08
Correlation with other pollutants					
$PM_{2.5}$	0.99	—	—	—	—
SO_2	0.45	0.46	—	—	—
NO_2	0.84	0.85	0.37	—	—
O_3	−0.40	−0.39	−0.41	−0.46	—
Intraclass correlation by practice†	0.87	0.85	0.77	0.90	0.94

Definition of abbreviations: NO_2 = nitrogen dioxide; O_3 = ozone; $PM_{2.5}$ = particulate matter with a median aerodynamic diameter less than 2.5 μm; PM_{10} = particulate matter with a median aerodynamic diameter less than 10 μm; SO_2 = sulfur dioxide.

* Income deprivation measures the proportion of the population experiencing income deprivation in an area. Employment deprivation measures deprivation conceptualized as involuntary exclusion of the working-age population from the labor market. Education deprivation measures the extent of deprivation in terms of education, skills, and training in a local area.

† Proportion of total variation explained by between-practice differences.

A total of 83,103 deaths (9.9% of all patients) were recorded between January 1, 2003 and December 31, 2007 with an underlying cause of death recorded in 80,505 (97%). There were 28,976 (35%) deaths from circulatory; 10,583 (13%) from respiratory; and 5,273 (6%) from lung cancer causes. A total of 37,443 (45%) had some mention of cardiovascular disease on the death certificate. Of all respiratory deaths, 7,740 (73%) had no mention of cardiovascular disease on the death certificate. Higher, age- and sex-adjusted, mortality rates were associated with greater deprivation, living in the North, abnormal BMI, and recorded smoking intensity at baseline (Table 2).

The relationships between residential air pollution concentrations in 2002 and all-cause mortality during 2003–2007 are shown in Table 3. Associations were positive for all pollutants, except for O_3, which were negative. After adjustment for smoking and BMI these ranged from 6–7% for interquartile range increases in PM_{10}, $PM_{2.5}$, SO_2, and NO_2, mostly reducing to 2–4% after adjustment for one of the area deprivation markers, with income having the biggest influence. For example, in a model adjusted for area income level, a 1.9 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with an HR of 1.02 (95% confidence interval [CI], 1.00–1.05). In two-pollutant models all associations were attenuated, with associations with SO_2 proving the most robust (*see* Table E3).

Analyses for specific causes of death (Table 4) revealed that the strongest associations were for respiratory deaths where all pollutants, except O_3, were positively associated with increases in mortality. For example, in a model adjusted for area income, a 1.9 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with an HR of 1.09 (95% CI, 1.05–1.13), whereas a 3.0 $\mu g/m^3$ increase in O_3 was associated with an HR of 0.94 (95% CI, 0.90–0.97). Comparable HRs were also observed for deaths from COPD and pneumonia (*see* Table E4). By contrast, there was less evidence of associations with cardiovascular causes of death (Table 4), where only SO_2 showed a relationship (HR, 1.04; 95% CI, 1.03–1.06). The pattern was similar with deaths from CHD, myocardial infarction, or stroke, although associations were observed between PM_{10} and $PM_{2.5}$ and deaths from heart failure as underlying cause (*see* Table E4). For lung cancer (Table 4), the strongest associations were seen with NO_2 (HR, 1.06; 95% CI, 1.00–1.12). Extending the definition of cardiovascular deaths to any mention on the death certificate, combining them with respiratory deaths, or restricting the definition of respiratory deaths to those without mention of cardiovascular disease, did not materially alter the above findings (*see* Table E5).

Further analyses of the association with respiratory deaths by selected covariates showed that for $PM_{2.5}$, PM_{10}, and NO_2 there was still evidence of a relationship with respiratory mortality in younger ages (40–64 yr), nonsmokers, and those without any COPD or asthma at baseline (*see* Table E6). For example, for $PM_{2.5}$ a 1.9 $\mu g/m^3$ increase produced an HR of 1.14 (95% CI, 1.08–1.20) for patients classed as nonsmokers at baseline. The association was strongest in more income-deprived areas for PM_{10}, $PM_{2.5}$, and NO_2, but highest for SO_2 in least-deprived areas.

Adjustment for within-practice clustering using frailty models attenuated the associations for all pollutants, especially for PM_{10} and $PM_{2.5}$ when also adjusted for area income (*see* Table E7). However, the associations between the pollutants and respiratory mortality remained robust (e.g., for $PM_{2.5}$ a 1.9 $\mu g/m^3$ increase produced an HR of 1.07; 95% CI, 1.03–1.11).

TABLE 2. AGE-SEX ADJUSTED PERCENTAGES OF PATIENTS WHO DIE DURING FOLLOW-UP BY BASELINE FACTORS (N = 835,607)

Baseline Variables	Level	No. Patients	No. Deaths	Adj %*
Sex	Male	404,716	41,207	10.2%
	Female	430,891	41,896	9.7%
Age	40–49	242,267	3,195	1.3%
	50–59	227,972	7,245	3.2%
	60–69	165,838	13,048	7.9%
	70–79	128,179	26,585	20.7%
	80-89	71,351	33,030	46.3%
Smoking	Non	386,591	31,404	8.0%
	Ex (unknown)	75,785	11,186	10.0%
	Ex (1–19 cigs/d)	54,344	6,572	10.7%
	Ex (20–39 cigs/d)	26,382	3,184	12.3%
	Ex (40+ cigs/d)	5,223	734	12.3%
	Current (unknown)	17,506	2,445	11.0%
	Current (1–19 cigs/d)	88,211	9,393	14.1%
	Current (20–39 cigs/d)	50,763	4,989	16.7%
	Current (40+ cigs/d)	4,552	602	19.7%
	Not recorded	126,250	12,594	10.0%
Body mass index	<20	33,078	4,189	14.5%
	⩾20 and <25	269,925	23,218	9.2%
	⩾25 and <30	243,289	23,950	9.1%
	⩾30	108,966	11,636	11.4%
	Not recorded	180,349	20,110	10.9%
Practice region	North	319,455	33,633	10.7%
	South (excl. London)	424,165	41,477	9.5%
	London	91,987	7,993	9.5%
Income deprivation quintile†	1 (most deprived)	104,137	13,724	12.8%
	2	147,788	17,752	11.3%
	3	180,382	18,495	9.9%
	4	197,066	18,020	9.2%
	5 (least deprived)	206,234	15,112	8.2%
Employment deprivation quintile†	1 (most deprived)	114,006	15,711	12.8%
	2	149,663	17,264	10.9%
	3	170,764	17,156	9.8%
	4	190,694	17,295	9.2%
	5 (least deprived)	210,480	15,677	8.3%
Education deprivation quintile†	1 (most deprived)	120,795	15,959	12.8%
	2	158,955	17,761	10.9%
	3	168,465	16,504	9.7%
	4	178,578	16,279	9.3%
	5 (least deprived)	208,814	16,600	8.3%

* Percentages adjusted to age–sex structure of overall population.
† Census-based national rankings.

DISCUSSION

This study of a national cohort has observed associations between annual concentrations of ambient air pollution and risk of subsequent death. These relationships were robust to adjustment for smoking and BMI, but attenuated when adjusting for small area SES markers. For cause-specific mortality, associations were larger for respiratory mortality and closer to unity for cardiovascular mortality. Associations with respiratory mortality were also found in nonsmokers and those without COPD or asthma at baseline.

Cohort studies of long-term exposure to air pollution and mortality are predominately based in the United States and have tended to focus on fine particulate matter ($PM_{2.5}$) (4, 6, 27–34). A 2010 review by the American Heart Association (2) reported HRs for $PM_{2.5}$ and all-cause mortality ranging from 0.99–1.21 per 10 $\mu g/m^3$, whereas a systematic review in 2008 calculated a pooled relative risk of 1.06 (1). Our estimate when scaled to a 10 $\mu g/m^3$ increment, and adjusted for area income, produced an HR of 1.13 (95% CI, 1.00–1.27).

Previous cohort studies have tended to emphasize associations with cardiovascular disease, in part because respiratory deaths are far fewer (4, 12) and in part because cardiovascular

TABLE 3. HAZARD RATIOS FOR ALL-CAUSE MORTALITY IN 2003–2007 FOR AN INTERQUARTILE RANGE CHANGE IN 2002 POLLUTANT CONCENTRATIONS

	PM_{10} ($n = 830,842$)		$PM_{2.5}$ ($n = 830,842$)		SO_2 ($n = 823,442$)		NO_2 ($n = 830,429$)		O_3 ($n = 824,654$)	
Baseline Variables Adjusted For	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
+ age, sex	1.08	1.05–1.11	1.09	1.06–1.12	1.07	1.05–1.09	1.09	1.06–1.12	0.93	0.90–0.96
+ age, sex, smoking, BMI	1.06	1.04–1.09	1.07	1.05–1.10	1.06	1.04–1.08	1.07	1.04–1.11	0.94	0.91–0.96
+ age, sex, smoking, BMI, income*	1.02	1.00–1.04	1.02	1.00–1.05	1.04	1.03–1.05	1.03	1.00–1.05	0.93	0.90–0.96
+ age, sex, smoking, BMI, employment*	1.04	1.01–1.06	1.04	1.02–1.07	1.03	1.02–1.05	1.04	1.01–1.07	0.94	0.91–0.97
+ age, sex, smoking, BMI, education*	1.04	1.02–1.06	1.04	1.02–1.06	1.03	1.01–1.05	1.06	1.03–1.08	0.96	0.93–0.98
10 unit change (income model)	1.07	0.99–1.16	1.13	1.00–1.27	1.20	1.12–1.28	1.02	1.00–1.05	0.86	0.78–0.94

Definition of abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 = ozone; $PM_{2.5}$ = particulate matter with a median aerodynamic diameter less than 2.5 μm; PM_{10} = particulate matter with a median aerodynamic diameter less than 10 μm; SO_2 = sulfur dioxide.

Number of deaths for each pollutant analysis was as follows: $PM_{10}/PM_{2.5}$ = 82,475; SO_2 = 81,636; NO_2 = 82,421; O_3 = 81,627. Interquartile ranges for each pollutant were as follows: PM_{10} = 3.0 μg/m^3; $PM_{2.5}$ = 1.9 μg/m^3; SO_2 = 2.2 μg/m^3; NO_2 = 10.7 μg/m^3; O_3 = 3.0 μg/m^3.

*Census deprivation score.

risks were found to be greater than respiratory (7, 35). US cohort studies of cardiovascular deaths and $PM_{2.5}$ have reported HRs (per 10 μg/m^3) in the range 1.12 (35) to 1.76 (30). Our finding of 1.01 for $PM_{2.5}$ (when adjusted for income) is considerably lower and is more in line with the two European studies (13, 15) listed in the American Heart Association review (2), which reported associations closer to 1.00. The only cardiovascular subgroup in our study to show evidence of an association with $PM_{2.5}$ was heart failure deaths. This corresponds to our analysis of disease incidence based on the same cohort (23). We have no firm explanation for the weaker associations between $PM_{2.5}$ and CHD in our study as compared with the ACS (8). Both studies used standard ICD coding of death certificates as the outcome but there remains the possibility of differences in the certification practice of clinicians. Other relevant differences to consider include time period; population characteristics (including the likely greater use of statins among our patients with CHD); pollution sources; and the spatial scale of the pollution model.

In contrast to the results for cardiovascular mortality, we observed larger and more robust associations with respiratory mortality. Cohort studies that investigated respiratory mortality, summarized in Table 5, have generally reported HR or risk ratios in excess of one, although many have lacked statistical power. The California Teachers Study focused results on cardiovascular rather than respiratory mortality, despite comparable HRs (36). The largest US study (the ACS) initially reported an HR of 0.92 (35); however, a more recent analysis based on almost twice as many respiratory deaths reported an HR of 1.03 (37). Elsewhere, population studies in Norway (13), Japan (18), New Zealand (17), and China (38) have all reported statistically significant, positive associations with respiratory mortality. In the United Kingdom, a national ecologic study (39) reported larger effects of black smoke (a reflectance measure of black carbon particles <4 μm in diameter) on respiratory mortality (HR, 1.19) in the most recent exposure periods (1990–1994), whereas a Scottish study (40) also found larger relationships with respiratory mortality (HR, 1.26). Our scaled findings for PM_{10} and $PM_{2.5}$ (HR, 1.30 and 1.54, respectively, per 10 μg/m^3) adjusted for area income deprivation exceed all but one (38) of the reported estimates in Table 5; however, we note the smaller mean and standard deviation of our modeled concentrations compared with other studies.

TABLE 4. HAZARD RATIOS FOR SPECIFIC CAUSES OF MORTALITY IN 2003–2007 FOR AN INTERQUARTILE RANGE CHANGE IN 2002 POLLUTANT CONCENTRATIONS

	PM_{10} ($n = 830,842$)		$PM_{2.5}$ ($n = 830,842$)		SO_2 ($n = 823,442$)		NO_2 ($n = 830,429$)		O_3 ($n = 824,654$)	
Cause of Death and Baseline Variables Adjusted For	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Circulatory*										
+ age, sex	1.06	1.03–1.09	1.07	1.03–1.10	1.07	1.05–1.09	1.07	1.03–1.10	0.94	0.91–0.97
+ age, sex, smoking, BMI	1.05	1.02–1.08	1.05	1.02–1.09	1.06	1.04–1.08	1.05	1.02–1.09	0.95	0.92–0.97
+ age, sex, smoking, BMI, income†	1.00	0.97–1.03	1.00	0.97–1.03	1.04	1.03–1.06	1.00	0.97–1.03	0.96	0.94–0.99
+ age, sex, smoking, BMI, education†	1.02	0.99–1.04	1.02	1.00–1.05	1.03	1.01–1.05	1.03	1.00–1.07	0.96	0.94–0.98
Respiratory*										
+ age, sex	1.19	1.14–1.24	1.20	1.15–1.25	1.13	1.09–1.17	1.22	1.16–1.27	0.89	0.85–0.94
+ age, sex, smoking, BMI	1.16	1.12–1.21	1.17	1.12–1.22	1.12	1.09–1.15	1.17	1.12–1.23	0.91	0.87–0.95
+ age, sex, smoking, BMI, income†	1.08	1.04–1.12	1.09	1.05–1.13	1.09	1.06–1.12	1.09	1.04–1.14	0.94	0.90–0.97
+ age, sex, smoking, BMI, education†	1.11	1.08–1.15	1.12	1.08–1.16	1.07	1.04–1.10	1.15	1.10–1.20	0.93	0.90–0.96
Lung cancer*										
+ age, sex	1.12	1.05–1.20	1.14	1.07–1.22	1.10	1.05–1.15	1.20	1.12–1.27	0.89	0.84–0.95
+ age, sex, smoking, BMI	1.07	1.02–1.13	1.08	1.03–1.14	1.07	1.03–1.11	1.13	1.07–1.19	0.92	0.88–0.97
+ age, sex, smoking, BMI, income†	1.01	0.96–1.06	1.02	0.97–1.07	1.05	1.01–1.08	1.06	1.00–1.12	0.94	0.90–0.99
+ age, sex, smoking, BMI, education†	1.03	0.98–1.08	1.04	0.99–1.09	1.03	0.99–1.06	1.11	1.05–1.17	0.94	0.90–0.98

Definition of abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 = ozone; $PM_{2.5}$ = particulate matter with a median aerodynamic diameter less than 2.5 μm; PM_{10} = particulate matter with a median aerodynamic diameter less than 10 μm; SO_2 = sulfur dioxide.

Interquartile ranges for each pollutant were as follows: PM_{10} = 3.0 μg/m^3; $PM_{2.5}$ = 1.9 μg/m^3; SO_2 = 2.2μg/m^3; NO_2 = 10.7 μg/m^3; O_3 = 3.0 μg/m^3.

* Number of deaths for each pollutant analysis was as follows. Circulatory: $PM_{10}/PM_{2.5}$ = 28,743; SO_2 = 28,441; NO_2 = 28,726; O_3 = 28,427. Respiratory: $PM_{10}/PM_{2.5}$ = 10,508; SO_2 = 10,408; NO_2 = 10,500; O_3 = 10,437. Lung cancer: $PM_{10}/PM_{2.5}$ = 5,244; SO_2 = 5,192; NO_2 = 5,241; O_3 = 5,210.

† Census deprivation score. Results adjusting for employment were similar to those adjusting for education (data not shown).

TABLE 5. RESULTS FROM PUBLISHED COHORT STUDIES OF LONG-TERM EXPOSURE TO PARTICULATE MATTER AND RESPIRATORY MORTALITY

Study	Setting	N	Age (*yr*)	Definition of Respiratory Disease	No. of Respiratory Deaths	Exposure Years	Mean Exposure ($\mu g/m^3$) (SD)	Key Adjustments	HR per 10 $\mu g/m^3$	95% CI per 10 $\mu g/m^3$
PM_{10}										
Abbey *et al.*, 1999 (27)	California, United States	6,338 (nonsmokers)	27–95	ICD-9: 460–519	272	1973–1992	51.3 (16.6)	Past smoking, education, BMI, exercise	1.06	0.99–1.15
Naess *et al.*, 2007 (13)	Oslo, Norway	143,842	51–90	ICD-10: J40–J47	1,455	1992–1995	Range, 6.6–30.1	Occupation, education	1.06–1.28	n/a
Hales *et al.*, 2010 (17)	New Zealand	1,051,464	30–74	ICD-9: 162, 470-478, 490-519	3,213	1995–2001	8.3 (8.4)	Smoking, BMI, census SES	1.14	1.05–1.23
Lipsett *et al.*, 2011 (36)	California, United States	61,181 (female teachers)	20–80+	ICD-9: 460–519 & ICD-10: J00-J98	453	1996–2005	29.2 (9.7)	Smoking, BMI, exercise, census SES	1.08	0.98–1.19
Hart *et al.*, 2011 (34)	United States	53,814 (male truckers)	15–85	ICD-10: J10–18, J40–J98	317	1985–2000	26.8 (6.0)	Census region	1.04	0.85–1.27
Dong *et al.*, 2012 (38)	Shenyang, China	9,941	35–103	ICD-10: J00-J99	72	1998–2009	154 (41)	Smoking, education, income, BMI, exercise	1.67	1.60–1.74
Present study	United Kingdom	831,788	40–89	ICD-10: J00-J99	10,518	2002	19.8 (2.3)	Smoking, BMI, income	1.30	1.15–1.47
$PM_{2.5}$										
Naess *et al.*, 2007 (13)	Oslo, Norway	143,842	51–90	ICD-10: J40–J47 (COPD)	1,455	1992–1995	Range, 6.6–22.3	Occupation, education	1.07–1.41	n/a
Beelen *et al.*, 2008 (15)	Netherlands	117,528	58–67	ICD-10: J00-J99	904	1987–1996	28.3 (3.1)	Smoking, education, BMI, diet	1.07	0.75–1.52
Jerrett *et al.*, 2009 (37)	United States	448,850	30+	ICD-9: 460–519	9,891	1999–2000	13.8 (n/a)	Smoking, education, BMI, exercise	1.03	0.96–1.11
Katanoda *et al.*, 2011 (18)	Japan	63,520 (no baseline respiratory disease)	40–70+	ICD-9: 460–519	677	1974–1983	Area range, 16.8–41.9	Smoking, occupation	1.16	1.04–1.30
Lipsett *et al.*, 2011 (36)	California, United States	73,489 (female teachers)	20–80+	ICD-9: 460–519 and ICD-10: J00-J98	404	1996–2005	15.6 (4.5)	Smoking, BMI, exercise, census SES	1.21	0.97–1.52
Hart *et al.*, 2011 (34)	United States	53,814 (male truckers)	15–85	ICD-10: J10–18, J40–J98	317	1985–2000	26.8 (6.0)	Census region	1.18	0.91–1.54
Lepeule *et al.*, 2012 (9)	Six cities, United States	8,096	25–74	ICD-10: J40–J47 (COPD)	247	1974–2009	15.9 (n/a)	Smoking, education, BMI	1.17	0.85–1.62
Cesaroni *et al.*, 2013 (16)	Rome, Italy	1,265,058	30+	ICD-9: 460-519	8,825	2005	23.0 (4.4)	Education, occupation, census SES	1.03	0.97–1.08
Present study	United Kingdom	831,788	40–89	ICD-10: J00-J99	10,518	2002	12.9 (1.4)	Smoking, BMI, income	1.54	1.27–1.86
Black smoke										
Elliot *et al.*, 2007 (39)	United Kingdom	662,343	30+	ICD-9: 460–519	8,471	1990–1994	13.3 (5.3)	Area SES	1.19†	1.05–1.36
Beelen *et al.*, 2008 (15)	Netherlands	117,528	58–67	ICD-10: J00-J99	904	1987–1996	13.9 (2.2)	Smoking, education, BMI, diet	1.22	0.99–1.50
Yap *et al.*, 2012 (40)	Scotland*	15,188/ 6,299	45–64/ 35–64	ICD-9: 480-487, 490-496, 786.0, 786.2	606/ 174	1970–1979	19.3 (3.9)/ 23.2 (7.5)	Smoking, BMI, social class, blood pressure	1.26/ 0.97	1.02–1.55/ 0.79–1.18
Total suspended particles										
Cao *et al.*, 2011 (19)	China	70,947	40+	ICD-9: "Respiratory"	921	1991–2000	289	Smoking, education, BMI, exercise	1.00	0.99–1.03

Definition of abbreviations: BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; HR = hazard ratio; ICD = International Classification of Diseases; $PM_{2.5}$ = particulate matter with a median aerodynamic diameter less than 2.5 μm; PM_{10} = particulate matter with a median aerodynamic diameter less than 10 μm; SES = socioeconomic status.

Where a study has produced multiple estimates over time (e.g. American Cancer Society), we have only included the most recent estimate.

* Study included two separate cohorts, so both sets of results are included.

† This was not a cohort study, and so relative risk is given.

Our associations with respiratory mortality were similar if we further subcategorized into COPD and pneumonia, each representing about 40% of all respiratory deaths. A Norwegian study (13) found positive associations for $PM_{2.5}$ and PM_{10} across different age and sex groups for COPD death (Table 5), whereas the ACS (35) and a Japanese study (18) reported positive associations with pneumonia but not COPD. Our associations with respiratory mortality were found in patients classed as nonsmokers, and those without COPD or asthma at the study outset. Other studies have reported little variation of their association with respiratory mortality across their smoking groups (27, 36, 38), or have lacked power to test this (35). A Japanese study (18) demonstrated an effect of $PM_{2.5}$ on respiratory mortality in female never-smokers (HR, 1.29). Only a Dutch study (15) reported stronger relationships for respiratory mortality and pollution exposure (in this case black smoke) in current smokers.

The evidence from cohort studies for an association between SO_2 and mortality is mixed (1). In the ACS reanalysis (8), SO_2 was associated with all-cause, cardiopulmonary, and ischemic heart disease mortality, and coefficients for fine particles and mortality were markedly reduced when SO_2 was included as a covariate (5). Our robust findings resonate with a UK study that found long-term associations between SO_2 and mortality (39), and found larger effects with respiratory deaths. Recent cohort studies from Japan (18) and China (19) have also reported associations with respiratory mortality, contrasting with earlier studies that found little evidence (15, 27). The causal nature of associations between SO_2 and mortality have been questioned in part because of the correlation between sulfur dioxide and particles and the lack of persuasive hypotheses linking exposure to low concentrations of sulfur dioxide and death (41).

NO_2 has been associated with increased all-cause mortality in some (11, 12, 15, 34, 38) but not all cohort studies (8, 36). Some studies have reported greater effects for respiratory deaths alone (15, 18, 34, 38). A large Dutch cohort found moderate associations with all-cause mortality (HR, 1.03 scaled to a 10 $\mu g/m^3$ change), and larger associations with respiratory mortality (HR, 1.12) (15), which compares closely with 3% and 9% increases in our adjusted HRs for a similar incremental change. Similarly to the Dutch study (15), we also found no associations with cardiovascular mortality, unlike US studies, which reported positive associations for CHD (8, 34, 36), or a small German study that found elevated effects for cardiopulmonary, of which over 90% were cardiovascular deaths (12).

Evidence for long-term health effects of exposure to ozone has come exclusively from US cohorts (8, 27, 29, 36, 37, 42); however, the picture has not been consistent. A study of nonsmokers found raised HR between mean monthly O_3 concentrations and respiratory mortality but lacked precision (27). Extensive analyses of the ACS suggested small, long-term associations with mortality for summer, but not annual, ozone concentrations (8). A further analysis involving two-pollutant models including particles ($PM_{2.5}$) suggested associations with summer ozone persisted only for respiratory mortality (37), whereas another found relationships with cardiopulmonary mortality alone (42). Our data found negative associations with mortality irrespective of cause, which may be partly explained by negative correlations between ozone and the other pollutants; however, they were not completely explained away in two pollutant models. Because there was little variation within our practice clusters, the modeled O_3 concentrations may be largely representing regional levels, where ozone was higher in southern England, where mortality is lower. Because ozone is a highly seasonal pollutant and its production depends on the presence of precursors and sunlight, a metric based on summer ozone concentrations might have been more discriminatory and informative (8).

In our study, air pollution concentrations were derived from emission-based dispersion models, which potentially improve on other methods, such as geostatistical interpolation and land use regression (43) but depend on the quality of data used. A comparison of modeling methods using a large Dutch cohort concluded that dispersion models performed favorably compared with land use regression (44). We have previously applied these models in cross-sectional analyses of national English health survey data (45) and they have been used extensively by the UK Government for reporting to the European Commission (25) and for policy purposes including burden estimation (26).

We have previously discussed the performance and validation of these models (23), and provide further details in the online supplement. Briefly, external validation of the model with monitoring sites in 2002 suggested better modeling of NO_2 compared with PM_{10} and SO_2. Because of a limited number of monitoring sites, model validation statistics for $PM_{2.5}$ were not available until 2009; however, the modeling for PM_{10} and $PM_{2.5}$ uses the same general methodology and model performance was similar between the two. The better relative performance of NO_2 is perhaps not surprising, because of the complexity of the PM mixture for which the sources are not well characterized. Although this suggests greater confidence in results for NO_2, we have emphasized our results with $PM_{2.5}$ because it is the most important regulated pollutant, is regarded as more likely to be causal, and is commonly used for health impact assessments. The R^2 reported for NO_2 and PM_{10} were comparable with those found in a study using land use regression models to estimate concentrations in the United Kingdom in 2001 (46).

Misclassification is also likely to have resulted from assigning pollution estimates at a 1 km^2 resolution. Although misclassification of exposure will likely bias effect estimates toward the null (47), and may explain the lack of associations found with cardiovascular mortality, it seems unlikely to explain why stronger associations were found with respiratory mortality. The exposure estimates used for existing cohort studies vary from those that are at a larger community level spatial scale (4, 6, 48) to those where the estimate is at the residential address (13, 16). Our study therefore lies somewhere between the two, and it is possible that this may explain some of the differences between our results and those of other cohorts.

One of the strengths of our study was that it incorporated data from the clinical record, and linked in deaths from a national data collection system. Although we adjusted for individual confounders, such as smoking, misclassification may have arisen, either because of missing values or because of patients being incorrectly classed as nonsmokers on their medical record. Even if recorded correctly, our variable fails to quantify the lifetime burden of current or ex-smokers. Although this limits the precision of our smoking adjustment, it seems unlikely to completely explain away associations seen in nonsmokers.

Although we were unable to adjust for individual socioeconomic markers, neighborhood indicators of socioeconomic deprivation have been shown to be acceptable proxies (49). In our models, this adjustment attenuated all air pollution associations especially with cardiovascular mortality. Because the SES indices may be measured on a smaller geographic scale than our modeled pollution in urban areas, they could be representing concentration gradients not captured by the pollution models. However, given the modest correlations that exist nationally between SES and pollution concentrations, it seems unlikely that the SES indices are over adjusting and erroneously explaining all of the associations observed. Indeed, even if this was not the case for associations with cardiovascular mortality, it cannot explain the stronger associations we found with respiratory mortality before and after SES adjustment. Although we found patients in more socially deprived areas have higher pollution concentrations (except ozone), this contrasted with the ACS (8) where similar census variables were not strongly related, and subsequently had little impact on their effect estimates. In a national Canadian cohort (48), higher concentrations were found in more affluent areas, and HRs associated with exposure to $PM_{2.5}$ increased after socioeconomic adjustment.

The potential limitations of using cause of death coding from death certificates to classify respiratory deaths has been identified by others (35). For example, a patient with their cause of death listed as pneumonia might have warranted a more appropriate underlying cause of death from long-term chronic conditions, such as CHD, stroke, or COPD (50). A recent report estimated that among all deaths in England and Wales, respiratory deaths are overrecorded by 7%, whereas circulatory deaths are underrecorded by 6% (51). However, for such misclassification to explain a spurious relationship with respiratory deaths and the absence of one with cardiovascular deaths, it requires that virtually all the excess deaths caused by air pollution were those being misclassified, and at a greater rate than the report suggested. Such a scenario seems unlikely. However, to account for potential misclassification we performed sensitivity analyses, which included any mention of circulatory death on the certificate, and restricted respiratory deaths to those with no mention of cardiovascular disease. These showed similar patterns to the underlying cause analyses, suggesting misclassification was unlikely to explain stronger associations with respiratory death. We also noted that associations with respiratory deaths remained when analyses were restricted to younger patients, who will have less comorbidity, and thus the issue of miscoding on their death certificate may be less relevant.

Because of the anonymous nature of the data, we were unable to investigate spatial autocorrelation beyond adjusting for clustering by practice. Patients from the same practice are likely to be

more similar to each other than patients from different practices, and this has implications for the precision of our estimates. We chose to conservatively account for this by using the modified sandwich estimate of variance to produce standard errors, which are robust to within practice correlation. As a sensitivity analysis we considered shared frailty models, which fit a random effect to explicitly model this correlation, and found an attenuation of all estimates. A similar attenuation was seen with other modeling approaches that estimated the within cluster effect by accounting for the mean practice concentration level or stratifying the model by practice (data not shown). The implication may be that differences in overall practice area concentrations are driving many of the associations, which is not surprising because this is where most of the variation in the pollution model arises. Although we advise caution when extrapolating our estimates to population impact calculations, we note that our associations with respiratory mortality remained whatever the approach.

This population-based, nationally representative English cohort extends the body of evidence linking air pollution to all-cause mortality but contrary to a number of studies from the United States and elsewhere found that the effects on respiratory mortality were greater than on cardiovascular mortality. When the evidence from existing published cohorts is considered as a whole it seems that there is important heterogeneity in the results for cause-specific mortality. The reasons may lie in differences in various aspects of the methods of investigation, population susceptibility, or toxicity of the air pollution mixture but remain to be elucidated.

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RESEARCH REPORT

Outdoor air pollution and infant mortality: analysis of daily time-series data in 10 English cities

Shakoor Hajat, Ben Armstrong, Paul Wilkinson, Araceli Busby, Helen Dolk

See end of article for authors' affiliations

Correspondence to: Dr S Hajat, Public & Environmental Health Research Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK; shakoor.hajat@lshtm.ac.uk

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Background: There is growing concern that moderate levels of outdoor air pollution may be associated with infant mortality, representing substantial loss of life-years. To date, there has been no investigation of the effects of outdoor pollution on infant mortality in the UK.

Methods: Daily time-series data of air pollution and all infant deaths between 1990 and 2000 in 10 major cities of England: Birmingham, Bristol, Leeds, Liverpool, London, Manchester, Middlesbrough, Newcastle, Nottingham and Sheffield, were analysed. City-specific estimates were pooled across cities in a fixed-effects meta-regression to provide a mean estimate.

Results: Few associations were observed between infant deaths and most pollutants studied. The exception was sulphur dioxide (SO2), of which a 10 μg/m^3 increase was associated with a RR of 1.02 (95% CI 1.01 to 1.04) in all infant deaths. The effect was present in both neonatal and postneonatal deaths.

Conclusions: Continuing reductions in SO2 levels in the UK may yield additional health benefits for infants.

There is now widespread acceptance that short-term increases in ambient air pollution are associated with increased mortality and morbidity, especially in elderly people and those with pre-existing health problems. However, there is now growing concern that there may also be a link with infant mortality and adverse pregnancy outcomes, representing substantial loss of life-years.[1]

Some recent reviews on this subject present mixed results and are only in agreement that further research is needed to confirm and clarify any links.[2–5] Infants may be particularly vulnerable to the adverse effects of air pollution.[6] The lung is not well developed at birth,[3] with 80% of alveoli being formed postnatally.[7] During the neonatal and post-neonatal periods, therefore, the developing lung is highly susceptible to environmental toxicants.[7–9]

Associations between particulate matter <10 μg/m^3 (PM_{10}) and infant mortality have been observed in time-series studies conducted in cities with notoriously high levels of pollution, such as Mexico City,[10] Seoul[11] and Sao Paulo.[12] However, it cannot be assumed that the much lower levels of exposure experienced currently on a daily basis in many Western cities have no harmful effects on susceptible subjects such as infants. Associations between post-neonatal mortality and ambient levels of particulates have been observed in spatial comparisons within the Czech Republic[13] and the US.[14 15]

To date, there has been no investigation on the effects of outdoor pollution on infant mortality in the UK. We analyse here time-series data of daily infant mortality counts in 10 major English cities to quantify any associations with short-term changes in air pollution.

METHODS

Data

Data on all-cause infant deaths (death within the first year of life) recorded between 1990 and 2000 were obtained from the Office for National Statistics for the following 10 major cities in England: Birmingham, Bristol, Leeds, Liverpool, London, Manchester, Middlesbrough, Newcastle, Nottingham and Sheffield. For each city, data were collapsed by date of death to generate a time series of daily infant death counts between 1990 and 2000. Further series were created separately for neonatal deaths (death within first 28 days) and post-neonatal deaths (after day 28 and within the first year).

Daily measures of the following six pollutants were also obtained for the period 1990–2000 from the UK Air Quality Network: carbon monoxide (CO), nitrogen oxide (NO), nitrogen dioxide (NO_2), ozone (O_3), particulate matter (PM_{10}) and sulphur dioxide (SO_2). A minimum of two monitoring sites were available for each city, except for Middlesbrough and Newcastle, where only one site was used. For each pollutant, sites providing <30% of missing data were combined to produce a single series for each city. For each pollutant, correlations between sites were high within each city ($r>0.74$).

For the same study period, daily maximum and minimum temperature (℃) and daily relative humidity (%) were obtained from the British Atmospheric Data Centre, using one weather station in each city. Daily mean temperature was estimated as the mean of the daily maximum and minimum values. Region-specific reports of laboratory-confirmed influenza A and respiratory syncytial virus activity were also collected from the Health Protection Agency.

Analysis

For each city, daily infant mortality was examined in relation to air pollution using Poisson generalised linear models allowing for overdispersion. Weekly reports of influenza A and respiratory syncytial virus activity were incorporated into each regression model as possible confounding variables, regardless of statistical significance. The non-linear effects of weather were also controlled for using natural cubic splines of mean temperature and relative humidity. In the case of relative humidity, the measure was modelled using the mean of levels on the day of death and the previous 2 days (lags 0–2), and the potential long-term effects of mean temperature were modelled using averaged values of lags 0–7. Three degrees of freedom (df) were used for each of these spline functions. Indicator variables were used to allow for any day-of-week effects.

Cubic smoothing splines of time with equally spaced df were used to control for secular trends (eg, demographic shifts) and any seasonal fluctuations in general birth numbers. Seven df

Abbreviations: df, degrees of freedom; PM_{10}, particulate matter <10 μg/m^3

Table 1 Summary statistics for infant mortality and air pollution data between 1990 and 2000

City	Total infant deaths	Neonatal, %	Mean daily pollution concentrations (25th, 75th centiles) (μg/m^3)					
			CO (mg/m^3)	NO	NO_2	O_3	PM_{10}	SO_2
Birmingham	2354	71.4	0.64 (0.4, 0.8)	24.3 (7, 27)	43.0 (29, 55)	33.5 (20, 45)	21.9 (14, 26)	17.5 (7, 22)
Bristol	644	64.3	1.01 (0.6, 1.2)	47.9 (18, 55)	66.3 (50, 78)	23.8 (12, 33)	23.1 (15, 28)	17.8 (7, 21)
Leeds	2027	62.1	0.73 (0.5, 0.9)	41.5 (18, 49)	48.0 (37, 58)	30.2 (19, 40)	24.0 (15, 28)	17.0 (6, 21)
Liverpool	1050	62.6	0.51 (0.3, 0.6)	37.7 (14, 49)	43.9 (30, 56)	34.8 (21, 47)	23.6 (15, 28)	21.3 (6, 28)
London	9037	66.1	0.77 (0.5, 0.9)	48.0 (22, 57)	66.1 (54, 75)	20.5 (10, 28)	26.3 (18, 31)	21.3 (9, 27)
Manchester	3404	63.2	0.63 (0.4, 0.7)	36.3 (12, 40)	49.0 (35, 58)	25.0 (14, 33)	22.6 (15, 27)	15.1 (9, 18)
Middlesbrough	574	62.9	0.37 (0.2, 0.4)	11.1 (4, 11)	28.3 (18, 37)	42.6 (31, 54)	18.4 (11, 22)	11.4 (4, 15)
Newcastle	986	66.6	0.67 (0.5, 0.8)	33.7 (14, 41)	41.0 (29, 52)	35.6 (23, 47)	21.5 (14, 26)	14.9 (7, 18)
Nottingham	963	67.3	0.62 (0.4, 0.7)	28.5 (11, 32)	45.1 (35, 54)	28.1 (17, 37)	20.7 (14, 24)	16.0 (10, 19)
Sheffield	1249	67.7	0.60 (0.3, 0.7)	60.1 (23, 74)	51.0 (38, 62)	34.5 (23, 45)	23.0 (15, 28)	16.5 (7, 21)

CO, carbon monoxide; NO, nitrogen oxide; NO_2, nitrogen dioxide; O_3, ozone; PM_{10}, particulate matter <10 μg/m^3; SO_2, sulphur dioxide.

per year (roughly equivalent to a 2-month moving average) were used for these smoothing splines. These parameters were constrained to be the same for all cities, although the sensitivity of estimates to the degree of seasonal control was also examined.

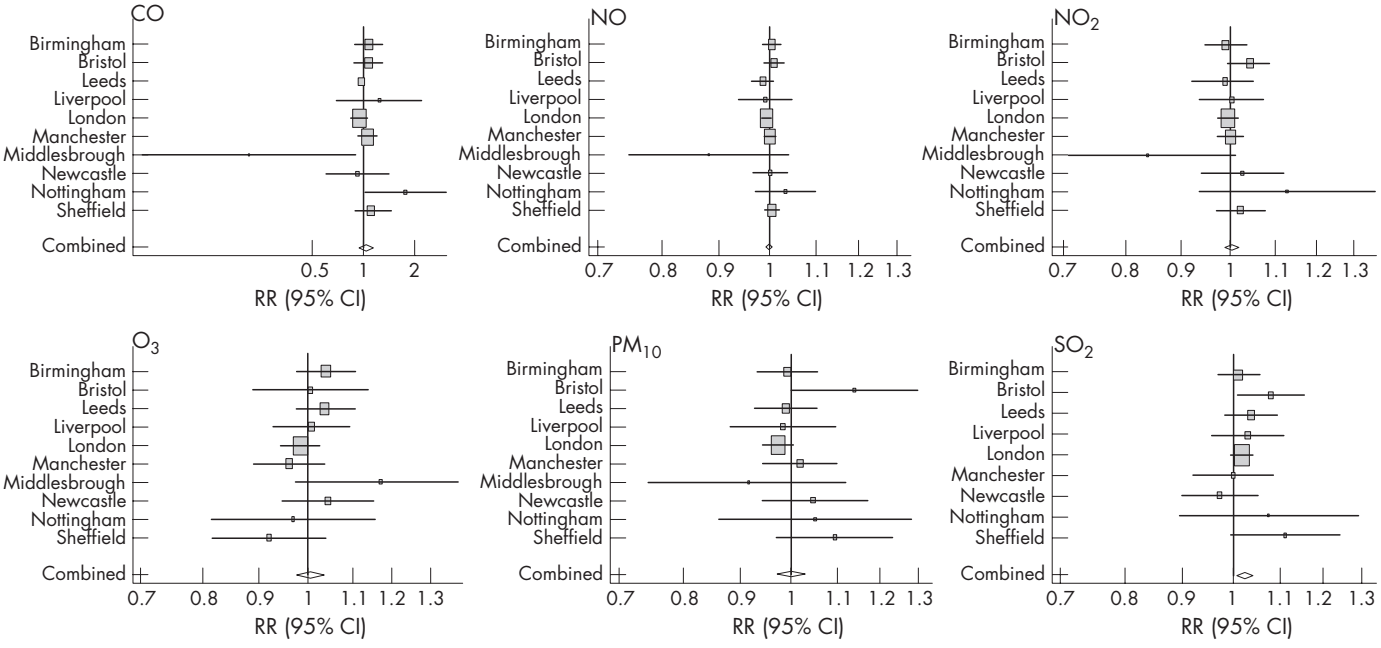
To assess the short-term effects of pollution exposure on infant mortality, each pollutant was modelled using the average value of lags 0–2 days before death. Each pollutant was modelled as a linear term and considered separately from other pollutants. Pollutant effects are presented as the relative risk of mortality associated with a 10-unit increase (1 unit for CO) in the pollutant measure. For each pollutant, city-specific estimates were pooled across cities in a fixed-effects meta-regression to provide a mean estimate.

Analyses were repeated separately for neonatal and post-neonatal deaths. All analyses were conducted in STATA version 9.

RESULTS

The average infant mortality rate in the 10 study cities in 2000 was 7.75 per 1000 deaths. The city-specific rates for Birmingham (10.54/1000) and Leeds (10.25/1000) were considerably higher than the average, and lower in Liverpool (5.36/1000), Bristol (5.46/1000) and Newcastle (5.78/1000). Table 1 provides summary statistics for infant deaths and averaged pollution data for each city between 1990 and 2000. Birmingham had a considerably higher proportion of neonatal deaths than other cities. London and Bristol generally experienced high levels of all pollutants compared with other cities, except for O_3, which tends to be negatively correlated with most of the other pollutants in winter months. In general, SO_2 and, to a lesser extent, PM_{10} levels decreased over the study period and O_3 levels have risen slightly.

Figure 1 shows the relative risk (RR) of infant death for every 10-unit increase in each pollutant (1 unit for CO). For each city, generally few associations were observed with any of the pollutants. Although Bristol had an increased risk with all pollutants, only in the case of SO_2 was the risk statistically significant at the 5% level. The combined estimates suggested no relationship between pollutants and infant deaths, except in the case of SO_2, for which a 10 μg/m^3 increase was associated with a RR of 1.02 (95% CI 1.01 to 1.04, p = 0.008). Restricting analysis to just the summer months (April–September) left the



Note: Middlesbrough SO2 model did not converge

Figure 1 RR of all infant mortality for 10-unit increase in pollutant (1 unit for carbon monoxide). Pollutant measure as average of lags 0–2 days. CO, carbon monoxide; NO, nitrogen oxide; NO_2, nitrogen dioxide; O_3, ozone; PM_{10}, particulate matter <10 μg/m^3; SO_2, sulphur dioxide.

Table 2 RR (95% CI) for 10-unit increase in pollutant (1 unit for carbon monoxide), for all infant deaths, and by neonatal and post-neonatal deaths. Only mean effects are presented. Pollutant measure was presented as an average of lags 0–2 days.

	CO	NO	NO2	O3	PM10	SO2
All infant deaths	1.02 (0.96 to 1.09)	1.00 (0.99 to 1.01)	1.00 (0.99 to 1.02)	1.00 (0.98 to 1.03)	0.99 (0.97 to 1.01)	1.02 (1.01 to 1.04)
Neonatal deaths	0.99 (0.92 to 1.07)	1.00 (0.99 to 1.01)	1.00 (0.98 to 1.02)	0.99 (0.96 to 1.02)	0.99 (0.97 to 1.02)	1.02 (1.00 to 1.04)
Post neonatal deaths	1.09 (0.94 to 1.25)	1.00 (0.99 to 1.01)	1.01 (0.98 to 1.04)	0.99 (0.92 to 1.06)	0.99 (0.95 to 1.03)	1.03 (0.98 to 1.08)

CO, carbon monoxide; NO, nitrogen oxide; NO_2, nitrogen dioxide; O_3, ozone; PM_{10}, particulate matter <10 μg/m^3; SO_2, sulphur dioxide.

effect estimate for O_3 largely unchanged, but the SO_2 effect was larger in the summer months: 1.03 (1.00 to 1.06). In winter (October–March), the SO_2 effect was 1.01 (0.99 to 1.04).

On repeating the analysis separately for neonatal and post-neonatal deaths, the SO_2 effect was found to remain for both age groupings (table 2). Very few other differences were observed, except a very strong adverse effect of CO in post-neonatal deaths, although CIs were wide due to small numbers.

Effect estimates were largely unchanged when more seasonal control (10 df/year) was used in all models.

Discussion

On the basis of previous evidence, our prior hypothesis was that PM_{10} may be adversely associated with infant mortality; however, our results suggested a link with SO_2 on both neonatal and post-neonatal mortality. Exposure to SO_2 may irritate the respiratory system, with high concentrations causing constriction of the bronchi and increasing mucous flow, making breathing difficult. Children may be particularly susceptible to such effects. A similar time-series study from Sao Paulo reported a 6% (95% CI 4 to 8) increase in neonatal deaths associated with the interquartile range (9.2 μg/m^3) of SO_2.[12] Our estimate of 2% (0 to 4) was roughly for a similar change in SO_2 levels. In a spatial study, Bobak and Leon found associations between infant mortality in the Czech Republic and both total suspended particles and SO_2, which were specific to respiratory mortality in the post-neonatal period.[13] These results were later reproduced in a case–control study, where an odds ratio (95% CI) of 1.74 (1.01 to 2.98) was estimated for a 50 μg/m^3 increase in SO_2 on post-neonatal respiratory mortality.[1] Results of our present study were much smaller, but were on all-cause deaths and only consider, effects of short-term changes in air pollution as opposed to cumulative exposures.

What this paper adds

- An adverse effect of SO_2 exposure was observed on both neonatal and post-neonatal mortality.
- No effects of particulate matter <10 μg/m^3 were observed.

Policy implications

- Continuing reductions in SO_2 levels in the UK may yield additional health benefits in infants.

Another spatial comparison from the US by Woodruff *et al*[14] estimated an OR (95% CI) of 1.10 (1.04 to 1.16) of total post-neonatal mortality in the highest tertile of PM_{10} exposure compared with the lowest tertile. An equivalent comparison from our current study for just PM_{10} levels in London and post-neonatal deaths gives a RR of 0.94 (0.87 to 1.01), suggesting no contribution from PM_{10} and no overlap with the Woodruff estimate.

Recent time-series and case-crossover studies have also implicated PM_{10}[10 16] or NO_2,[17] but no role for SO_2 was observed. Furthermore, no significant effect of CO was observed in these studies—our results suggested that CO may have a strong adverse effect on post-neonatal deaths, although our estimate was imprecise. Other temporal studies have only considered effects of PM_{10}.[11]

Recent work has demonstrated that correlations between ambient levels and personal exposure of gaseous pollutants such as SO_2 is lower than those for fine particles, and that ambient gaseous pollutant concentrations may be better surrogates of personal $PM_{2.5}$ exposures than they would be as surrogates of personal exposures to the gases themselves.[18 19] This is most likely to be the case in low-ventilated environments; however, our SO_2 effect was strongest in the summertime, when ventilation is at its highest in UK homes.

A long time-series was used in the present study—11 years of data from 10 major English cities allowed us to robustly estimate the effects on all-cause mortality. In addition, all effects were insensitive to the different levels of seasonal control, suggesting that our original model choice was satisfactory.

In conclusion, our results suggest an adverse effect of SO_2 exposure on both neonatal and post-neonatal mortality. Continuing reductions in SO_2 levels in the UK may yield additional health benefits for infants.

Authors' affiliations
Shakoor Hajat, Ben Armstrong, Paul Wilkinson, Araceli Busby, London School of Hygiene & Tropical Medicine, London, UK
Helen Dolk, University of Ulster, Newtownabbey, Co Antrim, UK

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SPEAKER'S CORNER

Publishing has become a ''Russian roulette''

As authors, every now and then we get rather prejudiced, biased or scientifically unfounded—if not fully unethical, because of conflicts of interest—comments from manuscript reviewers. Some journal editors seldom seem to feel accountable for the choice of reviewers.

Today, I seek advice from a colleague and friend, a widely recognised scientist at a top-ranking college in London, UK, about suitable journals to which we could resubmit a given paper. Other than the specific advice, his main reflection is:

Publishing has become a ''Russian roulette''.

Hopefully, not so in *JECH* and in most other journals. But the debate is worthwhile.[1 2]

Correspondence to: Professor M Porta, IMIM & UAB, Carrer del Dr Aiguader, 88, E-08003 Barcelona, Catalonia, Spain; mporta@imim.es

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Air pollution and children's respiratory symptoms in six cities of Northern China

Guowei Pan [a,*], Shujuan Zhang [a], Yiping Feng [a], Ken Takahashi [b], Jun Kagawa [c], Lianzheng Yu [a], Ping Wang [d], Meijuan Liu [e], Qinan Liu [f], Shuwen Hou [g], Bailing Pan [h], Jianping Li [i]

[a] *Department of Environmental Epidemiology, Liaoning Provincial Center for Disease Control and Prevention, 42-1 Jixian St, Heping Dis, Shenyang 110005, PR China*
[b] *Department of Environmental Epidemiology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Kitakyushu, Japan*
[c] *Dept. of Hygiene and Public Health, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan*
[d] *Shenyang Municipal Center for Disease Control and Prevention, Shenyang, PR China*
[e] *Anshan Municipal Center for Disease Control and Prevention, Anshan, PR China*
[f] *Dandong Municipal Center for Disease Control and Prevention, Dandong, PR China*
[g] *Benxi Municipal Center for Disease Control and Prevention, Benxi, PR China*
[h] *Liaoyang Municipal Center for Disease Control and Prevention, Liaoyang, PR China*
[i] *Panjin Oil Field Center for Disease Control and Prevention, Panjin, PR China*

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KEYWORDS
Air pollution;
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NO_2

Summary
OBJECTIVE: The associations between air pollution and children's respiratory health in the high pollution range have not yet been clearly characterized. We evaluated the effects of outdoor air pollution on respiratory morbidity in children selected from multiple sites in a heavy industrial province of northeastern China.
METHODS: The study included 11,860 children aged 3–12 years, selected from 18 districts of 6 cities in Liaoning province, the participation rate is 89.9%. Informed consent and written responses to surveys about children's historic and current health status, personal and household characteristics, and other information were obtained from parents. A two-stage regression approach was applied in data analyses.
RESULTS: There were wide gradients for TSP (188–689 $\mu g/m^3$), SO_2 (14–140 $\mu g/m^3$ and NO_2 (29–94 $\mu g/m^3$) across the 18 districts of 6 cities. The three air pollutants significantly increased the prevalence of persistent cough (21–28%), persistent phlegm (21–30%) and current asthma (39–56%) for each interquartile range increment (172 $\mu g/m^3$ for TSP, 69 $\mu g/m^3$ for SO_2, 30 $\mu g/m^3$ for NO_2), showing larger between-city effects than within-city. Rates of respiratory

* Corresponding author. Tel.: +86 24 8338 0014; fax: +86 24 2338 8218.
E-mail address: panpgw@yahoo.com.cn (G. Pan).

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symptoms were significantly higher for children with younger age, atopy, respiratory disease in early age, family history of asthma or chronic bronchitis, and tobacco smoke exposure.
CONCLUSION: The high levels of outdoor air pollution in north China are positively associated with children's respiratory symptoms, the associations with TSP appear to be stronger than SO_2 and NO_2.

Introduction

China has experienced rapid economic development and urbanization over the past three decades, the levels and patterns of outdoor and indoor air pollutants have altered dramatically. The levels of particulate matter and SO_2 are higher than those of the national standard and criterion concentration of WHO in many cities, although they have declined gradually in recent years.[1–4] With the rapid increase in motor vehicles, urban air pollution has changed from the coal combustion type to mixed coal smoke and motor vehicle emission type encountered at relatively high levels since the mid 1990s. Meanwhile, the levels of indoor coal smoke pollution have decreased rapidly since more people moved to new houses with gas or electric power. The new building materials used, pet raising, and tobacco smoke exposure have also affected the types and levels of indoor air pollution.[1,2] While a limited number of studies have evaluated the health effects of the changing and mixing air pollution in the past decade,[5–15] most were conducted in one city with heavy air pollution, the inconsistent results obtained to date do not provide a clear overall picture of health damage.

The air pollution levels were higher in cities of north China, since coal was the main fuel for industry and heating, especially in winter. Several cities in the Liaoning province, including Shenyang, Anshan and Benxi, are historically among the most polluted cities in China. Epidemiological studies reveal positive associations between high level air pollution and increased morbidity and mortality from respiratory diseases and lung cancer.[8,13,14] These studies have several limitations: (1) all were performed in one city with heavy air pollution, the relatively high and narrow pollution range between the nested districts in one city could not reveal between-city effects; (2) none included pre-school children, who are more susceptible to air pollutants; (3) some important confounding factors, such as family history of respiratory disease, respiratory infections in early life, and atopic status, were not effectively controlled.

To evaluate the associations between air pollution and children's respiratory symptoms and illnesses within a wider range of both air pollutants and subjects, we conducted a cross-sectional survey in 6 cities in Liaoning province.

Materials and methods

Detailed information on locations of study area, schools and participants selection, and ambient air pollution assessment, has been has been reported in previous paper on adults' respiratory health of the present study.[14] In brief, with the aim of maximizing between-city and within-city concentration gradients in the air pollutants, six cities (i.e., Anshan, Benxi, Dandong, Liaoyang, Panjin and Shenyang) and three districts (slight, moderate, heavy) within each city were selected based on historical monitoring data. A kindergarten and an elementary school that were located within 1 km of the monitoring sites were selected in each district. Two classes were randomly selected for each grade/age group in the kindergarten/schools.

The records obtained between 1997 and 2000 from environmental monitoring stations nearest to the subjects' residence (any one of each of the three stations in each city) were used to determine the levels of exposure to ambient air pollution for each subject. Ambient air pollution was determined by the annual average levels of three pollutants (TSP, SO_2, and NO_2). For comparison, the annual PM_{10} concentrations were estimated by multiplying TSP with 0.52 for each district using the method recommend by State Environmental Protection Administration of China.[15]

The Chinese language questionnaire was translated and back-translated from the Epidemiologic Standardization Project Questionnaire of American Thoracic Society (ATS-DLD-78-A).[16] We additionally included some questions, such as breast feeding, atopy, family history of respiratory disease, dwelling and classroom characteristics, methods of cooking and heating, pet raising, history of respiratory illnesses, and passive smoking. After obtaining written consent forms from parents, questionnaires were distributed simultaneously in all the districts. The questionnaire was self-completed by parents or other family members of the schoolchildren, either at school or at home between January and June 2002.

We focus on four respiratory symptoms and illnesses, specifically, persistent cough, persistent phlegm, current wheeze and current asthma. We used the similar definitions as adopted in the ATS-DLD-78-A questionnaire survey in Japan.[17] Respiratory symptoms and illnesses were determined based on questionnaire responses. (a) Persistent cough: had a cough on most days (≧4 days per week) for as long as 3 months of the year, either together with or separately from colds; (b) Persistent phlegm: seemed congested or brought up phlegm or mucus from the chest on most days (≧4 days per week) for as long as 3 months of the year, either together with or separately from colds; (c) Current wheeze: positive answers to all the four criteria: (1) occasional wheezing; (2) chest ever sound wheezy or whistling, either together with or separately from colds; (3) experienced two or more such episodes in the past 2 years; (4) not meet the criteria for 'current asthma'. (d) Current asthma: positive responses to all the six criteria: (1) have experience an attack of wheezing and/or short of breath; (2) have had two or more such attacks; (3) have been diagnosed with asthma by a doctor; (4) wheezing could be heard during an attack; (5) experienced shortness of breath and wheezing during an attack; (6) have experienced such

an attack or have received treatment for asthma in the past 2 years. Other risk factors, such as respiratory disease at early age, atopy and obesity, were defined as specified in the online data supplement.

To study the relationships between the air pollution levels and the prevalence of four respiratory symptoms/illnesses, we used a two-stage regression approach similar to the method used in other studies.[12,18–20] In the first stage, we used stepwise logistic regression models to determine which personal and household variables were associated with each symptom. Any variables that were significant at the $p < 0.15$ level for a given symptom will be included in all subsequent models of pollutant effects for that symptom. We fit a single logistic regression model for the prevalence rate of each symptom, including all of the significant personal/household variables and 18 separate intercept terms α_j for each community j. These intercept terms represent the logit of the community-specific prevalence rates, adjusted for the personal/household covariates. The adjusted prevalence rate can then be computed as $e^{\alpha j}/(1 + e^{\alpha j})$. In the second stage model, we firstly fitted one pollutant models by regressing the community-specific parameter estimates (α_j, $j = 1, \ldots,18$) on the community-specific ambient level of a given pollutant, using simple linear "ecologic" regression $\alpha_j = (\alpha_j = \alpha + \beta Z_j + E_j)$ where Z_j denotes the pollution variable(s) in community j. The expectation is that if there is a relationship between the condition and pollution, there will be a non-zero slope (β) in this model. The standard t test of zero slope for a regression model is utilized to determine whether rates of symptoms are correlated with pollutants. The quantity, e^{β}, can be translated to the prevalence odds ratios (ORs) and 95% confidence intervals (95% CIs), scaled so that the interquartile range corresponds to one unit change. Finally, we fitted three pollutant models to assess the independent effects of each pollutant while controlling the possible confounding from others.

Because the 18 districts were nested in the six cities, we used additional second stage models that tested separately for the between-city and within-city associations between prevalence and each pollutant.[12,20] The models can be described with two dimensional expression as follows: k denotes city ($k = 1, \ldots, 6$) and l denotes the three districts within a city ($l = 1, 2, 3$); then $\alpha_{kl} = a + b_1 X_k + b_2(X_{kl} - X_k) + e_{kl}$, where α_{kl} is the coefficient for district kl (similar to α_j in the first-stage model), X_k denotes the city-specific concentration for city k (the average of city k's three districts), X_{kl} denotes the pollutant concentration in district l of city k, and e_{kl} represents the error term. In this model, $b1$ and $b2$ represent between-city and within-city pollutant–outcome relationships, respectively. These coefficients were t-tested for zero slope and translated to ORs and 95% CIs.

Results

Table 1 presents the 4-year arithmetic means of TSP, SO_2 and NO_2, as well as the estimated PM_{10}, in the 18 districts. 94–100% of estimated PM_{10}, 44–94% of SO_2, 56–67% of SO_2 exceeded the National Standard of China[21] and WHO Air Quality Guidelines.[22] There are wide between-city and within-city gradients for TSP (188–689 $\mu g/m^3$), SO_2 (14–140 $\mu g/m^3$ and NO_2 (29–94 $\mu g/m^3$). The highest levels of TSP and SO_2 were observed in Anshan and Benxi, where the two largest iron-steel companies in China are located.

Table 2 contains detailed information about the final study samples of 12,879 children (89.9%) of 13,192 eligible children. The participation rates varied from 78.7% in Dandong to 96.1% in Benxi, which did not correlate with either pollution levels or disease prevalence. In total, 1019 children (153 aged <3, 127 aged ≥13, 739 residing in the current district for <3 years) were excluded from further analyses (exclusion rate of 7.9%). Among the 11,860 children analyzed, the average age was 8.4 ± 2.6 years, 50.7% were male, 79.9% were breast-fed, 3.3% were low birth weight, 6.9% were diagnosed with atopy, 13.0% displayed obesity, 22.9% had a respiratory disease history before 2 years of age, 54.0% were exposed to tobacco smoke at home. Within the parents and grandparents of the children, 1.4% and 8.4% had asthma history, and 2.7% and 10.5% had a history of chronic bronchitis, respectively. In terms of houses, 25.2% were close to a main road (<20 m), 31.1% were close to a factory or chimney (<100 m), 22.5% had been painted or re-built in the past 3 years, 6.2% use humidifier, 25.6% have pets. In total, 11.5% houses used coal for cooking or heating, with the highest rates reported in Benxin (31.2%) and Dandong (12.4%).

As shown in Table 3, the prevalence of persistent cough, persistent phlegm, current wheeze and current asthma were 9.5%, 4.6%, 6.0% and 1.4% respectively, which were significantly different among the 6 cities. The lowest levels of both air pollutants and prevalence of persistent cough and persistent phlegm were recorded in Panjin city. Preschool children aged <7 years displayed a significantly higher prevalence for all four symptoms than school children. No marked differences were observed between males and females.

Table 4 shows the results of first-stage logistic regressions. Respiratory disease history at an early age, atopy, parental history of asthma and/or chronic bronchitis, grandparents' history of asthma, and passive tobacco smoke exposure at home significantly increased the ORs for all four symptoms/illnesses. Significantly positive associations were observed between low birth weight and persistent cough; obesity and wheeze; grandparents' chronic bronchitis and persistent cough and wheeze; fewer room number and persistent phlegm; house close to main road and asthma; house close to factory/chimney and persistent cough, wheeze and asthma; classroom close to main road and persistent cough, persistent phlegm and asthma; house pet and persistent cough and persistent phlegm; house painting and wheeze and asthma; humidifier and persistent phlegm and asthma. Significantly negative associations were observed between elder age and persistent cough and wheeze; breast feeding and persistent cough and persistent phlegm; parents as responders and persistent cough, persistent phlegm and asthma.

Table 5 presents the results of second stage regression analyses. We observed significantly increased prevalence of persistent cough (21–28%), persistent phlegm (21–30%), asthma (39–56%) for each interquartile range of all the three air pollutants, but not for wheeze, in the one pollutant model. However, the significant associations with

Table 1 District-specific ambient air pollutant concentrations (g/m^3), 4-year (1997–2000) arithmetic means for TSP, PM_{10}, SO_2 and NO_2 in 18 districts of 6 cities.

City	TSP[d]			PM_{10}[e]			SO_2[f]			NO_2[g]		
	Heavy	Moderate	Slight	Heavy	Moderate	Slight	Heavy	Moderate	Slight	Heavy	Moderate	Slight
Anshan	689	391	307	358	203	160	117	91	72	94	91	58
Benxi	625	573	448	325	298	233	120	140	133	48	55	53
Dandong	212	199	188	110	103	98	26	25	14	47	38	35
Liaoyang	322	253	225	167	132	117	34	25	27	70	45	33
Panjin	286	208	194	149	108	101	41	27	26	38	30	29
Shenyang	351	334	314	183	174	163	96	82	50	67	74	57
Grand Mean ± SD	414 ± 195	326 ± 142	279 ± 99	215 ± 101	170 ± 74	145 ± 51	72 ± 43	65 ± 47	54 ± 44	61 ± 20	56 ± 23	44 ± 13
	340 ± 153			177 ± 79			64 ± 42			53 ± 44		
Interquartile range[a]	172			114			69			30		
National standard[b]	200			100			60			50		
% of > NS	83			94			44			56		
WHO guideline[c]	–			20			20			40		
% of > WHO	–			100			94			67		

[a] Range from 25th to 75th percentile of district-specific concentrations.
[b] China national ambient air quality standard.
[c] WHO air quality guidelines global update 2005.
[d] TSP: total suspended particle.
[e] PM_{10}: particulate matter with a mass median aerodynamic diameter <10 μm, estimated by multiplying TSP with 0.52.
[f] SO_2: sulfur dioxide.
[g] NO_2: nitrogen dioxide.

SO_2 do not exit in the three pollutants model analysis. When the overall associations were broken down into between-city and within-city associations (Table 6), we found significantly increased ORs in between-city associations in single pollutant model, most between-city ORs were higher than the corresponding within-city ORs, also no significantly increased or decreased ORs for wheeze. In the three pollutant molde analyses, the between-city ORs almost doubled for the associations between TSP and persistent cough (2.39/1.23) and persistent phlegm (2.81/1.22), all the within-city ORs for TSP also slightly increased. Most ORs for SO_2 decreased over 50%, especially for the significantly decreased between-city ORs for persistent cough (OR = 0.41, 95%CI = 0.26–0.67) and persistent phlegm (OR = 0.32, 95%CI = 0.16–0.64), and within-city OR for wheeze (OR = 0.31, 95%CI = 0.17–0.56). All the between-city ORs decreased, but within-city ORs increased for NO_2.

Discussion

The average levels of $PM_{10,}$, SO_2 and NO_2 of the 18 sites were 8.9, 3.2 and 1.3 times of WHO recommended limits, substantially extended the upper end of the pollution ranges of previous epidemiological studies conducted in North America, Europe and Japan,[11,18–20] also higher than that in former East Germany.[23–25] The wide gradients present a unique advantage in assessing the harmful heath effects of air pollution within the high pollution range, especially for particulate matters and SO_2.

The prevalence of persistent cough and persistent phlegm are higher than that of wheezing and asthmatic symptoms, confirmed the previous findings that the rates of 'non-allergic symptoms' were significantly higher than that of 'allergic symptoms' in Chinese children.[9–14] The prevalence of asthma (1.4%) was significantly lower than that of Japanese schoolchildren assessed with the same ATS questionnaire (6.51%),[17] close to the level of 'current asthma' in a national survey among 432,500 children in 43 Chinese cities (1.54%).[26] The definition of 'asthma ever diagnosed by a doctor' in ATS[17] is similar to 'ever had asthma' in ISSAC (the international study of asthma and allergies in childhood),[27] the rate of 'asthma ever diagnosed by a doctor' in the present study is 6.5%, close to that of 'ever had asthma' for ISSAC survey in Beijing (6.9%), Chongqing (7.1%) and Shanghai (7.1%),[27] but significantly lower than Japanese children (18.9%),[17] The data from both ATS and ISAAC surveys support that Chinese children has significantly lower prevalence of asthma than Japanese children, China is one of the countries with the lowest prevalence of asthma.[27] The prevalence of 'current asthma' reported in the ISSAC survey in Beijing (2.3%) and Guangzhou (2.1%) is lower than Hang Kong (3.3%),[28] the lower rate of 'current asthma' in the present study maybe partly related to the stricter criteria in ATS than ISSAC. The prevalence of current wheeze was 6.0%, close to the 12 month prevalence of wheeze in China (4.2%),[27] lower than that of the cities in south and west China (6.6–18.8%).[12]There are big geographic variations in asthmatic and wheeze symptoms in China,[12,26–28] we should be careful while comparing the prevalence of asthma between various surveys assessed with different questionnaire and/or definitions. The higher prevalence of respiratory symptoms in younger children supports the theory that the developing and maturing lung is more vulnerable to damage

Table 2 Personal and household characteristics of children in six cities.

Variable	All	City						*p*-Value
		Anshan	Benxi	Dandong	Liaoyang	Panjin	Shenyang	
Subjects administrated questionnaire [N (%)]	13192 (100)	1971(14.9)	2190(16.6)	2428(18.4)	2476 (18.8)	2089(15.8)	2019 (15.3)	<0.001
Respondents included in final analysis [N (%)]	11860.0	1772(14.9)	2105(17.7)	1911(16.1)	2303(19.4)	1966(16.6)	1803 (15.2)	<0.001
Response rate (%)	89.9	89.9	96.1	78.7	93.0	94.1	89.3	<0.001
Male [N (%)]	5847 (49.3)	883(49.8)	1030(48.9)	969(50.7)	1131(49.1)	969(49.3)	865(48.0)	0.681
Age (mean [SD]) (yr)	8.3 [2.6]	8.5[2.6]	8.1[2.7]	8.8[2.7]	8.3[2.4]	8.1[2.5]	8.3[2.5]	<0.001
Breast-fed (%)	79.9	76.1	81.1	87.3	78.3	85.6	70.4	<0.001
Low birth weight (%)	3.3	3.5	4.2	1.8	3.3	3.0	4.3	<0.001
Atopy (%)	6.9	5.5	7.0	8.9	5.1	7.2	8.0	<0.001
Obesity (%)	13.0	11.6	17.7	12.6	10.2	11.3	14.8	<0.001
Respiratory disease before 2 yr (%)	22.9	26.4	24.8	25.1	22.3	19.7	19.2	<0.001
Parental asthma (%)	1.4	1.8	2.2	1.8	0.9	0.7	0.9	<0.001
Parental chronic bronchitis (%)	2.7	3.1	3.2	3.3	2.1	1.9	2.8	<0.001
Grandparent asthma (%)	8.4	8.8	10.2	9.7	6.0	8.1	7.8	<0.001
Grandparent chronic bronchitis (%)	10.5	10.4	11.0	12.3	8.8	10.9	10.0	<0.001
Numbers of room ≥3 (%)	31.8	15.7	20.5	35.2	35.0	61.5	20.2	<0.001
House close to main road (%)	25.2	26.0	24.7	27.4	30.8	18.1	23.2	<0.001
House close to factory or chimney	31.1	27.0	24.8	40.5	32.3	20.4	42.9	<0.001
House painted or re-built in past 3 yr (%)	22.5	20.1	16.3	19.6	24.6	34.0	20.2	<0.001
Indoor coal use (%)	11.5	3.2	32.2	13.1	5.7	5.7	7.8	<0.001
Ventilation in kitchen (%)	76.8	75.7	49.6	79.4	85.8	93.2	77.6	<0.001
Air exchange in winter (%)	47.2	47.8	32.9	52.6	47.8	48.5	55.4	<0.001
Humidator use (%)	6.2	5.8	2.4	4.3	6.8	9.7	8.5	<0.001
House pets (%)	25.8	30.0	25.8	20.5	28.2	13.1	37.8	<0.001
Passive smoking exposure (%)								
Father	43.5	42.7	55.4	42.5	36.7	43.2	40.7	<0.001
Mother	1.0	1.3	2.4	0.4	0.3	0.9	0.8	<0.001
Anyone	54.0	53.1	64.9	51.2	48.8	51.4	54.6	<0.001
Parents as responders (%)	92.3	91.5	92.5	91.0	91.5	94.8	92.6	<0.001

Table 3 Prevalence (%) of respiratory symptoms and illnesses by city, gender and age groups.

	Persistent cough			Persistent phlegm			Current wheeze			Current asthma		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
City												
Anshan	9.4	9.8	9.6	4.4	6.0	5.2	3.7	4.3	4.0	2.0	2.2	2.1
Benxi	11.8	11.5	11.7	5.8	5.2	5.5	5.0	4.5	4.8	1.7	1.9	1.8
Dandong	8.2	9.4	8.8	3.7	4.5	4.1	5.8	6.2	6.0	1.0	1.6	1.3
Liaoyang	11.7	12.2	11.9	5.7	6.2	5.9	3.7	4.1	3.9	0.7	0.8	0.7
Panjin	4.9	5.0	4.9	2.1	2.5	2.3	5.7	4.8	5.2	1.2	1.0	1.1
Shenyang	9.7	9.0	9.3	4.3	4.4	4.3	3.8	3.9	3.9	1.0	1.2	1.1
p-Value*	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.1	0.2	<0.01	0.1	<0.05	<0.01
Age												
3—6	12.2	12.9	12.5	5.1	5.3	5.2	8.6	9.4	9.0	2.0	1.9	1.9
7—9	8.4	8.0	8.2	4.1	3.8	4.0	4.6	4.4	4.5	1.0	1.2	1.1
10—12	8.5	7.7	8.1	5.4	4.1	4.8	2.7	2.6	2.6	1.0	1.3	1.1
p-Value#	<0.01	<0.01	<0.01	0.1	0.1	0.0	<0.01	<0.01	<0.01	0.0	0.1	<0.01
Total	9.6	9.4	9.5	4.8	4.4	4.6	4.6	5.9	5.2	1.3	1.4	1.4
p-Value†	0.66			0.25			0.94			0.58		

*p-Value for the effect of city.
#p-Value for the effect of age.
†p-Value for the effect of sex.

Table 4 ORs of personal and household covariates associated with respiratory symptoms.

Variable	Persistent cough			Persistent phlegm			Current wheeze			Current asthma		
	OR	95%CI		OR	95%CI		OR	95%CI		OR	95%CI	
Age (ref: 3—6 yr)	0.80**	0.74	0.87	0.94	0.84	1.05	0.56**	0.49	0.63	0.71	0.57	0.88
Low birth weight (ref: normal l birth weight)	1.28*	0.96	1.72	1.49	1.02	2.18	1.04	0.70	1.56	0.78	0.32	1.93
Breast feeding (ref: not breast-fed)	0.85**	0.73	0.98	0.74**	0.61	0.91	0.96	0.79	1.17	0.72	0.50	1.04
Obesity (ref: not obesity)	1.14	0.96	1.36	1.05	0.81	1.34	1.44**	1.14	1.81	0.91	0.57	1.46
Atopy (ref: no atopy)	1.73**	1.41	2.12	2.09**	1.62	2.69	2.18**	1.73	2.76	3.83**	2.63	5.58
Res Dis History before 2 years old (ref: no history)	2.24**	1.96	2.55	2.24**	1.87	2.69	4.04**	3.44	4.75	9.53**	6.52	13.91
Parental asthma (ref: no history)	1.71**	1.14	2.56	1.68**	1.01	2.79	2.19**	1.40	3.42	4.09**	2.22	7.53
Parental chronic bronchitis (ref: no history)	1.80**	1.35	2.41	1.72**	1.18	2.51	2.35**	1.35	3.34	1.98**	1.13	3.44
Grandparent asthma (ref: no history)	1.43**	1.17	1.76	1.73**	1.35	2.22	1.74**	1.33	2.26	2.56**	1.68	3.91
Grandparent chronic bronchitis (ref: no history)	1.21*	1.00	1.46	1.59	1.25	2.03	1.41**	1.10	1.81	1.64	1.07	2.51
Mother smoking (ref: nonsmoking mother)	2.54**	1.63	3.97	2.07**	1.15	3.71	1.83	0.97	3.45	3.13**	1.19	8.23
Passive tobacco exposure at home (ref: no PTE at home)	1.26**	1.11	1.43	1.36**	1.13	1.64	1.48**	1.23	1.78	1.41*	0.99	1.99
Fewer room number (ref: room number≥3)	1.12	0.97	1.28	1.16*	0.95	1.41	0.88	0.75	1.03	0.81	0.59	1.13
House close to main road (ref: distance :≥20 m)	1.10	0.88	1.38	0.90	0.64	1.26	1.26	0.96	1.66	1.57*	0.96	2.58
House close to factory or chimney (ref: distance:≥100 m)	1.40**	1.12	1.76	1.62	1.20	2.18	1.34**	1.10	1.63	1.80**	1.11	2.91
Classroom close to main road (ref: distance: ≥20 m)	1.59**	1.27	2.00	1.88**	1.40	2.53	1.13	0.85	1.50	1.92**	1.14	3.24
House pets (ref: no pet at home)	1.19**	1.03	1.37	1.24**	1.02	1.50	1.09	0.91	1.30	1.02	0.71	1.46
House painted/re-built in 3 yr (ref: not in the past 3 yr)	0.94	0.81	1.10	1.04	0.85	1.27	1.16*	0.97	1.40	1.43**	1.00	2.02
Humidator use (ref: not use)	1.06	0.82	1.37	1.39**	0.99	1.94	0.97	0.71	1.33	1.82**	1.06	3.14
Parents as responders (ref: others as responders)	0.79**	0.63	1.00	0.66**	0.49	0.89	1.22	0.89	1.67	0.60*	0.34	1.07
Low education of the questionnaire responder (ref:≥Junior high school)	1.16	1.02	1.33	1.19*	0.99	1.43	0.83*	0.67	1.02	1.25	0.88	1.76

*$p < 0.15$; **$p < 0.05$.

Variables with asterisks are selected in the first-stage logistic stepwise regression model, and included in the second stage model for this symptom. The variables are adjusted for each other. The remaining variables without asterisks are adjusted for each other, as well as for age and sex.

caused by air pollutants.[29,30] The inclusion of these children enhanced sensitivity in detecting the harmful effects of air pollution.

The significantly increased ORs of family history of asthma and chronic bronchitis, as well as atopy of the subject, confirmed the strong influence of genetic-determined susceptibility and/or common environmental exposure. We observed strong effects of respiratory diseases in early life on wheeze and asthma. However, the lower prevalence of asthma (1.4%) and higher rate of early respiratory infection (22.9%), as reported in other developing countries[27] and East Germany,[23—25] does not support a causal link between respiratory infection and asthma, further studies are warranted to establish whether infection in early life plays different roles in the etiology of asthma in countries with varying levels of asthma. As expected, breast feeding was a significant protective factor for persistent cough and persistent phlegm.

We observed significant effects of some indoor air pollutions on various respiratory symptoms, the rapidly increasing trend of pet raising, humidifier usage, and house painting is expected to cause more health damage in the

Table 5 Associations between air pollutants and respiratory symptoms and illnesses.

Pollutant	Persistent cough			Persistent phlegm			Current wheeze			Current asthma		
	OR	95%CI		OR	95%CI		OR	95%CI		OR	95%CI	
Single pollutant model												
TSP	1.21*	1.14	1.29	1.21*	1.10	1.32	0.92	0.83	1.01	1.41*	1.22	1.65
SO_2	1.24*	1.13	1.36	1.21*	1.06	1.38	0.88	0.77	1.00	1.52*	1.21	1.92
NO_2	1.27*	1.16	1.38	1.30*	1.15	1.48	0.87	0.76	1.00	1.39*	1.11	1.74
Three pollutant model												
TSP	1.27*	1.10	1.46	1.31*	1.07	1.60	1.02	0.82	1.29	1.57*	1.12	2.21
SO_2	0.85	0.70	1.04	0.77	0.58	1.04	0.90	0.66	1.23	0.81	0.49	1.35
NO_2	1.14*	1.02	1.27	1.20*	1.03	1.40	0.91	0.77	1.08	1.10	0.84	1.45

Single and three pollutant models adjusted for personal and household factors with asterisks in Table 2.
OR is scaled to the interquartile range for each pollutant as follows: 172 $\mu g/m^3$ of TSP, 69 $\mu g/m^3$ of SO_2, 30 $\mu g/m^3$ of NO_2.
*$p < 0.05$.

future. We confirmed the strong harmful effects of passive tobacco smoke, especially for mother smoking. Consistent with the findings in a recent study in four Chinese cities,[12] we could not find significantly increased ORs for indoor coal use, which maybe related to the dramatically decreased level and frequency of indoor coal smoke exposure over the past decade. The increased ORs of close proximity of houses or classrooms to main roads or chimneys/factories for various respiratory symptoms suggest the harmful effects of local and/or traffic air pollution.

The significantly increased ORs of persistent cough, persistent phlegm and current asthma for each interquartile increment of TSP, SO_2 and NO_2 in single model analyses, both for overall and within-city ORs, confirmed the similar positive associations found in several one-city studies in China, such as Whuan,[5] Lanzhou,[6] Beijing[7] and Shenyang.[8] The prevalence of persistent cough,[5–8] persistent phlegm,[5–8] wheeze,[6–8] and asthma[7,8] were significantly elevated in the heavily air polluted areas compared with that in the control areas within each city. A recent one-city study could not observe significant associations between the levels of SO_2 and NO_2 and increased ORs of wheeze and asthma in Taiyuan.[9] Although we could not find significantly increased ORs for wheeze as other respiratory symptoms, we did find significantly increased wheeze prevalence among atopic children (data not shown). By selecting 18 districts from 6 cities, we have observed the larger effects of the wider between-city air gradient than the narrow range of within-city, and demonstrated the characteristics of the overall harmful effects which could not have been evaluated in one-city studies.

Several multi-city studies have reported positive associations between these air pollutants and the prevalence of a number of respiratory symptoms. The Harvard Six Cities Study found TSP was positively associated with the morbidity of cough or persistent cough, bronchitis, chest illness, wheeze, lower respiratory diseases.[31,32] A Slovakian study has also found that the prevalence of non-asthmatic symptoms and hospitalization was associated with elevated TSP.[33] A study involving 4 areas of East Germany and 2 areas of West Germany found the higher prevalence of non-allergic respiratory illness in East German children was associated with TSP and SO_2, the sharp decline in TSP and SO_2 in East Germany was mirrored by similar reductions

Table 6 Between and within-city modeled ORs, scaled to interquartile range of concentration for each air pollutants.

Pollutant	TSP						SO2						NO2					
	Between			Within			Between			Within			Between			Within		
	OR	95%CI		OR	95%CI		OR	95%CI		OR	95%CI		OR	95%CI		OR	95%CI	
Single pollutant model																		
Persistent cough	1.23*	1.14	1.33	1.15*	1.02	1.31	1.25*	1.14	1.37	1.14	0.81	1.59	1.27*	1.14	1.41	1.33*	1.14	1.55
Persistent phlegm	1.22*	1.10	1.36	1.15	0.96	1.38	1.23*	1.07	1.40	1.04	0.64	1.68	1.33*	1.14	1.55	1.23	0.97	1.57
Current wheeze	1.03	0.94	1.13	1.09	0.93	1.28	1.05	0.93	1.18	0.72	0.47	1.08	0.91	0.8	1.04	1.22	0.98	1.51
Current asthma	1.46*	1.21	1.77	1.40*	1.04	1.88	1.61*	1.27	2.05	0.94	0.41	2.18	1.56*	1.19	2.04	1.19	0.78	1.81
Three pollutant model																		
Persistent cough	2.39*	1.62	3.54	1.23	0.96	1.32	0.41*	0.26	0.67	0.64	0.39	1.05	1.07	0.93	1.22	1.34*	1.07	1.69
Persistent phlegm	2.81*	1.59	4.96	1.77	0.94	1.48	0.32*	0.16	0.64	0.54	0.26	1.09	1.14	0.94	1.39	1.34	0.97	1.85
Current wheeze	0.96	0.6	1.54	1.14	0.92	1.4	1.19	0.67	2.12	0.31*	0.17	0.56	0.84	0.71	0.99	1.65*	1.22	2.22
Current asthma	1.52	0.56	4.41	1.65*	1.13	2.4	0.56	0.25	2.9	0.33	0.10	1.09	1.23	0.89	1.71	1.94	0.64	2.24

*$p < 0.05$.

in the prevalence of non-allergic, but not allergic symptoms.[21–23] A four-city study in south and west China found significantly increased prevalence of persistent cough (OR = 1.35, 95%CI = 1.02–1.79), persistent phlegm (OR = 2.52, 95%CI = 1.91–3.21), as well as non-significantly increased prevalence for wheeze (OR = 1.28, 95% CI = 0.83–1.99) and asthma (OR = 1.32, 95% CI = 0.75–1.41) for each interquartile increment of TSP (263 $\mu g/m^3$), only weakly positive associations between SO_2, NO_2 and the respiratory symptoms.[12] The status of air pollution and respiratory diseases of the present study was similar to that of East Germany[21,22] and the four cities in China,[12] all the positive findings (overall, between-city and within-city) supported the casual relationships between air pollutants and non-allergic symptoms, especially for particulate materials. The low prevalence of asthma observed in the six cities, and other cities in China[12] and East Germany[23–25] despite high level of air pollutants, argues against that air pollutants contribute to the initial development of asthma. We believe that the significant positive associations between air pollutants and asthma, as well as wheeze in atopic children, reflect their triggering effects, rather than a direct causal link between asthma prevalence and air pollutants.[34,35]

The strong or moderate correlations between TSP and SO_2 ($r = 0.889$, $p < 0.01$), TSP and NO_2 ($r = 0.606$, $p < 0.01$), SO_2 and NO_2 ($r = 0.577$, $p = 0.012$) make it difficult to distinguish the effects of individual air pollutant. The increased ORs for TSP and decreased ORs for SO_2 and NO_2 in multi-pollutant models may reflect the dominated influence of the particulate material pollution in the 'coal smoke' style air pollution in the six cities.[2,36] Rather than being itself responsible for the increased risks of respiratory symptoms, TSP maybe operating as the best surrogates of the mixed air pollutants in this context. The significantly decreased ORs for SO_2 could be caused by the limited effectiveness of multi-pollutant regression models in controlling for confounding by copollutants.[37]

This cross-sectional study has known limitations with regard to etiological research, could not establish a temporal relationship between exposure and outcome.

The study confirmed the between-city and within-city harmful effects of the high level outdoor air pollution on children's respiratory health in north China. Accumulating rates of female smoking, childhood obesity, pet raising, and traffic air pollution tend to increase the incidence of various respiratory symptoms.

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Conflict of interest

We hereby declare that there were no conflicts of interest involved in the conduct of this study.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rmed.2010.07.018.

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Characterization of $PM_{2.5}$, gaseous pollutants, and meteorological interactions in the context of time-series health effects models

KAZUHIKO ITO[a], GEORGE D. THURSTON[a] AND ROBERT A. SILVERMAN[b]

[a]*NYU School of Medicine, Nelson Institute of Environmental Medicine, Tuxedo, New York, USA*
[b]*Department of Emergency Medicine, Long Island Jewish Medical Center, New Hyde Park, New York, USA*

Associations of particulate matter (PM) and ozone with morbidity and mortality have been reported in many recent observational epidemiology studies. These studies often considered other gaseous co-pollutants also as potential confounders, including nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO). However, because each of these air pollutants can have different seasonal patterns and chemical interactions, the estimation and interpretation of each pollutant's individual risk estimates may not be straightforward. Multi-collinearity among the air pollution and weather variables also leaves the possibility of confounding and over- or under-fitting of meteorological variables, thereby potentially influencing the health effect estimates for the various pollutants in differing ways. To investigate these issues, we examined the temporal relationships among air pollution and weather variables in the context of air pollution health effects models. We compiled daily data for PM less than 2.5 μm ($PM_{2.5}$), ozone, NO_2, SO_2, CO, temperature, dew point, relative humidity, wind speed, and barometric pressure for New York City for the years 1999–2002. We conducted several sets of analyses to characterize air pollution and weather data interactions, to assess different aspects of these data issues: (1) spatial/temporal variation of $PM_{2.5}$ and gaseous pollutants measured at multiple monitors; (2) temporal relationships among air pollution and weather variables; and (3) extent and nature of multi-collinearity of air pollution and weather variables in the context of health effects models. The air pollution variables showed a varying extent of intercorrelations with each other and with weather variables, and these correlations also varied across seasons. For example, NO_2 exhibited the strongest negative correlation with wind speed among the pollutants considered, while ozone's correlation with $PM_{2.5}$ changed signs across the seasons (positive in summer and negative in winter). The extent of multi-collinearity problems also varied across pollutants and choice of health effects models commonly used in the literature. These results indicate that the health effects regression need to be run by season for some pollutants to provide the most meaningful results. We also find that model choice and interpretation needs to take into consideration the varying pollutant concurvities with the model co-variables in each pollutant's health effects model specification. Finally, we provide an example for analysis of associations between these air pollutants and asthma emergency department visits in New York City, which evaluate the relationship between the various pollutants' risk estimates and their respective concurvities, and discuss the limitations that these results imply about the interpretability of multi-pollutant health effects models.
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Keywords: *particulate matter, nitrogen dioxide, weather, health effects.*

Introduction

A large number of studies have examined the short-term associations between air pollution and morbidity and mortality outcomes, but a surge in the increasing number of these studies has occurred over the last two decades. The most common study design is time-series analysis, comparing day-to-day fluctuations of community average air pollution and corresponding fluctuations in the daily citywide aggregate counts of morbidity or mortality, while adjusting for temporal trends and weather effects. The basic modeling concept goes back to several studies conducted in London, England in the 1950s and 1960s (e.g., Scott, 1958; Martin and Bradley, 1960) in which attempts were made to quantitatively link particulate matter (PM), sulfur dioxide (SO_2) and daily deaths, adjusting for temporal trends. Several studies also reported associations between PM and mortality in the U.S. in the 1970s (e.g., Schimmel and Greenburg, 1972; Schimmel and Murawski, 1976; Schimmel, 1978), using increasingly more elaborate techniques. The 1980s brought a re-evaluation of the London data sets by several researchers to quantify the relationship between air pollution and mortality (Ware et al., 1981; Mazumdar et al., 1982; Shumway et al., 1983; Schwartz and Marcus, 1986; Thurston et al., 1989). Most of the above studies focused on PM and SO_2, the "classic" primary air pollution products of coal burning. In addition to the main objective of quantifying the exposure–response relationships, the relative importance of PM and SO_2 was often examined in these studies.

The surge in the number of time-series studies in the 1990s appears to have started with a series of reported associations

1. Address all correspondence to: Dr. K. Ito, NYU School of Medicine, Environmental Medicine, 57 Old Forge Road, Tuxedo, New York 10987, USA.
Tel.: +1 845 731 3540. Fax: +1 845 351 5472.
E-mail: kaz@env.med.nyu.edu
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between daily morbidity/mortality and PM whose levels were mostly well below the ambient air quality standard (Pope, 1989; Fairley, 1990; Dockery et al., 1992; Pope et al., 1992; Schwartz and Dockery, 1992a, b). The PM controversy (Utell and Samet, 1993) led to more analyses and increased funding for PM research. Many of the respiratory morbidity studies whose main interest was the effects of summer haze air pollution, which includes ozone (O_3) and secondary fine particles, also applied similar time-series concepts (e.g., Bates and Sizto, 1983, 1987; Thurston et al., 1994, 1997). However, an increasing number of studies expanded to examine other gaseous pollutants, with the rationale that they may be potential confounders in the PM-health effects association.

These analyses then expanded to consider multiple cities, to increase statistical power. Many of these year-round multi-city studies found that some of these gaseous pollutants were also significantly associated with morbidity and mortality. The Air Pollution and Health—A European Approach (APHEA) study reported positive and significant associations between mortality and NO_2 (Touloumi et al., 1997), and a later report suggested that PM mortality risk estimates were higher in cities where NO_2 levels were higher (Katsouyanni et al., 2001). A systematic time-series analysis of the largest 90 U.S. cities (Samet et al., 2000; Dominici et al., 2003) found that PM was associated with mortality, but their results also showed that other gaseous pollutants were also associated with mortality in single-pollutant models, although less consistently than PM. A meta-analysis of PM and gaseous pollutants also showed that PM, NO_2, CO, and SO_2, all showed a positive and significant mortality risk estimates (Stieb et al., 2002, 2003). Burnett et al.'s (2004) analysis of 12 Canadian cities also suggested that NO_2 was most consistently associated with mortality. Since many of these pollutants come from the same sources (e.g., traffic and other combustion sources) and day-to-day fluctuations of air pollution are strongly influenced by weather conditions, it is not surprising that these air pollutants are temporally correlated and that the collinearity possibly leads to conflicting associations.

Despite the statistical power advantages of the multi-year and multi-city studies, the challenge of choosing the most appropriate model specification remains, and is potentially worsened by the fact that the population make up and pollutant-meteorological interactions may vary from city to city, and season to season. The difficulty in interpreting each individual pollutant's risk estimate is also that it is often not clear as to what extent each gaseous pollutant's risk estimate represents its own effects or whether the pollutant in question acts as a surrogate marker of PM sources. For example, the presence of high NO_2 levels is likely also associated with periods of elevated impacts of PM from motor vehicles. Most studies analyze each of the multiple pollutants in the same health effects regression model as if each pollutant's risk estimate represents its own (chemical entity's) independent effect, but each pollutant's correlation with other covariates in the regression model (e.g., temporal trends, weather variables, day of week) is expected to be different from other pollutants'. Therefore, the optimal extent of model "adjustment" applied is likely to vary from pollutant to pollutant, city to city, and season to season, depending upon the interactions that are occurring among the base model (i.e., the model without a pollutant included) meteorological and seasonal "controlling" terms and the particular pollutant(s) under consideration. The correlation among air pollution and weather variables can also vary across seasons, and thus the correlation matrix (and regression) for the year-round data may be misleading. Furthermore, the measurement error associated with each of the pollutants in representing the city's population exposure may vary across pollutants and between seasons. Therefore, the aim of this study was to systematically investigate the influences of the temporal relationships among the air pollution and weather variables beyond the usual extent of consideration given in most time-series epidemiological literature, and including all of the criteria air pollutants ($PM_{2.5}$, O_3, NO_2, SO_2, and CO). In addition, we provide an example analysis of health outcome data (asthma emergency department (ED) visits) using these air pollutants, and discuss the relationship between the results from the above analysis and the pollutants' corresponding risk estimates in New York City.

Methods

Data

The data from all the air quality monitors within a 20-mile radius from the geographic center of New York City were obtained, and the average of multiple monitors were computed for each day. We retrieved all the relevant air pollution variables from the EPA's Air Quality System (AQS): PM less than 2.5 μm ($PM_{2.5}$), collected by the 24-h filter samples using the Federal Reference Method (FRM), $PM_{2.5}$, and PM_{10} data measured by the tapered element oscillating microbalance (TEOM) procedure, ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO). There were 17 ozone monitors with this inclusion criterion, but the data from a monitor at the top of the World Trade Center was excluded because of its height (it read higher readings than the nearby monitors on the ground level), and because the site was destroyed during the attack on 9/11/01. There were 30 monitors for the FRM $PM_{2.5}$, 24 monitors for TEOM $PM_{2.5}$, 18 monitors for CO, 15 monitors for NO_2, and 19 monitors for SO_2. The average values across the monitors were then computed for further analyses.

$PM_{2.5}$ data were available from 1999; therefore, we evaluated the influence of $PM_{2.5}$ and other co-pollutants

for the years 1999–2002. Hourly readings were available for the gaseous pollutants and the TEOM PM data. We computed the daily summary exposure index for each pollutant based on the averaging time used for the National Ambient Air Quality Standard (NAAQS). Thus, 24-h average values were computed for TEOM $PM_{2.5}$ (FRM $PM_{2.5}$ was available as a 24-h average), NO_2 (there is no daily NAAQS for NO_2), and SO_2. The daily maximum of the 8-h average values were computed for O_3 and CO.

We retrieved and analyzed the daily 24-h average temperature, dew point, maximum relative humidity, resultant wind speed, and barometric pressure from La Guardia airport using EarthInfo (Boulder, Colorado, USA), which compiled the First Order Summary of the Day data from the National Climatic Data Center.

The asthma ED visits data considered here were obtained from the 11 New York City Health and Hospitals Corporation medical centers with emergency receiving facilities. These hospitals are municipally run and serve a largely poor and minority population located within the five boroughs of New York City. The asthma ED visits for all ages were considered in this analysis. More details of the asthma ED visits data set can be found in Silverman et al. (2005).

Data Analysis

We conducted several sets of analyses to characterize the interactions among the air pollution and weather variables, and to describe these interactions' effects on the modeling of time-series analysis of health effects outcomes. The three sets of data interaction analyses were as follows: (1) spatial/temporal variation of $PM_{2.5}$ and gaseous pollutants measured at multiple monitors; (2) temporal relationships among air pollution and weather variables; and (3) extent and nature of the multi-collinearity of the air pollution and weather variables in the context of health effects models. Our primary objectives were (2) and (3), but (1) affects the interpretation of (2) and (3). In addition, we present an example analysis of asthma ED visits data using these air pollution variables.

Spatial/Temporal Error of $PM_{2.5}$ and Gaseous Pollutants Measured at Multiple Monitors There are several types of exposure errors associated in the time-series air pollution data in representing the population exposure of the city in question, including (1) analytical (chemical/physical) measurement errors; (2) discrepancy between personal exposures and ambient concentrations; and (3) error in a community monitor's ability to represent the population exposure of the city. The first type of error is generally considered small, provided that the concentration levels are well above the detection limits (which is usually the case for $PM_{2.5}$ and gaseous pollutants, but not as usually the case for many of $PM_{2.5}$ chemical species). The second type of error has been characterized for PM in several personal exposure studies (e.g., Lioy et al., 1990; Janssen et al., 1998, 1999) and less frequently for gaseous pollutants in addition to $PM_{2.5}$ (Sarnat et al., 2001, 2005). These studies generally find that, while personal levels of air pollution differ between personal vs. central site monitors, the population mean of the personal exposures correlate well with the central site monitor over time, causing this source of error to be relatively small in the population-based time-series studies considered here. The third type of error, which may be called ecologic-level exposure error, has to do with the spatial/temporal uniformity of temporal fluctuations of air pollution. A few past studies have previously examined this type of error (e.g., Ito et al., 2001, 2005; Pinto et al., 2004). Examining the variability and effects of this ecologic-level exposure error across pollutants and models is the primary focus of this analysis.

There are two aspects of this ecologic-level error: (1) errors in correlation of temporal fluctuations at multiple locations within the city (i.e., the extent to which the correlation coefficient, r, between data from different sites over time is less than 1.0) and (2) the difference in absolute concentration levels of pollutants across the city. In the first case, if temporal fluctuations of an air pollutant measured at multiple locations are not highly correlated with each other, that is indicative of an ecologic-level error of that air pollutant, and the relationship between the data from a central-site community monitor (or the average of a few monitors) for such an air pollutant with health outcomes would be biased toward null. In the second case, a difference in the absolute concentration levels of an air pollutant across the city does not necessarily affect the strength of association between that pollutant and the health outcome, but the slope (risk estimate) can still be biased if the average level of the monitor's data is lower (which would result in a positive bias) or higher (a negative bias) relative to the true citywide average.

We estimate each of these two ecological error terms for each pollutant in the case of New York City. We compute the first term by calculating the monitor-to-monitor temporal correlations from multiple monitors for each pollutant considered. Since the correlation of two time series can be heavily influenced by trends and seasonal cycles, and since such trends are routinely "controlled for" in health effects regression models, we computed the monitor-to-monitor temporal correlation after removing the temporal trends from each series using the Generalized Additive Model (GAM) (note that there is only one smoothing term in the model, which should not result in biased results) and smoothing splines with 8 d.f. per year. Although there are at least 15 monitors available for each of the pollutants, and their sampling periods did not always overlap. Therefore, we computed temporal correlation only when at least 60 overlapping observations were available in each pair of monitors. To estimate the second aspect of ecologic error, we

computed the coefficient of variation (CV) of the average values across monitors.

Temporal Relationships among Air Pollution and Weather Variables To characterize the temporal relationships among air pollution and weather variables, we computed the cross-correlation function (CCF) (correlation with lags) for each variable considered. For air pollution variables, we used the average of multiple monitors as the input to the CCF. These cross-correlations can indicate the sequence of temporal fluctuations (i.e., which variable leads the other in time). Again, the correlation between the two time series can be strongly influenced by shared trends and seasonal cycles. Therefore, to remove the influence of these temporal patterns and to focus on the short-term relationships between the variables, each of the weather and air pollution time series was first pre-filtered in the GAM using smoothing splines function with 8 d.f. per year prior to computation of CCF. Also, since the lag-structure of CCF in the short-term span (e.g., days) can also be influenced by each series' day-of-week pattern, we also removed this trend by including day-of-week indicator variables in the same data filtering GAM. Furthermore, since relationships among the weather and air pollution variables can change across seasons, the CCF was computed in a series of 12 3-month blocks centered on each month of the year, and pooled for the entire 4-year study period.

Extent and Nature of Multi-Collinearity of the NYC Air Pollution and Weather Variables To characterize the extent and nature of the multi-collinearity in the context of current air pollution short-term health effects studies, we computed the variables' concurvity (i.e., the nonlinear analogue of multi-collinearity) using the regression models similar to those used in the time-series air pollution literature. Concurvity was computed by regressing each of the air pollution variables on the same covariates usually used in the health effects regression models, except that the Gaussian model was used rather than the Poisson model (used for counts), and the extent of concurvity was expressed as the correlation between the original series and the predicted series from the regression, as has been carried out previously in other studies (Dominici et al., 2002; Ramsay et al., 2003). Because we were interested in which of the meteorological or seasonal covariate(s) were correlated with each of the air pollutants, we computed concurvity in sets of building models that included one added term with each new model, as follows: (1) adjustment term for temporal trends; (2) model (1) plus weather terms; (3) model (2) plus day-of-week indicators; (4) model (3) plus one of the other pollutants, and so on. On the basis of the fact that the majority of the reviewed pollution health effects studies showed associations between today's health with 0- or 1-day lagged pollution concentrations (i.e., same day or day before pollution), we included the average of 0- and 1-day lagged pollution indices in this analysis. To adjust for seasonal cycles and other temporal trends, we included a smoothing function of days using natural splines with 8 d.f. per year as a base model and, as a sensitivity analysis, we also used 4 and 16 d.f. per year for comparison. This range covers the extent of temporal smoothing used in most past published time-series health effects studies.

On the basis of the types of weather models most commonly used in the published literature, we considered three alternative weather models: (A) two smoothing terms including: (i) one with natural splines of same-day temperature (d.f. = 3) and (ii) another with natural splines of same-day dew point (d.f. = 3) (i.e., a model similar to that used in Schwartz et al., 1996; Klemm et al., 2000; Schwartz, 2003; Klemm and Mason, 2003); (B) four smoothing terms, including: (i) natural splines of same-day temperature (d.f. = 6), (ii) natural splines of the average of lag 1 through 3-day temperature (d.f. = 6), (iii) natural splines of same-day dew point (d.f. = 3), and (iv) natural splines of the average of lag 1 through 3 day dew point (d.f. = 3) (i.e., similar to the model used in Samet et al., 2000; Dominici et al., 2003, 2006; Bell et al., 2004), and; (C) a more parsimonious version of model (B) that has (i) natural splines of same-day temperature (d.f. = 3) and (ii) natural splines of the average of lag 1 through 3 day temperature (d.f. = 3). The model (C) did not include dew point, because dew point was so highly correlated with temperature in this data set ($r = 0.93$), which may lead to unstable fits if placed in the model simultaneously with temperature when they are so highly correlated. Since the relationships among the weather and air pollutants are expected to change across seasons, the above analysis was repeated for both the warm season (April through September) and the cold season (October through March).

For the analysis of asthma ED visits data, we used a Poisson's Generalized Linear Model to estimate the impact of ozone on the asthma ED visits while adjusting for the effects of temporal trends, day-of-week, weather, and accommodating over-dispersion of the ED visit series. We used the same three weather models as those used in the concurvity analysis above. We analyzed the data for all year, warm months and cold months, but to avoid the influence of the fall peaks in asthma ED visits (Silverman et al., 2005), we excluded September and October. To adjust for temporal trends, we used natural splines with 8 and 4 d.f. per season (warm and cold months). As in the concurvity analysis above, the average of 0- and 1-day lag pollution was included in the model. Single- and two-pollutant models were examined.

Results

Table 1 shows the distribution of air pollution variables for the all-year, warm seasons, and cold seasons, respectively.

Seasonal contrasts are clear for O_3 (higher in the warm season) and SO_2 (higher in the cold season). Figure 1 presents the raw data time-series plots of each of the air pollution variables. Note that all the pollutants show some extent of seasonality, except for NO_2, which shows white noise-like fluctuations around the mean of approximately 30 p.p.b. CO exhibits a declining trend during the 4-year period.

Spatial/temporal Variation of $PM_{2.5}$ and Gaseous Pollutants Measured at Multiple Monitors

Figure 2 presents the paired monitor-to-monitor correlation vs. corresponding separation distance for each of the air pollutants as a function of separation distance between the sites. $PM_{2.5}$ (FRM and TEOM) monitors showed the highest monitor-to-monitor correlation, followed by NO_2 and O_3. SO_2 and CO generally showed poorer correlation. Table 2 shows median values of these correlations as well as the CV of the monitors' mean values (i.e., within-city variation of the mean). Again, $PM_{2.5}$ (FRM and TEOM) monitors showed the smallest spatial variation ($\sim$10%) in the mean levels across the monitors, followed by NO_2 (17%) and O_3 (19%). In contrast, SO_2 and CO had much larger spatial variation (36%) of the mean values. Since the FRM $PM_{2.5}$ and TEOM $PM_{2.5}$ are highly correlated ($r = 0.92$), the following analyses will only examine FRM $PM_{2.5}$.

Table 1. Distribution of air pollution variables in NYC 1999–2002, all year (first row for each pollutant), warm months (second row, April–September), and cold season (third row, October–March).

	N	Mean	SD	5%	25%	50%	75%	95%
$PM_{2.5}$	1297	15.1	8.9	5	9	13	19	32
FRM	732	17.5	9.9	7	11	15	22	38
(mg/m^3)	652	15	8.5	5	9	13	19	31
$PM_{2.5}$	1460	15.7	8.4	7	10	14	19	32
TEOM	732	17.5	9.9	7	11	15	22	38
($\mu g/m^3$)	728	14	6.1	7	10	12	17	26
NO_2	1460	31.1	8.7	18	25	30	37	47
(p.p.b)	732	30.4	8.8	17	24	30	36	47
	728	31.8	8.6	19	26	31	37	48
O_3	1460	30.4	19	6	16	27	41	68
(p.p.b.)	732	42.7	18.2	18	30	40	52	77
	728	18	9.2	4	11	17	24	33
SO_2	1460	7.8	4.6	3	5	7	10	17
(p.p.b.)	732	5.4	2.2	3	4	5	7	10
	728	10.2	5.1	4	6	9	13	19
CO	1460	1.31	0.43	0.77	1.02	1.23	1.52	2.11
(p.p.m.)	732	1.22	0.32	0.75	1	1.19	1.39	1.82
	728	1.41	0.5	0.78	1.04	1.31	1.67	2.33

Temporal Relationships Among Air Pollution and Weather Variables

Because of the large number of CCF results, we have shown them here only as figures. Also, because the pattern of results for SO_2 and CO was similar to that for NO_2 but weaker, we show results for $PM_{2.5}$, O_3, and NO_2 only.

Figure 3 shows the CCFs for wind speed vs. $PM_{2.5}$, O_3, and NO_2. NO_2 showed the strongest negative associations with wind speed year-round, whereas $PM_{2.5}$'s negative associations with wind speed are weaker during warm seasons, likely due to the domination of transported secondary sulfate, which is regionally distributed and therefore less wind dependent. O_3's associations with wind speed changed signs across seasons. Note that, in these results, the strongest associations are on the same day, but the lag structure of associations is generally not symmetric (low wind speed tends to lead the air pollution).

Figure 4 shows the CCFs for temperature and air pollutants. The lag structure of associations is generally not symmetric. For $PM_{2.5}$ and NO_2, in cold seasons, colder temperature days result in higher air pollution levels a few days later in cold seasons, likely due to the setting up of a high-pressure cell over the NYC area in the days following the passage of a cold front. However, the higher NO_2 or $PM_{2.5}$ levels are also predictive of the following days' warmer temperature, likely due to the tendency for warmer southwest winds on the "back-side" of a high-pressure cell. O_3's association with temperature was positive in summer and negative in winter, suggesting different mechanisms for the temporal fluctuations of the ozone in the two different seasons. Figure 5 shows the CCFs for barometric pressure and air pollutants. Barometric pressure is positively associated with the following days $PM_{2.5}$ and NO_2, especially in colder seasons, consistent with the setting up of a high-pressure dome over the metropolitan area on those days.

Figure 6 shows the CCF's relationships between $PM_{2.5}$ vs. O_3 and NO_2. The lag structure of associations between $PM_{2.5}$ and O_3 is generally symmetric, but the correlation is positive in the warm season and negative in the cold season. The association between $PM_{2.5}$ and NO_2 is strongest on the same day, but the lag structure of association is not symmetric—higher NO_2 levels are positively predictive of the following day's $PM_{2.5}$. These results generally suggest that the correlation among air pollution and weather variables have varying lag structure of associations and the association can differ across pollutants and also change across seasons.

Extent and Nature of Multi-Collinearity of the Air Pollution and Weather Variables

Table 3 shows computed concurvity of air pollution variables using three alternative weather models and using d.f. = 8 per year for fitting temporal trends in the all-year data. Sensitivity analysis using 4 d.f. and 16 d.f. per year showed nearly identical results once the weather terms are included

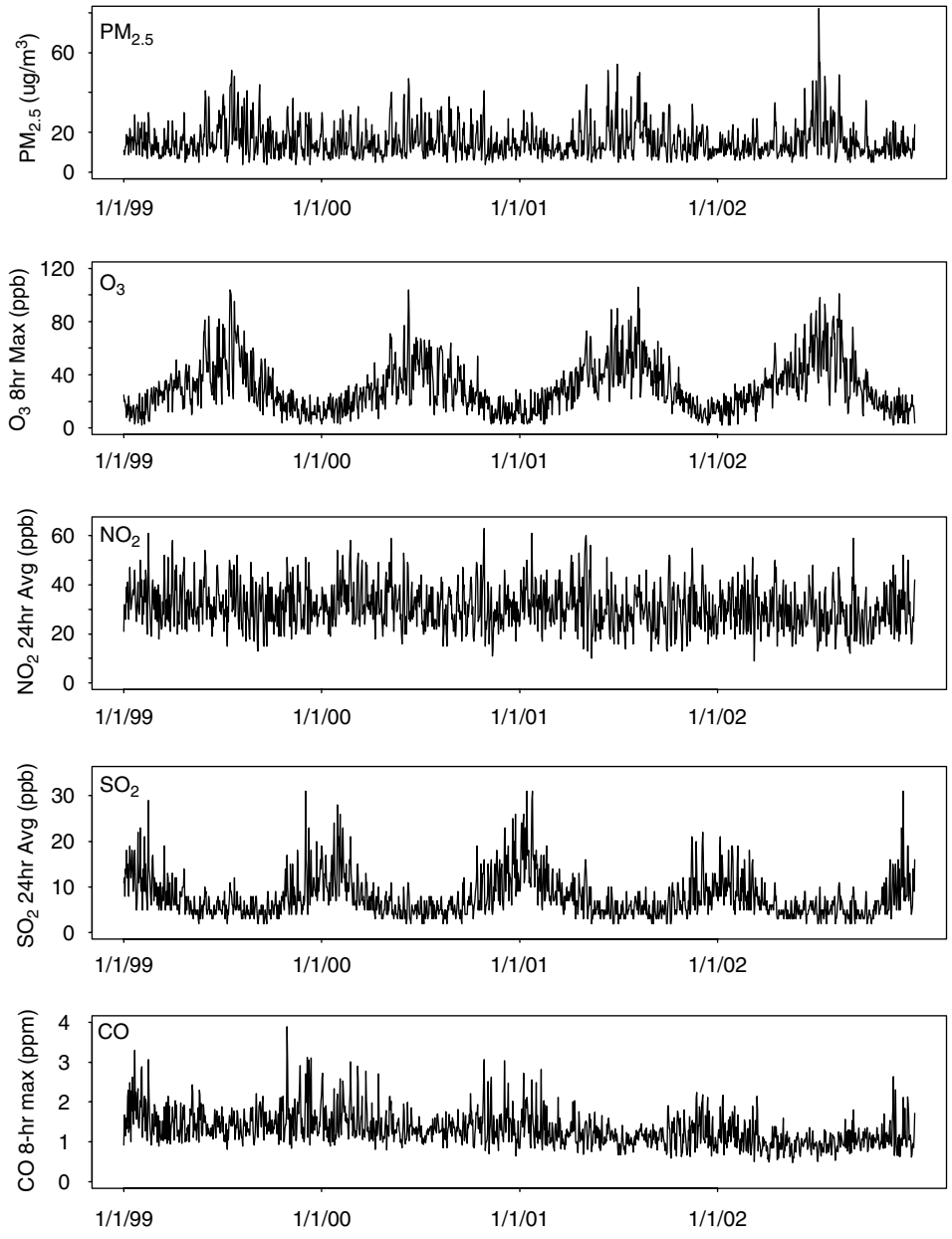

Figure 1. Time-series plots of air pollution variables in New York City, 1999–2002.

(likely because the weather terms have seasonal trends), and therefore not shown here. $PM_{2.5}$ and NO_2 showed the two lowest correlations with temporal trends. O_3 showed the strongest association with temporal trends. When weather terms are added, concurvity increased substantially for $PM_{2.5}$ and NO_2, but NO_2 still showed the lowest concurvity of all the pollutants considered, indicating that it would be least affected by the co-presence of the temperature variables to the model. The inclusion of the day-of-week term increased concurvity slightly for NO_2 and CO. Adding $PM_{2.5}$ in the model increased concurvity problems for the gaseous pollutants, except O_3. Adding O_3 did not change concurvity for $PM_{2.5}$ and other pollutants. The three alternative weather models showed very similar results, although the model B (the model that has the most number of terms and degrees of freedom) almost always showed the strongest concurvity problems among the three models. Thus, these analyses indicate that NO_2 is most likely to be identified independent of the other pollutants in this city, and that the concurvity problems of all pollutants grow with the year-round model that most aggressively controls for seasonality and long-term trends.

The results for the warm (Table 4) and cold (Table 5) seasons showed generally similar patterns to those in the

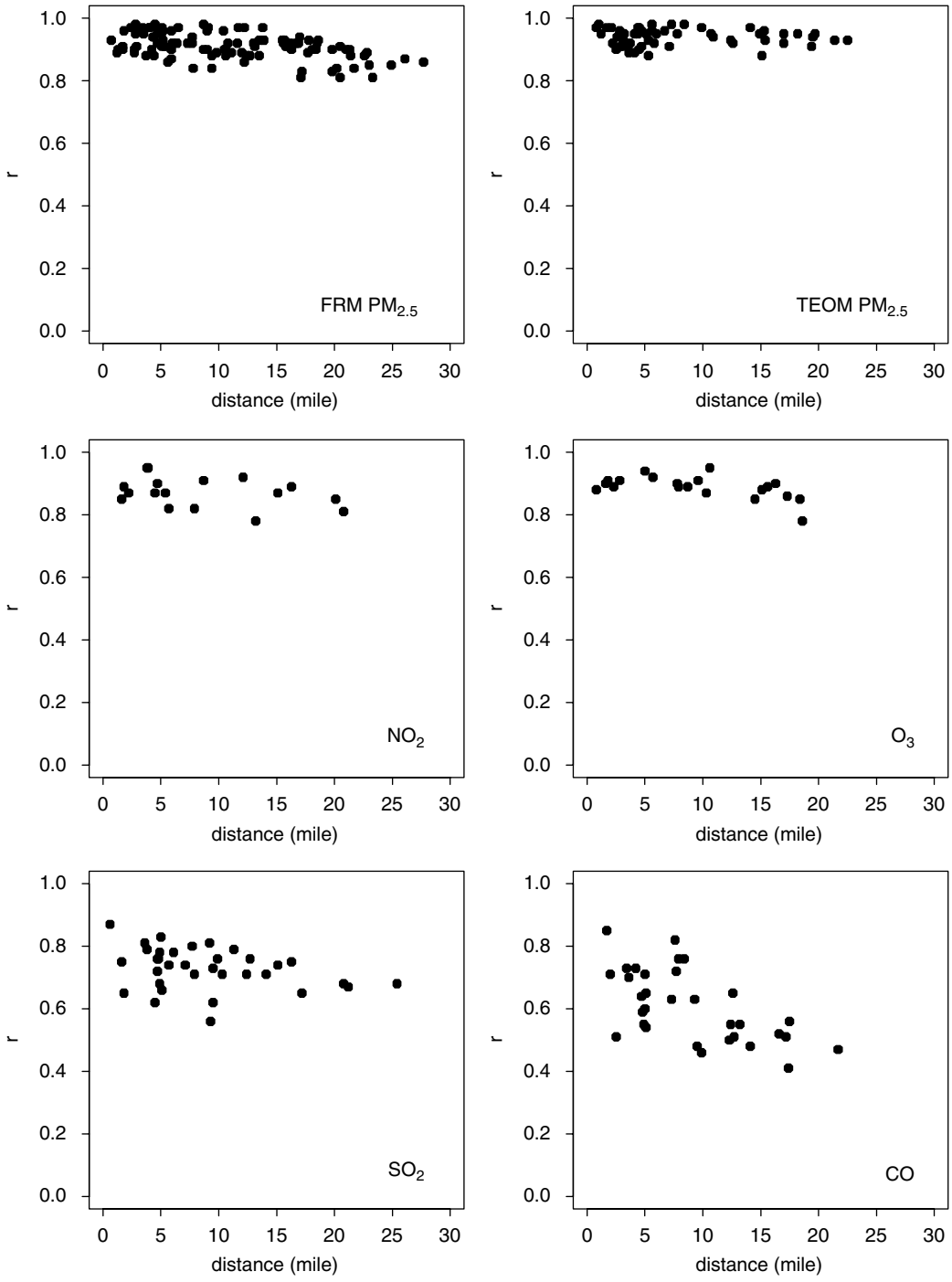

Figure 2. Monitor-to-monitor correlation and separation distance.

all-year data, but with a few notable exceptions. The extent of correlation with temporal trends is reduced for O_3 and SO_2, as expected because these two pollutants showed the strongest seasonal cycles. $PM_{2.5}$'s concurvity is larger in the warm season than in the all-year data, likely because $PM_{2.5}$ in the warm season in this locale is dominated with secondary sulfate, which positively correlates with temperature. Interestingly, in contrast to the all-year and warm season results, adding O_3 increased concurvity problems for $PM_{2.5}$ and other gaseous pollutants in the cold season. Thus, the pollutant–pollutant and pollutant–weather interactions can vary by season, and concurvity problems are reduced by separately analyzing the seasons in this city, suggesting the need for season-specific analyses of health effects.

An Example Analysis of Asthma ED Visits

Figure 7 shows results of asthma ED visits risk estimates per 5th to 95th percentile of air pollution increment in the single-pollutant models for all-year, warm months, and cold months. NO_2 was generally the most significant (and the largest in effect size per the same distributional increment) predictor of asthma ED visits among these pollutants for all-year and warm months (e.g., for Model C, RR = 1.14 (95% CI: 1.09, 1.19) per 24 p.p.b. increase and 1.32 (95% CI: 1.23, 1.42) per 25 p.p.b. increase, respectively). However, it is important to examine this result in the context of corresponding pollutants' concurvity (see Tables 3–5). NO_2 exhibited the lowest concurvity with the temporal trend plus weather terms among the pollutants in the all-year and warm months. O_3's risk estimates in cold months are negative, but given the very low levels of O_3 in cold months, it is unlikely that such associations are causal health effects. These associations may arise because of O_3's negative associations with temperature or $PM_{2.5}$ in cold months (see Figures 4 and 6). The three alternative weather models generally did not make substantial difference in risk estimates, except for O_3 in all-year and warm months in which Model B resulted in much smaller risk estimates than those from Model A or C. This is not surprising because Model B adjusts for temperature more aggressively than Model A or C. Thus, these health effect results are consistent with the patterns found in the CCF and concurvity results.

Table 2. Median monitor-to-monitor correlation and coefficient of variation (CV) of mean levels across multiple monitors.

	Median monitor-to-monitor correlation	CV of mean levels (%)
$PM_{2.5}$ FRM	0.91	11
$PM_{2.5}$ TEOM	0.95	8
NO_2	0.87	17
O_3	0.89	19
SO_2	0.74	36
CO	0.60	36

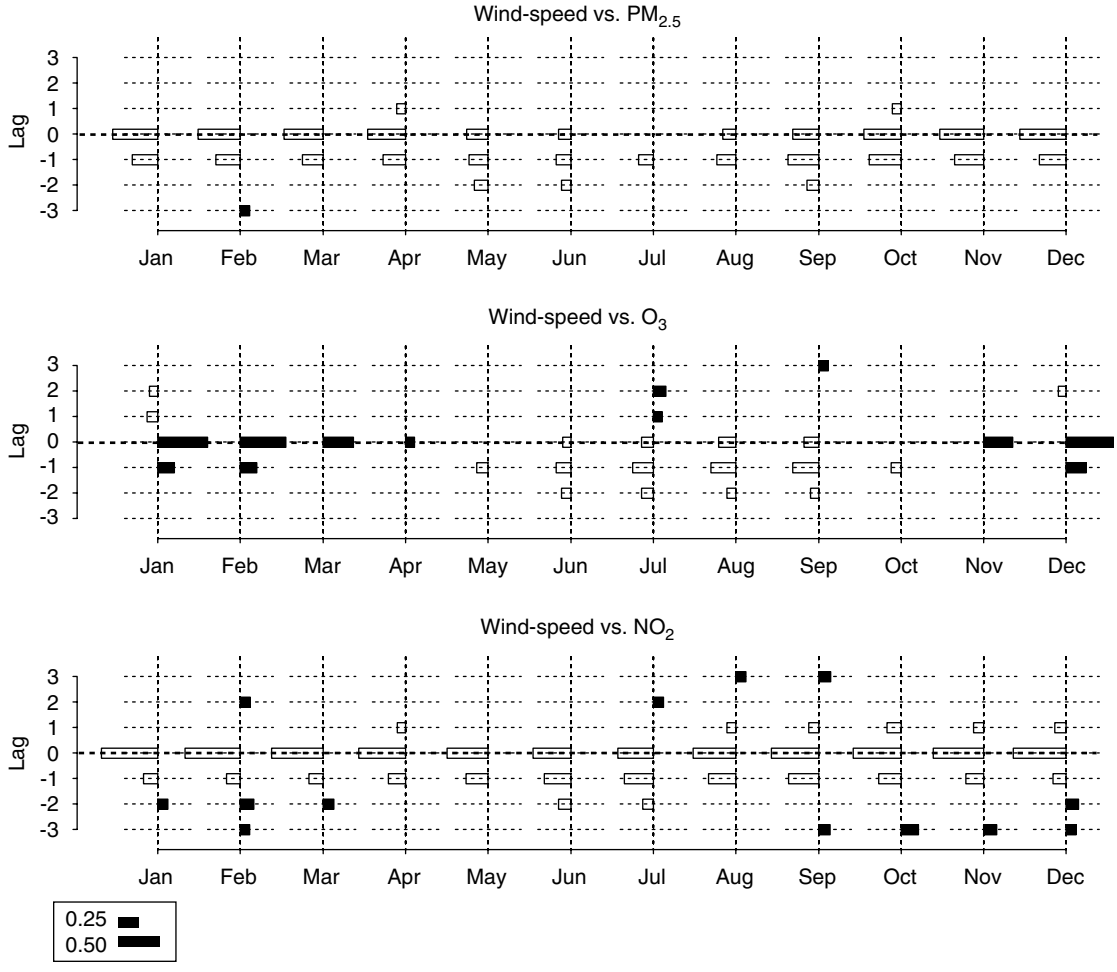

Figure 3. Cross-correlation functions of wind speed vs. air pollutants. The correlation below the center line (lag 0) indicates that wind speed leads air pollution. Correlations $< \pm 0.1$ are not shown.

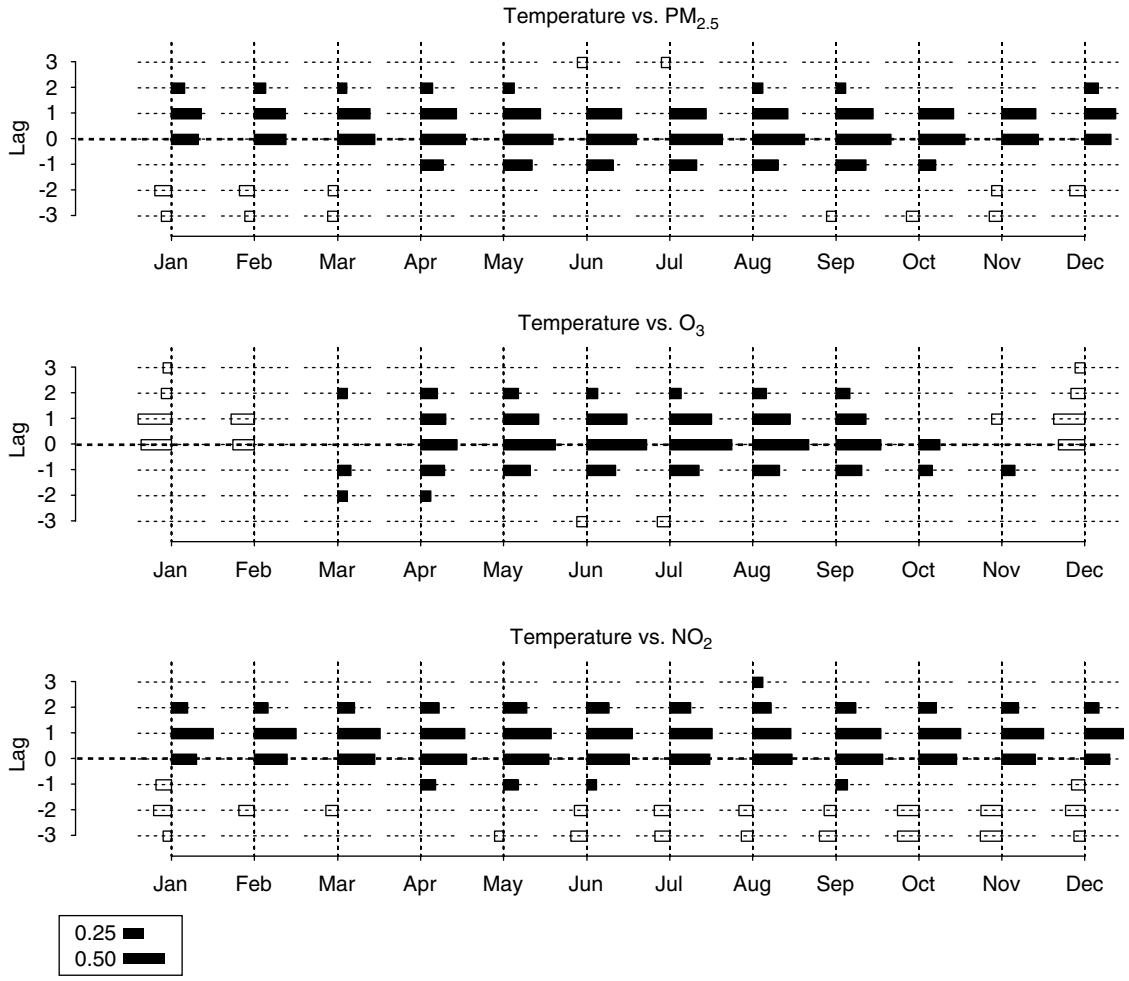

Figure 4. Cross-correlation functions of temperature vs. air pollutants. The correlation below the centerline (lag 0) indicates that temperature leads air pollution. Correlations $< \pm 0.1$ are not shown.

Figure 8 shows two-pollutant model results for warm months using Model C. NO_2's risk estimates were most robust to the addition of other pollutants in the model, and the addition of NO_2 reduced other pollutants' risk estimates most consistently. CO and SO_2's associations with asthma ED visits (RR = 1.15 (95% CI: 1.07, 1.25) per 1.3 p.p.m. increase and 1.20 (95% CI: 1.13, 1.28) per 6 p.p.b. increase, respectively) were "eliminated" once NO_2 was included in the model, which is consistent with the result of monitor-to-monitor correlations, suggesting that NO_2 has less exposure error than CO or SO_2 in this data set. We do caution that these differences may also reflect the corresponding differences in toxicity, but it is impossible to differentiate such factors in multi-pollutant models.

Discussion

This analysis examined three issues that affect interpretations of short-term health-risk estimates for multiple air pollutants: (1) ecologic error associated with $PM_{2.5}$ and gaseous pollutants in representing a city's population exposure; (2) lag structure of temporal correlation among air pollution and weather variables; and (3) multi-collinearity of the $PM_{2.5}$ and gaseous pollutants in the prevailing health effects model specifications. These issues are typically not described or investigated in detail in most of time-series studies in the literature, but nevertheless, are important in interpreting, and especially in inter-comparing, individual pollutant health effect estimates from multi-pollution exposures. We found that, in this locale, $PM_{2.5}$ showed the best characteristics, on an ecologic-level, in representing the citywide population exposures in terms of high monitor-to-monitor correlation ($r > 0.9$) and high precision (CV $\sim$ 10%) of the mean levels within the city. NO_2 and O_3 also showed high monitor-to-monitor correlation ($r \sim 0.9$), but the precision of the mean levels (CV $\sim$ 20%) was lower than that for $PM_{2.5}$. Ozone also varied most between seasons, suggesting that annual analyses will not provide meaningful results for this pollutant. SO_2 and CO showed lower monitor-to-monitor correlation

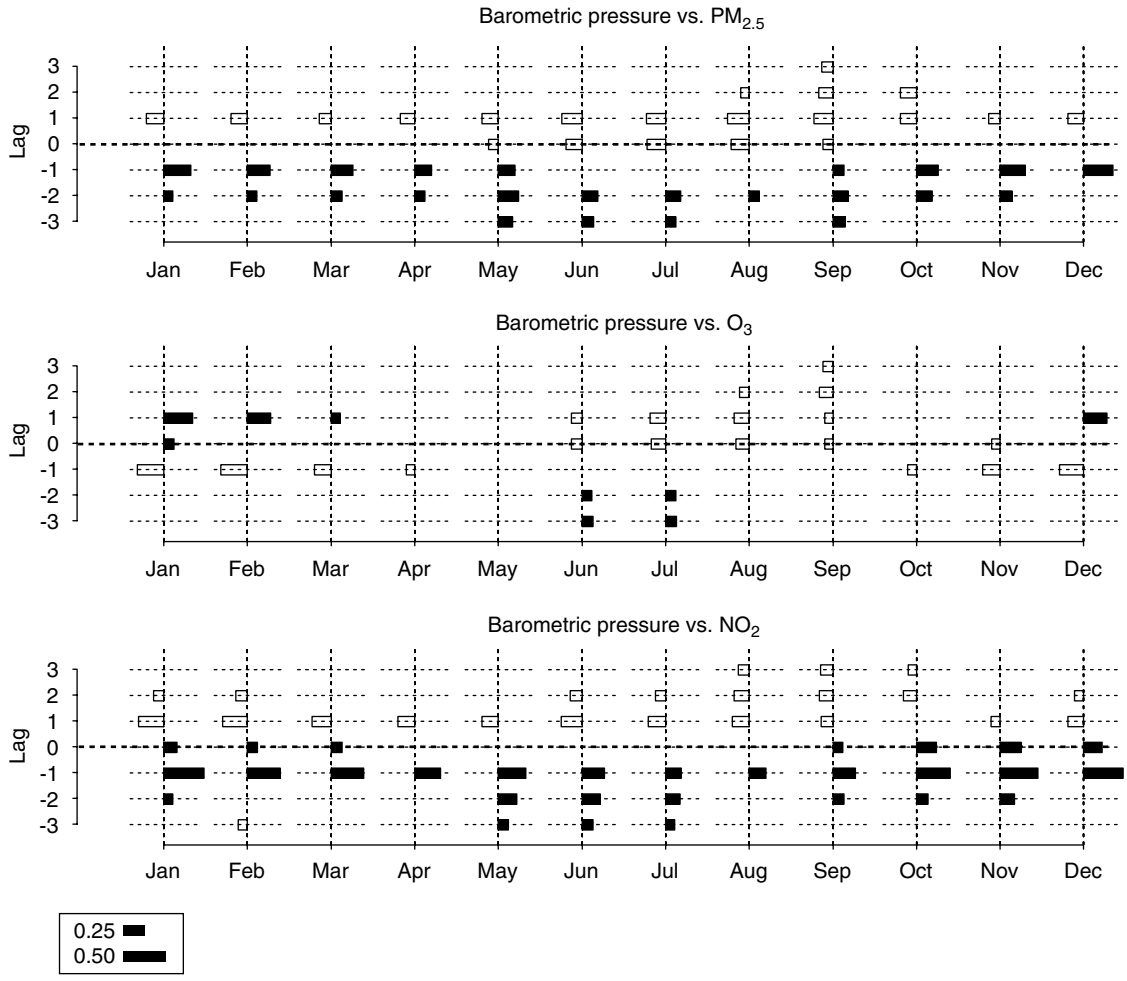

Figure 5. Cross-correlation functions of barometric pressure vs. air pollutants. The correlation below the center line (lag 0) indicates that barometric pressure leads air pollution. Correlations $< \pm 0.1$ are not shown.

($r \sim 0.7$ and 0.6, respectively) and low within-city precision of the mean levels (CV = 36%), indicating that these pollutants' risk estimates could be biased in short-term health effects models.

Most of the current time-series studies of health effects of air pollution employ regression models that adjust for the effects of weather. Both extreme heat waves and cold spells are known to affect a variety of health end points, and therefore adjusting for such events is clearly important. However, less is known regarding the health effects of temperature in the "milder" middle range of temperature. The weather condition is a major driving force of day-to-day fluctuations of air pollution concentrations, and temperature may be an indicator of the change in weather conditions. Our result shows that NO_2 (after removing long-term trends) is positively associated with the current and the following days' temperature (i.e., NO_2 leads temperature to some extent), although cold temperature (which is followed by higher barometric pressure, poor dispersion, and increased NO_2 a few days later. Moreover, O_3's association with temperature even changed sign across seasons. Thus, the relationship between temperature and air pollution can be complex and vary with season. In fact, it is not clear whether the temperature terms in the health effects regression models actually "control" for the weather effects, or are actually acting as surrogates for pollutants in the middle range of temperature, where direct temperature health effects are unlikely. If true, this would lead to over-adjustment of health effects for weather, and an underestimation of pollutants most correlated with temperature. Further research is needed on the extent of weather adjustment terms needed or desirable in air pollution models.

The results from an analysis of concurvity indicated that the extent of multi-collinearity with covariates in typical time-series health effects models varies across the pollutants. $PM_{2.5}$ and NO_2 showed the least correlation with temporal trends. With weather terms in the model, NO_2 showed the lowest concurvity among the pollutants, but the day-of-week term

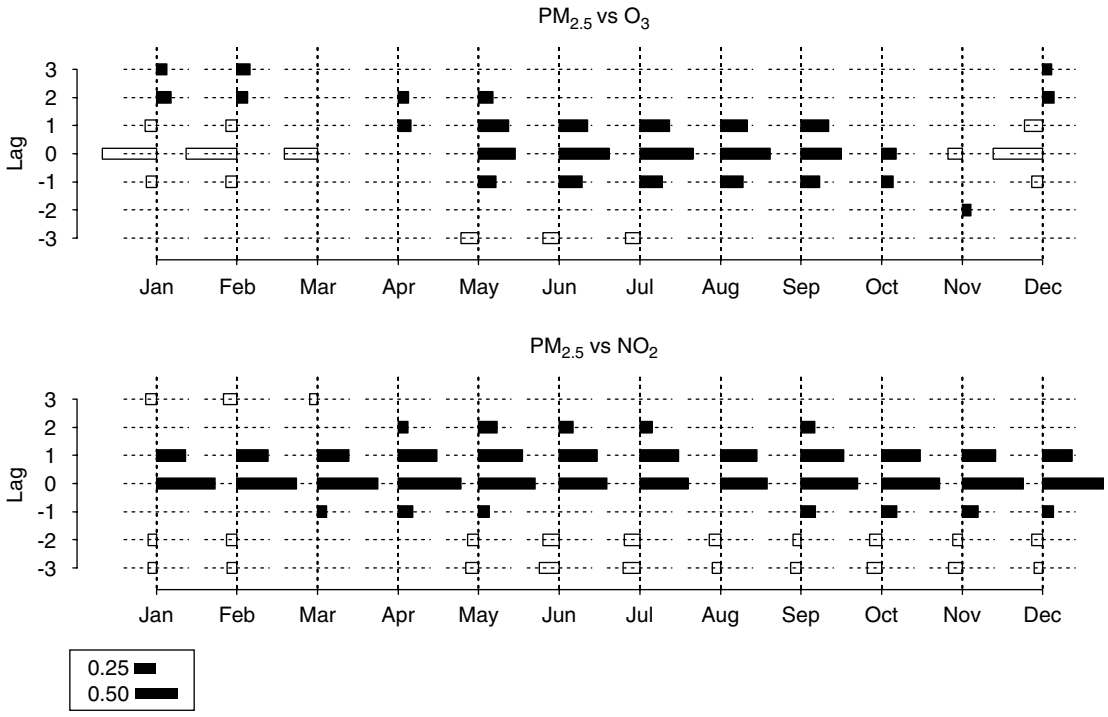

Figure 6. Cross-correlation functions of $PM_{2.5}$ vs. O_3 and NO_2. The correlation below the centerline (lag 0) indicates that $PM_{2.5}$ leads O_3 or NO_2. Correlations lt&; ± 0.1 are not shown.

Table 3. Concurvity of air pollutants in selected health effects models for all-year data.

Model	(1)Trend (d.f. = 8 per year)	(2): (1) + weather	(3): (2) + day-of-week	(4): (3) + $PM_{2.5}$	(5): (3) + NO_2	(6): (3) + O_3	(7): (3) + SO_2	(8): (3) + CO
$PM_{2.5}$								
A:	0.33	0.66	0.66	—	0.81	0.66	0.83	0.79
B:		0.69	0.70	—	0.81	0.70	0.83	0.80
C:		0.64	0.65	—	0.78	0.65	0.79	0.79
NO_2								
A:	0.28	0.52	0.60	0.78	—	0.60	0.83	0.82
B:		0.62	0.68	0.81	—	0.68	0.85	0.85
C:		0.58	0.64	0.78	—	0.64	0.83	0.82
O_3								
A:	0.77	0.89	0.90	0.90	0.90	—	0.91	0.91
B:		0.90	0.91	0.91	0.91	—	0.91	0.91
C:		0.88	0.89	0.89	0.89	—	0.89	0.89
SO_2								
A:	0.68	0.71	0.72	0.85	0.88	0.73	—	0.84
B:		0.76	0.76	0.86	0.88	0.78	—	0.86
C:		0.75	0.75	0.85	0.88	0.76	—	0.84
CO								
A:	0.52	0.65	0.68	0.80	0.86	0.69	0.82	—
B:		0.68	0.70	0.81	0.86	0.71	0.83	—
C:		0.63	0.66	0.79	0.83	0.69	0.78	—

Weather Model A: two smoothing terms, one with natural splines of same-day temperature (d.f. = 3) and another with natural splines of same-day dew point (d.f. = 3); Model B: four smoothing terms including natural splines of same-day temperature (d.f. = 6), natural splines of the average of lag 1 through 3 day temperature (d.f. = 6), natural splines of same-day dew point (d.f. = 3), natural splines of the average of lag 1 through 3 day dew point (d.f. = 3); Model C: two smoothing terms, natural splines of same-day temperature (d.f. = 3), natural splines of the average of lag 1 through 3 day temperature (d.f. = 3).

Table 4. Concurvity of air pollutants in selected health effects models for warm seasons (April–September).

Model	(1)Trend (d.f. = 8 per year)	(2): (1) + weather	(3): (2) + day-of-week	(4): (3) + $PM_{2.5}$	(5): (3) + NO_2	(6): (3) + O_3	(7): (3) + SO_2	(8): (3) + CO
$PM_{2.5}$								
A:	0.33	0.74	0.74	—	0.81	0.79	0.81	0.79
B:		0.76	0.77	—	0.82	0.80	0.82	0.80
C:		0.70	0.71	—	0.78	0.72	0.78	0.78
NO_2								
A:	0.30	0.59	0.67	0.77	—	0.72	0.86	0.84
B:		0.66	0.73	0.80	—	0.76	0.87	0.87
C:		0.60	0.68	0.77	—	0.71	0.86	0.83
O_3								
A:	0.52	0.83	0.84	0.87	0.86	—	0.85	0.84
B:		0.85	0.85	0.88	0.87	—	0.86	0.85
C:		0.80	0.80	0.81	0.82	—	0.81	0.81
SO_2								
A:	0.40	0.64	0.66	0.75	0.85	0.69	—	0.75
B:		0.69	0.71	0.78	0.86	0.72	—	0.77
C:		0.65	0.67	0.75	0.85	0.69	—	0.74
CO								
A:	0.59	0.72	0.76	0.8	0.88	0.76	0.82	—
B:		0.74	0.78	0.81	0.89	0.78	0.83	—
C:		0.65	0.69	0.77	0.83	0.7	0.76	—

See Table 3 for weather model descriptions.

Table 5. Concurvity of air pollutants in selected health effects models for cold seasons (October–March).

Model	(1)Trend (d.f. = 8 per year)	(2): (1) + weather	(3): (2) + day-of-week	(4): (3) + $PM_{2.5}$	(5): (3) + NO_2	(6): (3) + O_3	(7): (3) + SO_2	(8): (3) + CO
$PM_{2.5}$								
A:	0.27	0.54	0.55	—	0.82	0.68	0.85	0.80
B:		0.60	0.62	—	0.83	0.72	0.85	0.82
C:		0.56	0.58	—	0.80	0.71	0.81	0.81
NO_2								
A:	0.26	0.49	0.55	0.82	—	0.69	0.86	0.84
B:		0.61	0.66	0.84	—	0.76	0.87	0.87
C:		0.58	0.63	0.82	—	0.72	0.86	0.84
O_3								
A:	0.63	0.74	0.78	0.83	0.84	—	0.87	0.83
B:		0.75	0.79	0.84	0.85	—	0.88	0.84
C:		0.70	0.74	0.81	0.80	—	0.82	0.81
SO_2								
A:	0.52	0.58	0.60	0.86	0.87	0.78	—	0.81
B:		0.66	0.67	0.87	0.87	0.82	—	0.83
C:		0.63	0.64	0.84	0.86	0.76	—	0.79
CO								
A:	0.44	0.60	0.63	0.83	0.86	0.73	0.82	—
B:		0.63	0.66	0.84	0.87	0.74	0.82	—
C:		0.59	0.62	0.82	0.84	0.73	0.78	—

See Table 3 for weather model descriptions.

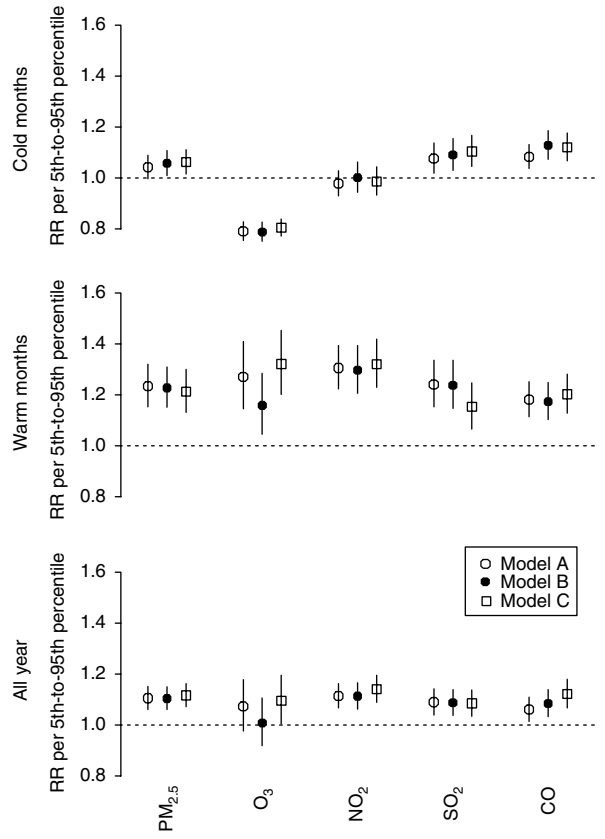

Figure 7. Relative risks per 5th to 95th percentile of air pollutants for asthma ED visits in NYC, in single-pollutant models, three alternative weather models, and for all-year, warm months and cold months.

increased NO_2's concurvity the most. Adding any of $PM_{2.5}$, NO_2, SO_2, or CO to these pollutants' models generally increased concurvity for these pollutants to a similar extent, suggesting possible confounding among them. Although adding O_3 in the model generally did not increase concurvity of $PM_{2.5}$, NO_2, SO_2, or CO, it did increase their concurvity in the cold season, despite the fact that O_3 levels are quite low in the cold season, possibly an indication that wintertime O_3 may be acting as a surrogate for specific weather conditions. For all the pollutants, a combination of temporal trends, weather term, day-of-week, and a co-pollutant made concurvity in the range between 0.8 and 0.9. These results suggest the importance of analysis by season and also the limitation of two-pollutant models.

NO_2 was also most negatively associated with wind speed (and wind speed leads NO_2), indicating that NO_2 may also be serving as a good indicator of general local air stagnation. $PM_{2.5}$ and O_3 are less correlated with wind speed, likely because these pollutants are distributed regionally and are therefore less affected by local wind speed or direction. Thus, NO_2 may be a good indicator of more air pollution from local combustion sources. NO_2 is sometimes referred to as a surrogate marker of traffic-related air pollution. Seaton and Dennekamp (2003) suggested that NO_2 may be a surrogate for ultrafine particles, especially the number concentrations. Since both NO (which gets converted to NO_2) and ultrafine particles are generated by the combustion process, NO_2 and ultrafine particles are likely to correlate. In their measurements over 6 months in Aberdeen city, the correlation between NO_2 and the number concentration ($r = 0.89$) was much higher than that between NO_2 and $PM_{2.5}$ ($r = 0.55$) and that between NO_2 and PM_{10} ($r = 0.45$). Thus, NO_2 may also be a marker of another agent that may not be measured routinely and yet has some potential health effects. Whether it is a surrogate or not, NO_2 in our data showed desirable characteristics in the context of time-series health effects analysis, in that it has small ecologic error and relatively small concurvity among the air pollutants. Thus, it would not be surprising where models that input all pollutants at once, NO_2 becomes the apparent individual "winner" in simultaneous regressions, since it is the pollutant that varies least like all the rest of the pollutants, and is least affected by concurvity in such a multi-pollutant model.

The question of relationship between ambient concentration and personal exposures of multiple air pollutants is another important issue in interpreting health-risk estimates of multi-pollutants that was beyond the scope of our analysis. There are a few studies that have examined this issue. Sarnat et al. (2001) conducted a study in Baltimore, Maryland, USA and measured personal exposure levels of $PM_{2.5}$, NO_2, O_3, SO_2, and CO for 56 subjects. Ambient concentrations were not associated with their corresponding personal exposures for any of the pollutants, except for $PM_{2.5}$. Interestingly, however, some of the ambient gaseous pollutants were significant predictors of personal $PM_{2.5}$. The results from Sarnat et al.'s (2005) another study in Boston, Massachusetts, USA generally support their findings in Baltimore in that summertime gaseous pollutant concentrations may be better surrogates of personal $PM_{2.5}$ exposures than they are surrogates of personal exposures to the gases themselves. These studies may be limited in size and locations, and clearly more studies like these in other locales are needed.

This study characterized the relationships among $PM_{2.5}$, gaseous pollutants, and weather variables in New York City, but the results may not yet be generalized for other cities. New York City is large in terms of population, but relatively small in terms of geographic scale compared to other large cities in the United States (e.g., Chicago and Los Angeles). The types of air pollution sources in New York City are not unlike other east-coast cities, with the mixed influences of transported secondary aerosols, traffic-related pollution, and other local combustion sources. However, characterization of air pollution in the context of health effects studies needs to be conducted in other locations with different pollution sources and climate to obtain a more comprehensive understanding of the relationships among weather and air

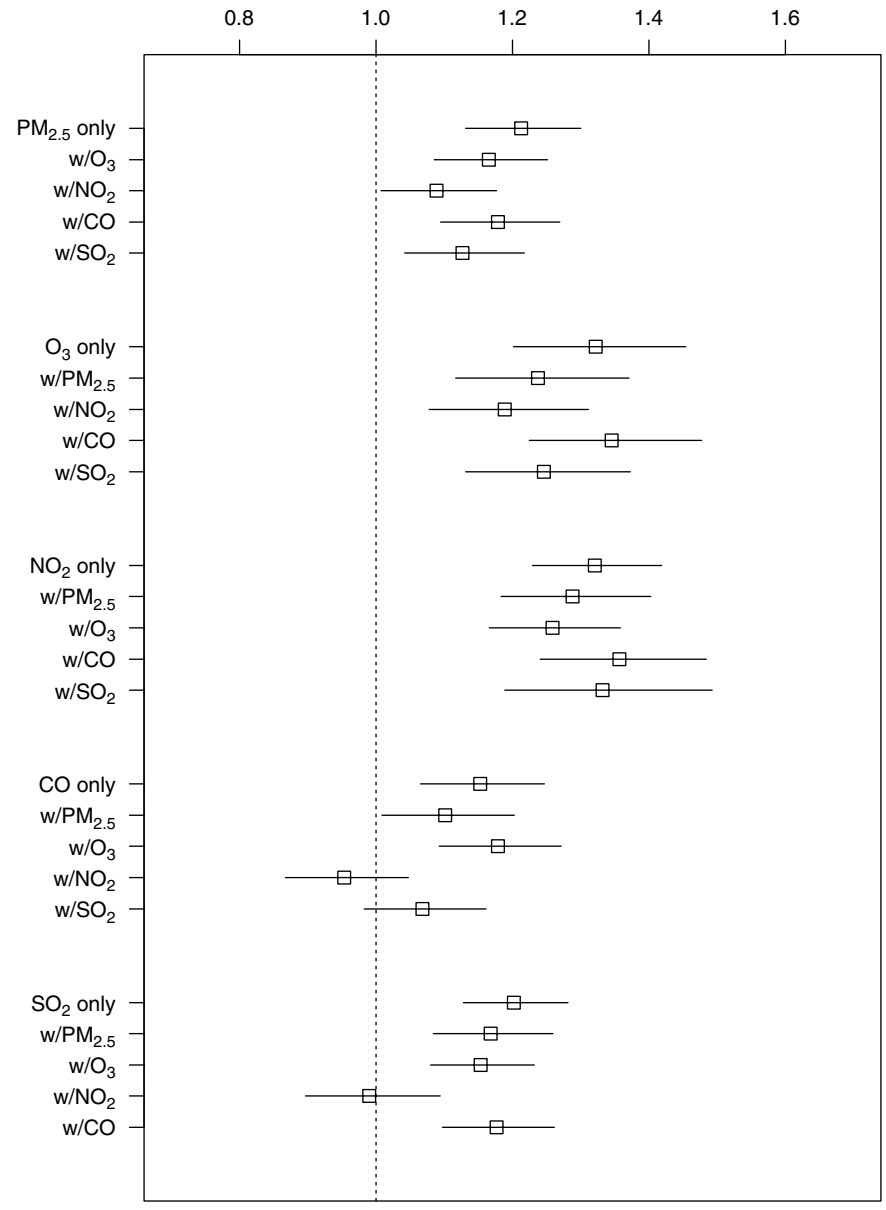

Figure 8. Relative risks per 5th to 95th percentile of air pollutants for asthma emergency department (ED) visits in single- and two-pollutant models using weather model C, NYC during warm season (April through August), 1999–2002.

pollution variables and their influences on the individual air pollutant effect estimates.

The results from the example analysis of asthma ED visits were generally as expected from the concurvity analysis: NO_2, which showed the lowest concurvity with temporal trend and weather terms among the pollutants, was the most independent predictor of asthma ED visits in the warm season when the pollutants were considered simultaneously. The fact that this was so predictable on the basis of the model specification interactions alone without consideration of the health effects) places great suspicion on the practice of interpreting multi-pollutant regressions as indicative of the pollutants' relative health effects, when it is much more likely that it is a product of the pollutants' respective model term interactions. The result that CO and SO_2's associations with asthma ED visits were eliminated once NO_2 was included in the model was also consistent with NO_2's smaller expected exposure error compared with CO and SO_2. However, obviously, these results may reflect actual difference in toxicity of either the corresponding pollutants themselves, or the pollution mixture that these pollutants are surrogate for. On the basis of the CCF results between weather and air pollutants, NO_2 appears to be most reflective of local air pollution (as opposed to regional pollution), likely combustion sources including traffic-related air pollution. More source-specific information may be useful in clarifying the

responsible pollutants or pollution sources. We are currently investigating this issue using $PM_{2.5}$ chemical speciation data.

In summary, our analysis described some of the complexities of the relationships among air pollution and weather variables, and cautions against including each of the PM and gaseous pollutants in the health effects model simultaneously, as if each is an ''independent'' variable. These results are a cautionary exercise, and throw into question the now commonplace practice of using multi-pollutant models in health effects analyses. The proper interpretation of risk estimates across the various pollutants in a city will need to much more carefully take into consideration the different extent of exposure error across the pollutants and the varying concurvity of the pollutants in a given model specification. Indeed, modeling of each of the various pollutants may require different long-wave and meteorological base model specifications, to minimize concurvity to achieve as unbiased a pollutant effect estimate for each pollutant as possible.

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SALUD AMBIENTAL

De lo global a lo local

Howard Frumkin, Editor

Organización Panamericana de la Salud

Oficina Regional de la
Organización Mundial de la Salud

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Índice analítico

Para más información

Varios de los libros enlistados en la bibliografía son de interés general.

Managing the Environment, Managing Ourselves, de R.N.L. Andrews es un trabajo escolar de valor duradoero, ofrece un descripción sobresaliente de políticas pasadas y actuales de la administración ambiental de Estados Unidos.

Making Environmental Policy de D. J. Fiorino (caps. 1, 2, y 3) presenta una buena explicación de los retos en el diseño de políticas y las instituciones federales involucradas en el diseño de políticas ambientales. Actualmente no hay ningún libro disponible sobre la historia de la Environmental Protection Agency de Estados Unidos pero *The Environmental Protection Agency: Asking the Wrong Questions from Nixon to Clinton* de M. K. Landy, M. J. Roberts, y S. R. Thomas, se acerca. Para personas que deseen saber cómo evolucionó la EPA, es requisito leer Impact of Hazardous Waste on Human Health de B. L. Johnson porque es el único libro que describe los retos políticos presentados por la administración de tiraderos peligrosos no controlados.

Además, muchas personas consideran la Ley del Aire Limpio como el principal estatuto ambiental federal en relación con el diseño de políticas. Para una revisión excelente de los retos de la política en el manejo de contaminantes del aire, vea

National Research Council. *Air Quality Management in the United States.* Washington, D.C.: National Academies Press, 2004.

La evaluación de riesgos conduce muchas políticas ambientales. El siguiente pequeño y agudo libro describe la historia y prácticas de la evaluación de riesgos mejor que ningún otro:

Rodricks, J. V. *Calculated Risks: The Toxicity and Human Health Risks of Chemicals in Our Environment.* Nueva York: Cambridge University Press, 1992.

Por último, para una revisión excelente de política ambiental durante un periodo de cambios y retos políticos para el diseño de políticas ambientales federales de Estados Unidos.

Vig, N. J., and Kraft, M. W. *Environmental Policy in the 1990s* (2nd ed.) Washington, D.C.: Congressional Quarterly, 1994.

CAPÍTULO TREINTA Y CUATRO

COMUNICACIÓN DE RIESGOS

Vincent T. Covello

Los miembros de una comunidad saben que una fábrica cercana ha contaminado el agua subterránea local con solventes durante tres años de manejo inadecuado. Los trabajadores saben que los niveles de mercurio en su lugar de trabajo exceden periódicamente los estándares aplicables. Los consumidores saben que se pueden encontrar niveles detectables de plaguicidas en muchas de las frutas y verduras que ellos compran. En cada caso, las personas comprenden que una exposición al ambiente puede poner en riesgo su salud, y eso les preocupa. Aun cuando el riesgo resulta ser bajo, la preocupación puede ser alta. Para comprender el riesgo y actuar adecuadamente ante él, las personas necesitan información. La comunicación de riesgos es la práctica que proporciona esta información.

La comunicación de riesgos ha sido definida de varias maneras. Por ejemplo, de acuerdo al National Research Council (1989), comunicación de riesgos es "un proceso interactivo de intercambio de información y opiniones entre individuos, grupos e instituciones". La comunicación de riesgos es exitosa al grado que "eleva el nivel de comprensión de temas o acciones relevantes para aquellos involucrados y los satisface porque están adecuadamente informados dentro de los límites del conocimiento disponible" (p. 4).

En este capítulo, se define la *comunicación* de riesgos como un enfoque basado en la ciencia que se utiliza típicamente para guiar la comunicación con una diversidad de audiencias en situaciones de alto estrés, alta preocupación o controversiales. Se refiere a cualquier comunicación pública o privada que informa a los individuos

El tamaño de una partícula está relacionado con su origen. El tamaño determina la forma como se transporta en la atmósfera, donde se deposita en el ambiente y en el sistema respiratorio. Las partículas más pequeñas son motivo especial de preocupación para la salud, puesto que penetran con mayor profundidad en el pulmón. Tales partículas por lo regular se generan mediante procesos de combustión. Los gases de combustión de diesel, una combinación de gases y partículas, son particularmente preocupantes debido al extenso uso de diesel y a que estas partículas son muy pequeñas (<1 micrón) (Kagawa, 2002). Además, la fase de gas del diesel contiene diversos contaminantes riesgosos como benceno, formaldehído e hidrocarburos aromáticos policíclicos.

Los niveles ambientales de la materia particulada, como lo indican las mediciones de MP_{10} y $MP_{2.5}$ entre otras, han tenido que ver con efectos de salud como un mayor número de ingresos al hospital y emergencias, síntomas respiratorios, decadencia de la función pulmonar, exacerbación de enfermedades respiratorias y cardiovasculares crónicas, y mortalidad prematura (EPA, 2003). Los animales de laboratorio expuestos a la MP experimentaron una variedad de respuestas, incluyendo inflamación y lesiones pulmonares (Broeckaert y cols., 1997; Dye y cols., 2001). Los estudios de serie de tiempo, que rastrean la variación cotidiana en los niveles de MP y la mortalidad, han demostrado que la exposición aguda a la MP está relacionada con un mayor índice de mortalidad, que alcanza su punto máximo unos días después de la exposición, reminiscente de los episodios de Londres y Donora ya descritos, pero que ocurrieron en niveles inferiores de exposición a la MP de hoy (ver, por ejemplo, Health Effects Institute [HEI], 2003; Samet y cols., 2000a, 2000b; Schwartz, 2000). Los estudios longitudinales como el estudio de seis ciudades y CPS II (recién mencionado) también demuestran un vínculo entre la exposición de largo plazo a la MP y la mortalidad (ver, por ejemplo, Dockery y cols., 1993; Krewski y cols., 2000; Pope y cols., 1995, 2002). Un comité del National Research Council examinó recientemente el estado de esta evidencia (National Research Council, 2004).

Las regulaciones han evolucionado en respuesta a un mayor entendimiento sobre cómo la MP afecta la salud humana. Cuando se estableció originalmente en 1971 el National Ambient Air Quality Standard sobre materia particulada, tenía que ver con el total de las partículas suspendidas totales (PST), pero este estándar fue sustituido por uno específicamente para MP_{10} cuando quedó claro que estas partículas más pequeñas estuvieron más estrechamente vinculadas con los efectos en la salud. De acuerdo con pruebas posteriores, las partículas aún más pequeñas, $MP_{2.5}$, eran responsables de efectos adversos en la salud, y se añadió el estándar $MP_{2.5}$ en 1997.

Si bien se han estudiado ampliamente las MP y la salud, sigue habiendo mucho por conocer. Por ejemplo, el riesgo para la salud que implica la exposición

a las partículas puede depender de las características de la MP; de su contenido de metales, acidez, contenido orgánico, sulfatos o combinaciones de estos componentes (HEI, 2002). Se requiere una investigación crítica para determinar los aspectos dañinos de la MP (National Research Council, 2004). Del mismo modo, aún no se comprenden del todo los mecanismos biológicos por medio de los cuales la MP causa muertes prematuras. Las principales hipótesis se concentran en reflejos del pulmón, que provocan cambios automáticos en el sistema nervioso, autónomo quizás predisponiendo a los individuos a arritmias, y en la inflamación que, por su parte, predispone para la trombosis o cambios similares (Brook y cols., 2004). Las investigaciones adicionales aclararán también el impacto que probablemente tendrá la MP en la regulación.

Dióxido de azufre

El SO_2 es un gas soluble en agua que fue un componente primario de la neblina de Londres en 1952. Los óxidos de azufre se producen en la combustión de combustibles y materiales que contienen azufre, como carbón y minerales metálicos. Un poco de carbón, como el del este de Estados Unidos, tiene un contenido de azufre particularmente alto. Las centrales eléctricas son la principal fuente de emisiones de SO_2. Otras fuentes son calderas industriales, trenes, barcos, e instalaciones de procesamiento de metales. El uso de carbón en casa también puede contribuir con cantidades significativas de SO_2. En algunas regiones, como en ciertas partes de China, el carbón es el principal combustible para cocinar y calentarse, lo que provoca altos niveles de SO_2 en el interior. Entre las fuentes naturales de SO_2 se incluyen los volcanes.

El SO_2 puede convertirse en ácido sulfúrico (Seinfeld y Pandis, 1998), y por lo tanto contribuye a la deposición ácida, lo que daña la vegetación, los materiales y la fauna. El SO_2 también contribuye a la formación de materia particulada. Los aerosoles de sulfato, importante componente de la materia particulada fina, pueden viajar lejos de su lugar de origen. Las altas chimeneas de las centrales eléctricas a menudo liberan contaminación por encima de la capa de inversión, lo que reduce la contaminación local, pero permite que los contaminantes emitidos recorran distancias mucho más grandes.

Como el SO_2 es muy soluble en agua, la mayor parte del SO_2 que se inhala es absorbido por las membranas mucosas de las vías aéreas superiores, y muy poco llega al pulmón; sin embargo, un aumento en la ventilación y la respiración oral, durante el ejercicio por ejemplo, pueden elevar la dosis que recibe el pulmón (Schlesinger, 1999). Se ha relacionado la exposición al SO_2 con una reducción en la función pulmonar, broncoconstricción (mayor resistencia de la vía aérea), síntomas respiratorios, hospitalizaciones debido a problemas cardiovasculares y

respiratorios, irritación de ojos, resultados adversos en el embarazo y mortalidad. Sin embargo, es difícil atribuir estas asociaciones reportadas únicamente al SO_2, porque el SO_2 es un precursor de la materia particulada y generalmente existe como el componente de una compleja mezcla de contaminantes, relacionada con la combustión. Los estudios experimentales sugieren que algunas personas con asma podrían ser particularmente sensibles al propio SO_2. Los estudios de exposición controlados han demostrado que en algunas personas con asma pueden presentarse efectos después de exposiciones muy breves (por ejemplo, diez minutos), mientras que la investigación epidemiológica ha demostrado efectos relacionados con la exposición a largo plazo (por ejemplo, niveles anuales).

Óxidos de nitrógeno

Los óxidos de nitrógeno (NO_x) constituyen una categoría de gases altamente reactivos que contienen nitrógeno y oxígeno, como el dióxido de nitrógeno (NO_2) y el óxido nítrico (NO). Estos contaminantes reaccionan en la atmósfera para formar contaminantes adicionales y compuestos tóxicos, incluso nitroarenos. El NO_x se produce mediante la combustión, incluso la de combustible fósil, cuando se oxida el nitrógeno que comprende casi 80% de aire. Por lo tanto, entre las fuentes de NO_x se incluyen automóviles y motores de camión, aparatos eléctricos e industrias. La contaminación del aire en el interior también puede aportar NO_2 por medio de calentadores de keroseno, hornos y calentadores de gas sin ventilación, y humo de tabaco. Las fuentes naturales de NO_x incluyen la intrusión estratosférica (cuando el NO_x pasa de la estratósfera a la troposfera), los procesos biológicos en la tierra, los incendios forestales y los relámpagos, pero hoy en día las principales fuentes son centrales eléctricas y automóviles. En Estados Unidos, los automóviles actualmente representan la mitad de todas las emisiones de NO_x.

Como el ozono, el NO_2 es casi insoluble en el agua y puede alcanzar las vías respiratorias inferiores. Los efectos del NO_2 en la salud incluyen irritación de ojos, nariz y garganta en concentraciones más altas, una reducción a corto plazo en la función pulmonar, al igual que un posible incremento en las infecciones respiratorias y los síntomas en niños. Es difícil separar los efectos del NO_x de los componentes relacionados con la contaminación del aire, como ozono y materia particulada (Ackermann-Liebrich y Rapp, 1999). Tanto el NO como el NO_2 son gases tóxicos, y el NO_2 es regulado como un contaminante criterio según la Ley de Aire Limpio. Los óxidos de nitrógeno también desempeñan un papel indirecto pero importante como precursores. El NO_x es un precursor del ozono troposférico y la materia particulada secundaria y desempeña un papel crucial en la formación de la lluvia ácida. El óxido nitroso (N_2O) es un gas de invernadero, que contribuye al calentamiento global (ver el capítulo once). El NO_x y las especies de contaminantes que se forman al someterse a reacciones químicas son capaces de recorrer grandes

distancias, por lo que los efectos en la salud pueden ocurrir lejos del origen. Aunque las emisiones hayan disminuido en décadas recientes, aproximadamente en 15% entre 1983 y 2002, las emisiones de algunas fuentes se elevan, como la de los motores de vehículos todoterreno (EPA, Office of Air Quality Planning and Standards, 2003).

Compuestos orgánicos volátiles

Los compuestos orgánicos volátiles (VOC, por sus siglas en inglés) son una categoría de productos químicos orgánicos con una presión de vapor alta que fácilmente se evaporan a una temperatura y presión normales. Éstos incluyen el benceno, cloroformo, formaldehído, isopreno, metanol y monoterpenos, junto con cientos de compuestos adicionales. Los VOC provienen de fuentes naturales, incluyendo árboles como el arce y el roble; las centrales eléctricas y de procesamiento industrial como los que involucran productos químicos y solventes; y el transporte, incluyendo automóviles y transporte no terrestre como aviones, equipo de construcción y segadoras. Las emisiones de automóviles explican aproximadamente 75% de las emisiones VOC relacionadas con el transporte, y la mayor parte de estas emisiones provienen aproximadamente de 20% de los vehículos que son más viejos y tienen poco mantenimiento (EPA, 1996). En muchos lugares, las fuentes biogénicas contribuyen con más VOC que las emisiones antropogénicas. Por ejemplo, en 1990, 77% de las emisiones de VOC en el centro de la región atlántica eran biogénicas (Mid-Atlantic Regional Air Management Association, 1997). De hecho, el aspecto natural que da su nombre a las montañas Blue Ridge y Great Smoky Mountains es resultado de los VOC biogénicos (sobre todo isopreno) que forman aerosoles. Los VOC son precursores del ozono, pero también tienen efectos independientes en la salud, como irritación de las vías respiratorias, dolores de cabeza y carcinogenicidad.

Ozono troposférico

El ozono está presente en la troposfera, la capa atmosférica más baja, que se extiende hasta aproximadamente 10 a 15 kilómetros por encima de la superficie de la tierra, y en la estratósfera, que se extiende desde la troposfera hasta aproximadamente 45 a 55 kilómetros por encima de la superficie de la tierra. El *ozono estratosférico* forma la capa natural de ozono que cubre la superficie de la Tierra de las radiaciones ultravioletas, mientras que el ozono troposférico, que en ocasiones recibe el nombre de *ozono de nivel de tierra*, es un contaminante dañino. Para establecer la diferencia entre el ozono estratosférico y el troposférico, la EPA introdujo el lema "Bueno arriba y malo de cerca".

El ozono troposférico es un gas incoloro y un oxidante fotoquímico que se forma a través de reacciones químicas complejas, no lineales, que implican a los

GLOSSARY

Indicators of socioeconomic position (part 1)

Bruna Galobardes, Mary Shaw, Debbie A Lawlor, John W Lynch, George Davey Smith

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This glossary presents a comprehensive list of indicators of socioeconomic position used in health research. A description of what they intend to measure is given together with how data are elicited and the advantages and limitation of the indicators. The glossary is divided into two parts for journal publication but the intention is that it should be used as one piece. The second part highlights a life course approach and will be published in the next issue of the journal.

Socioeconomic position (SEP) is a commonly used concept in health research. Although researchers have an intuitive sense of what SEP means, the numerous ways of measurement indicate the complexity of the construct. A variety of other terms, such as social class, social stratification, social or socioeconomic status, are often used interchangeably despite their different theoretical bases and, therefore, interpretations. These issues have been discussed in detail by Krieger *et al*[1] and we use SEP rather than socioeconomic status in line with their suggestion. ''Socioeconomic position'' refers to the social and economic factors that influence what positions individuals or groups hold within the structure of a society,[1 2] and encompasses concepts with different historical and disciplinary origins, which will briefly be reviewed here. SEP is related to numerous exposures, resources, and susceptibilities that may affect health. This glossary presents a comprehensive list of indicators of SEP used in health research, together with a description of what they intend to measure, how data are elicited, and their main advantages and limitations. The glossary builds on previous work[2–6] by providing updated information on the use and meaning of each measure, specifically in relation to epidemiological and health research.

There is no single best indicator of SEP suitable for all study aims and applicable at all time points in all settings. Each indicator measures different, often related aspects of socioeconomic stratification and may be more or less relevant to different health outcomes and at different stages in the life course. The choice of SEP measure(s) should ideally be informed by consideration of the specific research question and the proposed mechanisms linking SEP to the outcome. This is the case when SEP is the exposure of interest as well as when it is being considered as a confounding/mediating factor. If the central interest is to show the existence of a socioeconomic gradient in a particular health outcome then the choice of indicator may not be crucial. However, even in a case such as this, using different indicators of SEP may result in gradients of varying slopes. Furthermore, while a single measure of SEP may show an association with a health outcome, it will not encompass the entirety of the effect of SEP on health. This issue is of particular importance when SEP is a potential confounding factor. Multiple SEP indicators, preferably measured across the life course, will be needed to avoid residual confounding by unmeasured socioeconomic circumstances.[7 12] The notion that the choice of SEP measure should be determined by the particular research question is exemplified by Snow's work on exposures related to people working in the ''offensive trades''.[8 9] With respect to socially patterned exposures that have aetiological effects specific to particular stages of the life course it is clear that the socioeconomic indicators should relate to these life stages.[10] Other researchers have emphasised the importance of theoretically grounded measures of social position in recent contributions.[11] However, in practice, the measures used tend to be driven by what is available or has been previously collected. Even when a researcher cannot influence the particular SEP measure(s) available in a study, an understanding of their theoretical basis is important to making appropriate inferences.

In this glossary we highlight the theoretical basis, measurement, interpretation, strengths, and limitations of each indicator. Where possible we present the interpretation or mechanism that may be of particular relevance to each indicator, but this is difficult because most of these indicators are strongly correlated. For example, despite education reflecting some particular aspects of SEP such as possession of a richer score of knowledge, it does, at the same time, help determine a person's adult occupation and income, and therefore shares some of the health effects of these other indicators. This is particularly evident when a life course approach is considered (see fig 1 and part 2 of this glossary).

Most work on health inequalities has been conducted in developed countries and has generated indicators appropriate to this context. Further research is necessary to develop indicators that might be more appropriate in developing country settings. The glossary is organised such that individual level indicators are considered first, and within this they are presented in alphabetical order. Various forms of aggregate indicators (composite indicators and indices of area deprivation) follow. Finally, we briefly discuss life course SEP and multilevel approaches to considering SEP influences. The glossary is divided in two parts for journal

See end of article for authors' affiliations

Correspondence to: Dr B Galobardes, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, UK; bruna.galobardes@bristol.ac.uk

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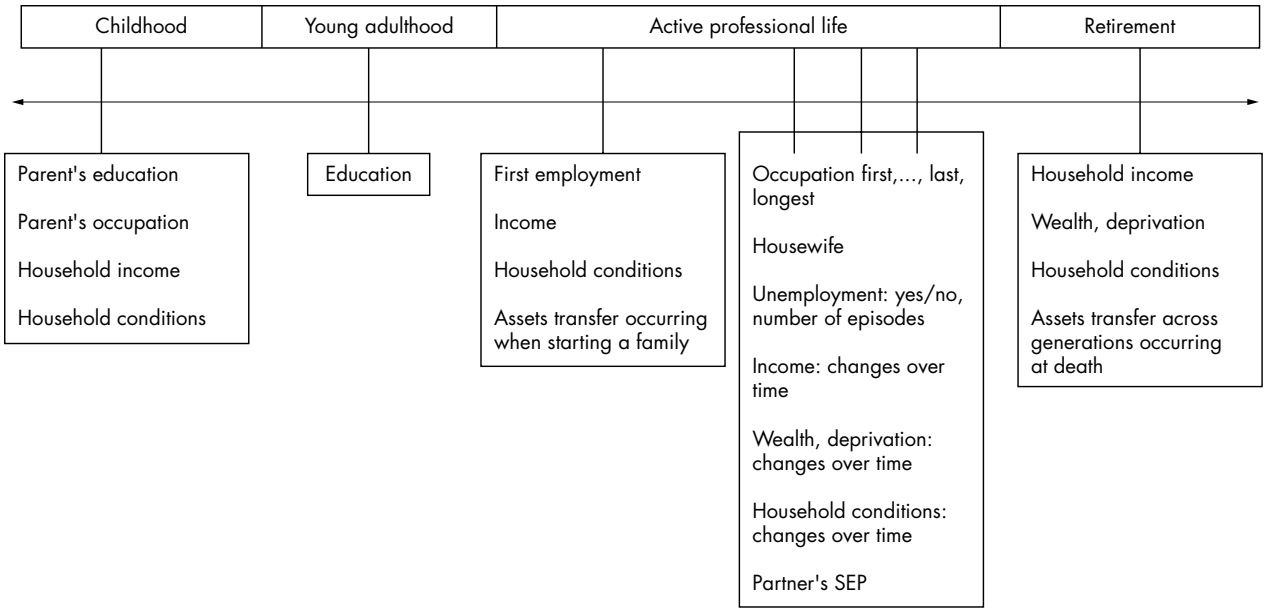

Figure 1 Examples of indicators measuring life course socioeconomic position.

publication, but the intention is that it should be used as one piece.

THEORETICAL ORIGINS

Many of the concepts underlying the use of SEP in epidemiological research have their origin in the work of two social theorists, Karl Marx and Max Weber. For Marx, SEP was entirely determined by ''social class'', whereby an individual is defined by their relation to the ''means of production'' (for example, factories, land). Social class, and class relations, are characterised by the inherent conflict between exploited workers and the exploiting capitalists or those who control the means of production. Despite the palpable political weight of Marxist ideology in the 20th century we are aware of only two classifications used in epidemiological research that are based on Marx's theory of social class, these are Erik Olin Wright's classification[13] and others developed in South America.[14] In contrast with Marx, who viewed social stratification in capitalist societies as both source and outcome of the conflict between two necessarily opposed social groups, Weber's theory suggests that society is hierarchically stratified along many dimensions, creating groups whose members share a common market position leading to shared ''life chances''. For Weber, market position is not necessarily only defined by Marx's class relations. For a more detailed summary of these sociological theories see Bartley.[15]

EDUCATION

Theoretical basis

Education is a frequently used indicator in epidemiology. The use of education as an SEP indicator has its historical origins in the status domain of Weberian theory,[3] and it attempts to capture the knowledge related assets of a person.[2] As formal education is normally completed in young adulthood and is strongly determined by parental characteristics, it can be conceptualised within a life course framework as an indicator that in part measures early life SEP.[16 17]

Measurement

Education can be measured as a continuous variable (years of completed education), or as a categorical variable by assessing educational milestones such as completion of primary or high school, higher education diplomas, or degrees. The continuous measure assumes that every year of education contributes similarly to a person's attained SEP and that time spent in education has greater importance than educational achievements, whereas the latter assumes that specific achievements are important in determining SEP.[3]

Interpretation

Although education is often used as a generic measure of SEP, there are specific interpretations to explain its association with health outcomes[3 18–20]:

- Education captures the transition from parents' (received) SEP to adulthood (own) SEP and it is also a strong determinant of future employment and income.[2 17] It reflects material, intellectual, and other resources of the family of origin, begins at early ages, is influenced by access to and performance in primary and secondary school and reaches final attainment in young adulthood for most people. Therefore it captures the long term influences of both early life circumstances on adult health, as well as the influence of adult resources (for example, through employment status) on health.[17 21 22]
- The knowledge and skills attained through education may affect a person's cognitive functioning, make them more receptive to health education messages, or more able to communicate with and access appropriate health services. A recent attempt to measure knowledge in terms of ''cultural literacy'' and assess its role in the association between education and health highlighted the great difficulty in trying to unpack some of the specific ways in which education and knowledge may affect health.[23 24]
- Ill health in childhood could limit educational attendance and/or attainment and predispose to adult disease, generating a health selection influence on health inequalities.[25]

Strengths and limitations

Education is comparatively easy to measure in self administered questionnaires, garners a high response rate, and is relevant to people regardless of age or working circumstances, unlike many other SEP indicators.[3] In addition, the

collection of information on education may be less contentious in some contexts than other SEP indicators such as income.

The meaning of educational level varies for different birth cohorts. In addition to secular trends in improving educational attainment, there have been considerable changes in educational opportunities for women and some minority groups over recent decades. Such cohort effects can be important but are seldom accounted for in epidemiological studies. The results from studies that use years of education or educational qualifications that include participants from a number of different birth cohorts may be biased if cohort effects are not taken into account, because older cohorts will be over-represented among those classified as less educated.[26] There are examples of how cohort effects have been accounted for in epidemiological studies. In one study the authors classified participants into low, medium, or high levels of education, these categories being defined with specific relevance to their birth cohort.[16] This will help account for the fact that cohorts born earlier who have, in absolute terms, fewer years of education, may be classified in the same relative group of education than cohorts born later, despite these having greater absolute number of years of education. Another option is to stratify the analysis by age group, for example examining health inequalities by educational attainment within five year age groups.[27] A further limitation of educational levels exists if individuals have obtained their education outside the country of residence—that is, in a different educational regime in which indicators of education may have very different implications than within the host country. Finally, measuring the number of years of education or levels of attainment may contain no information about the quality of the educational experience, which is likely to be important if conceptualising the role of education in health outcomes specifically related to knowledge, cognitive skills, and analytical abilities but may be less important if education is simply used as a broad indicator of SEP.

HOUSING TENURE, HOUSING CONDITIONS, AND HOUSEHOLD AMENITIES

Theoretical basis

Housing characteristics measure material aspects of socioeconomic circumstances. Housing based indicators are used in industrialised and non-industrialised countries, although the characteristics assessed differ. Moreover, these may be very specific to the area where they were developed. A recent glossary presents some of these indicators.[28] We mention here those that are more directly related to SEP.

Measurement

The most commonly used characteristic is *housing tenure*—whether housing is owner occupied (owned outright or being bought with a mortgage), or rented from a private or social landlord. In rural populations ownership of a farm and farm size may better define housing characteristics.[29]

A number of *household amenities* are used in epidemiological studies, including access to hot and cold water in the house, having central heating and carpets, sole use of bathrooms and toilets, whether the toilet is inside or outside the home, having a refrigerator, washing machine, or telephone. These household amenities are markers of material circumstances and may also be associated with specific mechanisms of disease. For example, lack of running water and a household toilet may be associated with increased risk of infection.[29 30] In addition the meaning of these amenities will vary by context and cohort (see the example of car access below). Very few people in contemporary advanced industrial societies will be without running hot water, indoor toilet or bathroom facilities and, therefore, some of these measures are not able to differentiate individuals in these populations. However, these indicators or other household amenities will have relevance in developing country populations (see below), and as indicators of childhood SEP in older adults in contemporary developed country populations (see for example their use in some articles[12 31 32]). One amenity that has proved to be a useful SEP indicator in the UK, but that has been used less in other populations, is *car access*.[33–35] In rural areas of industrialised countries car ownership may not be a useful indicator of SEP as even the poorest households often own cars, out of sheer necessity.[36] In non-industrialised countries, other assets that have been used as indicators of SEP in health related research include the number of livestock, owning a bicycle, refrigerator, radio, sewing machine, TV, or a clock.[37–39]

In addition to household amenities, *household conditions* such as the presence of damp and condensation, building materials, rooms in the dwelling, and *overcrowding* are housing related indicators of material resources. These are used in both industrialised and non-industrialised countries.[40–43] Crowding is calculated as the number of persons living in the household per number of rooms available in the house (usually excluding kitchen and bathrooms). Overcrowding is then defined as being above a specific threshold (commonly two or more people per room). Overcrowding can plausibly affect health outcomes through a number of different mechanisms: overcrowded households are often households with few economic resources and there may also be a direct effect on health through facilitation of the spread of infectious diseases.

Recent efforts to better understand the mechanisms underlying socioeconomic inequalities in health have lead to the development of some innovative area level indicators that use aspects of housing. For example, a ''*broken windows*'' *index* measured housing quality, abandoned cars, graffiti, trash, and public school deterioration at the census block level in the USA.[44] This indicator was more useful in explaining the variance in gonorrhoea rates than a poverty index that included income, unemployment, and low education. Similarly, an indicator of the ''*social standing of the habitat*'' combined characteristics of the building, their immediate surroundings and the local neighbourhood of residential buildings can be used to assign SEP.[45] Concordance of this measure with education or occupation was good for people of either high or low socioeconomic position, but not for those with medium education and/or occupation, showing the heterogeneity of socioeconomic circumstances among people labelled as middle class.[45]

Interpretation

These indicators are mainly markers of material circumstances. Housing is generally the key component of most people's wealth, and accounts for a large proportion of the outgoings from income. Housing (and its context) is an important, multifaceted and sometimes difficult to interpret indicator of SEP. As discussed above, some housing characteristics may be direct exposures or markers of exposures for specific diseases.

Strength and limitations

Housing characteristics and amenities are extensively used as measures of SEP. They are comparatively easy to collect and may also provide some indications of specific mechanisms linking SEP to particular health outcomes (for example, crowding). Their main limitation is that, although measuring the same underlying concept, these indicators may be specific to the temporal and geographical context where they were developed and thus be difficult to compare across studies.

INCOME

Theoretical basis

Income is the indicator of SEP that most directly measures the material resources component. As with other indicators such as education, income has a ''dose-response'' association with health,[46 47] and can influence a wide range of material circumstances with direct implications for health.[2 3] Income also has a cumulative effect over the life course[48] and is the SEP indicator that can change most on a short term basis, although this dynamic aspect is rarely taken into account in epidemiological studies.[49] It is implausible that money in itself directly affects health, thus it is the conversion of money and assets into health enhancing commodities and services via expenditure that may be the more relevant concept for interpreting how income affects health. Consumption measures are, however, rarely used in epidemiological studies.

Measurement

People can either be asked to report their absolute income or can be asked to place themselves within predefined categories. Most often income of the household rather than of individuals is measured. While individual income will capture individual material characteristics, household income may be a useful indicator, in particular for women, who may not be the main earners in the household. Using household income information to apply to all the people in the household assumes an even distribution of income according to needs within the household, which may or may not be true. For income to be comparable across households, additional information on family size or the number of people dependent on the reported income should be elicited.[1] This can be then transformed into ''equivalised income'',[47 50] which adjusts for family size and its associated costs of living.[3]

Income may be measured as a relative indicator establishing levels of *poverty* (for example, percentage above or below the official poverty level in a given year[48]).

Interpretation

Income primarily influences health through a direct effect on material resources that are in turn mediated by more proximal factors in the causal chain such as behaviours. The mechanisms through which income could affect health are:

- Buying access to better quality material resources such as food and shelter.
- Allowing access to services, which may improve health directly (such as health services, leisure activities) or indirectly (such as education).
- Fostering self esteem and social standing by providing the outward material characteristics relevant to participation in society.
- Reverse causality may also be considered as income level can be affected by health status.

Strengths and limitations

Income is arguably the best single indicator of material living standards. There is evidence that personal income is a sensitive issue and people may be reluctant to provide such information,[51] although this may have been overstated.[52] In different settings (including different countries, different birth cohorts, different sexes) income may be a more or less ''sensitive'' indicator (with respect to participants' willingness to disclose this information accurately) relative to educational attainment and occupation. Ideally we want to be able to collect disposable income as this reflects what individuals/households can actually spend, but often we collect gross incomes or incomes that do not take account of in-kind transfers that function as hypothecated income (such as food stamps in the USA). While income may be a sensitive question and potentially subject to greater non-response than other SEP questions, more sophisticated methods for eliciting accurate income information (especially for in-person interviews) have been developed, but of course these come at a cost of having to devote more space and time to collect these data. The meaning of current income for different age groups may vary and be most sensitive during the prime earning years. Income for young and older adults may be a less reliable indicator of their true SEP because income typically follows a curvilinear trajectory with age.

OCCUPATION BASED MEASURES

Theoretical basis

Occupation based indicators of SEP are widely used. Occupation can: represent Weber's notion of SEP as a reflection of a person's place in society related to their social standing, income and intellect; characterise working relations between employers and employees; or, less frequently, characterise people as exploiters or exploited in class relations.

Measurement

Most studies use the current or longest held occupation of a person to characterise their adult SEP. However, with increasing interest in the role of SEP across the life course, some studies include parental occupation as an indicator of childhood SEP in conjunction with individuals' occupations at different stages in adult life.[53] Occupational measures are in some sense transferable: measures from one individual, or combinations of several individuals, can be used to characterise the SEP of others connected to them. For example, the occupation of the ''head of the household'', or the ''highest status occupation in the household'', can be used as an indicator of the SEP of dependants (for example, spouse, children) or the household as a unit.

Interpretation

Different occupational classification schemes measure particular aspects of SEP, although it may be difficult to disentangle the specific effects of individual indicators. Some of the more general mechanisms that may explain the association between occupation and health related outcomes are presented here (for each classification we highlight the specific aspect it focuses on):

- Occupation (parental or own adult) is strongly related to income and therefore the association with health may be one of a direct relation between material resources—the monetary and other tangible rewards for work that determines material living standards—and health.
- Occupations reflect social standing and may be related to health outcomes because of certain privileges—such as easier access to better health care, access to education, and more salubrious residential facilities—that are afforded to those of higher standing.
- Occupation may reflect social networks, work based stress, control, and autonomy and thereby affect health outcomes through psychosocial processes.
- Occupation may also reflect specific toxic environmental or work task exposures such as physical demands (for example, transport driver, labourer).

Strengths and limitations

An important strength of these measures is their availability in many routine data sources, including census data and on death certificates. One of the most important limitations of

occupational indicators is that they cannot be readily assigned to people who are not currently employed. As a result, if used as the only source of information on SEP, socioeconomic differentials may be underestimated through the exclusion of some of the population.[54] Groups commonly excluded are retired people, people whose work is inside the home (mainly affecting women), the unemployed, students, and people working in unpaid, informal, or illegal jobs. Although previous occupation can be assigned to those who are retired and to some unemployed people, and husband's occupation is often used to assign women's SEP, this may inadequately index current social circumstances. Furthermore, other groups are less readily defined or willing to disclose their ''occupation''. People who are self employed can be difficult to classify, for example it is unclear in some occupationally based classifications whether someone who is a self employed builder with a team of 20 workers working for her is classified as a manager or a skilled manual worker. Some contemporary classification systems (see part 2) operationalise the classification of the self employed in a more meaningful way.

As with education, occupation may have different meanings for different birth cohorts and in different geographical settings (which may make international comparisons problematic). For example, for older generations the allocation of a husband's occupation to define a woman's SEP may have been appropriate and acceptable, but this is unlikely to be the case for many contemporary working populations where the participation rates of women, and their expectations of recognition, are much higher. Cohort influences are also relevant in terms of the changing structure and composition of the workforce—in industrialised societies fewer contemporary school leavers go into unskilled or semi-skilled occupations, whereas computer or IT based occupations are increasingly common. Additionally, the exposure consequences of working in different jobs may change with the advent of stricter occupational health legislation and new technologies that eliminate toxic exposures.

The second part of the glossary continues by describing specific occupation based indicators.

Authors' affiliations

B Galobardes, M Shaw, D A Lawlor, G Davey Smith, Department of Social Medicine, University of Bristol, Bristol, UK
M Shaw, South West Public Health Observatory, UK
J W Lynch, Department of Epidemiology, School of Public Health and Center for Social, Epidemiology and Population Health, University of Michigan, USA

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ECHO

Evaluation of the National Congenital Anomaly System in England and Wales

T Misra, N Dattani, A Majeed

Please visit the *Journal of Epidemiology and Community Health* website [www.jech.com] for a link to the full text of this article.

Objective: To evaluate the National Congenital Anomaly System (NCAS).
Methods: The NCAS in England and Wales based at the Office for National Statistics and the various regional registers that exchange data with it were examined, based on guidelines for evaluating public health surveillance systems, published by the Centres for Disease Control (CDC). Data relating to congenital anomaly notifications received from 1991 to 2002 were analysed.
Main outcome measures: The main outcome measures were based on CDC standards and included the level of usefulness of the system, simplicity, flexibility, data quality, acceptability, sensitivity, representativeness, timeliness, and stability of the system.
Results: The NCAS has two main tiers: the "passive" system of voluntary notifications and the anomaly registers, but many reporting sources within these. It receives about 7000 notifications a year. It is inflexible and has variable data quality. The voluntary nature of reporting affects the system's acceptability. The sensitivity as compared with two regional registers (Trent and Wales) is about 33%. The congenital anomaly registers reporting to the NCAS achieve high levels of coverage and completeness. From 2003, they cover 42% of all births and account for the major proportion of the notifications.
Conclusions: The NCAS serves the important function of monitoring birth defects in England and Wales, but is not currently operating in a timely or effective way. It should be adapted to meet its main objectives more effectively. More regional anomaly registers should be instituted and existing registers supported through central funds.

▲ *Archives of Disease in Childhood Fetal and Neonatal Edition* 2005;**90**:F368–F373.

GLOSSARY

Indicators of socioeconomic position (part 2)

Bruna Galobardes, Mary Shaw, Debbie A Lawlor, John W Lynch, George Davey Smith

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This is the second part of a glossary on indicators of socioeconomic position used in health research (the first part was published in the January issue of the journal).

OCCUPATIONAL BASED MEASURES (CONTINUED FROM FIRST PART OF THE GLOSSARY)

British occupational based social class (prior to 1990 known as the registrar general's social class)

Theoretical basis

The practice of classifying the population in Britain according to occupation and industry began as early as 1851 but it was not until the registrar's general's annual report for 1911 that occupation and industry were differentiated with a summary of occupations representing ''social grades'' separately presented. The main initial purpose was the analysis of fertility data, although mortality was also analysed; indeed there is evidence suggesting that revisions to the classification were constructed ''in the light of knowledge of mortality rates''.[1]

This scale is based on the prestige or social standing that a given occupation has in society. After revisions in 1990 this measure was more explicitly related to the skills needed to perform a particular occupation.[1] It is widely used in Britain and in other European countries.

Measurement

Occupations are categorised into six levels or classes (table 1), ranked from higher to lower prestige, which can also be reduced to two broad categories of manual and non-manual occupations; a seventh category includes all people in the armed forces irrespective of their rank therein, which is generally excluded in health studies.

Strengths and limitations

A key strength of this measure is its past official status in Britain and hence its widespread use in vital statistics, as well as many population censuses and surveys over a long time period. Adaptations have been extensively used in other countries, making comparability between studies easier. However, a key limitation is the subjectivity of its theoretical basis. In addition, it does not account for recent changes in the occupational structure, such as the increase in service jobs and the decrease in unskilled and semi-skilled manual occupations, or the increasing number of women in the labour market. Based on these criticisms, the Office for National Statistics in the UK has since 2000 used the new UK National Statistics socioeconomic classification as its official occupation classification (see below). Despite limitations the registrar general's social class system has been widely used to describe the socioeconomic gradient of health outcomes.

Interpretation

As (theoretically) a measure of prestige or social standing, it could be argued that the relation of this classification to health should be interpreted as due to the advantages bestowed by elevated social standing and increased prestige. In practice it is often interpreted as an indicator of both social standing and material reward and resources.

The Cambridge scale (or CAMSIS, the Cambridge social interaction and stratification scale)

Theoretical basis

This scale uses patterns of social interaction to determine the nature of social structure and a person's position within it; it is a hierarchical measure of social distance. The distance is defined by similarities in the lifestyles, social interactions, and resources that occupational groups share and is thus based on Weberian notions of what is important about social stratification.[2 3] The scale was originally constructed by grouping occupations according to friendship, which gave a numerical indication of how similar (socially close) or dissimilar (socially distant) any two occupations were.[2]

Measurement

The Cambridge scale provides a continuous measure that can be categorised into groups from the most to least advantaged (table 1). Although this classification bears resemblance to the registrar general's, its derivation (based on actual social networks rather than perceived status) means that some occupations will be differently classified by the two systems.[2]

Interpretation

The scale reflects general social and material advantage, and because it is based on social interaction it is also considered to represent lifestyles and health behaviours.[2 4]

Erikson and Goldthorpe class schema (also known as the Goldthorpe schema)

Theoretical basis

This classification is based on employment relations, classifying occupations that entail relations based on high levels of trust and independent working practices combined with delegated authority, to occupations based on a labour contract with very little job control.[4 5]

See end of article for authors' affiliations

Correspondence to: Dr B Galobardes, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR, UK; bruna.galobardes@bristol.ac.uk

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Table 1 Occupational based socioeconomic indicators: theoretical basis and group allocation

Prestige, skills	Working relations	Social distance (in lifestyle, social interactions, resources)	Property of means of production and class relations—social class
Registrar general's social class	**Erikson and Goldthorpe class scheme**	**Cambridge Scale**	**Wright**
I Professional	I Higher grade professionals, administrators and officials; managers in large industrial establishments; large proprietors	Continuous scale, can be arbitrarily grouped	1 Capitalist
II Intermediate			2 Small employer
III-N Skilled non-manual	II Lower grade professionals, administrators and officials; higher grade technicians; managers in small industrial establishments; supervisors of non-manual employees		3 Petty bourgeoisie
III-M Skilled manual			4 Expert manager
IV Partly skilled			5 Skilled manager
V Unskilled	IIIa Routine non-manual: higher		6 Non-skilled manager
VI Armed forces	IIIb Routine non-manual: lower		7 Expert supervisor
	IVa Small proprietors with employees	I Least advantaged	8 Skilled supervisor
	IVb Self employed without employees	II	9 Non-skilled supervisor
	IVc Farmers/smallholders	III	10 Experts
	V Foremen and technicians	IV	11 Skilled workers
	VI Skilled manual	… Most advantaged	12 Non-skilled workers
	VIIa Semi and unskilled manual		
	VIIb Agricultural workers		
Education and income			
American census classification	**UK National Statistics classification (NS-SEC)**		**Lombardi, *et al***
I Managerial and professional	1 Higher managerial and professional employers		Underproletariat (unemployed and seasonal workers)
II Technical, sales and administrative support	2 Lower managerial and professional		Typical proletariat (unskilled and semiskilled workers in manual occupations)
III Service occupations	3 Intermediate employees		Atypical proletariat (unskilled and semiskilled in commerce and services)
IV Farming, forestry, fishing	4 Small employers and own account workers		Traditional small bourgeoisie (self employed, small business owners)
V Precision production, craft, repair	5 Lower supervisory, craft and related employees		New small bourgeoisie (university-trained professionals)
			Bourgeoisie (large business owners)
VI	6 Employees in semi-routine occupations		
	7 Employees in routine occupations		
	8 Never worked and long term unemployed		

This scheme does not have an implicit hierarchical rank and therefore it does not necessarily capture a gradient in health across its groups. It has been used as an indicator of scioeconomic position in international comparisons of socio-economic inequalities in health across Europe.[6–8]

Measurement
Occupations are classified into 11 groups. This classification is not a hierarchy (despite the numbering that is used to refer to each group) (table 1).

Interpretation
Differences in health outcomes between groups can be mainly attributed to differences in working relations and work autonomy; different contract and reward system terms of remuneration; and different job promotion prospects.[4] However, the scheme also inherently reflects material resources as aspects of employment relations such as decision latitude are often co-terminus with material rewards accorded to different types of jobs.[9]

Strengths and limitations
This classification has a clear theoretical basis and it has been used in international comparisons. In addition, several studies have been conducted that permit assessment of its construct and criterion validity. However, working relations are likely to change over time and, therefore this scheme will also require continuous updating.[10]

Marxist based social class classifications
Theoretical basis
These indicators are based on Marx's theory of class and therefore categorise people as to whether they are exploited workers or those who own the means of production. Strictly speaking, this is the correct interpretation of *social class* as first coined by Marx. However, in practice the terms socio-economic position and social class are frequently used interchangeably in the epidemiological literature and the British registrar general's occupation based classification (although not based on Marxist theory) is referred to as social class.[11]

Interpretation
The results reported using these classifications in relation to health outcomes are explained in terms of exploitation between classes and in terms of the conflict generated by contradictory locations within this class system.[12]

To our knowledge there have been two explicit adaptations of Marx's theory of social class that take into account contemporary employment and social circumstances.

(a) Wright's social class classification
In this scheme people are classified according to the interplay of three forms of exploitation: (a) ownership of capital assets, (b) control of organisational assets, and (c) possession of skills or credential assets. This defines 12 locations (see figure 1) where cells 1 and 2 represent the capitalist class, cell 3 the petty bourgeoisie or self employed, cells 4 to 10 include contradictory class locations, and cells 11 and 12 the working class. People in the contradictory class locations belong simultaneously to the capitalist and the working class (capitalist in terms of controlling skills and credentials and exploiting workers; workers because they do not own capital assets and are controlled by capitalists).[13 14] In his later book, Wright uses variations of this classification. For example, in analysing time trends of the American class structure he used an eight location classification: employers, petty bourgeoisie, managers, supervisors, expert managers, experts, skilled workers, and workers. In a permeability analysis (analysis of friendship ties, family composition, and intergenerational

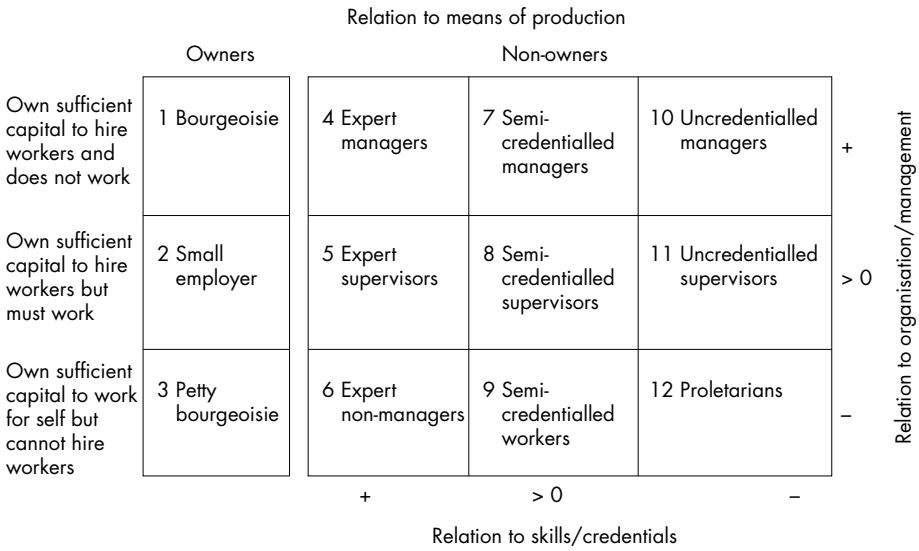

Figure 1 Wright's social class classification.

class mobility) Wright operationalises the social class classification in employers, petty bourgeoisie, experts managers, managers/supervisors, professionals, skilled workers, and workers.[15] Some of these variations were driven by data availability and by theoretical reasons, as was the case for a different operationalisation of the skill dimension in the permeability analysis.[15]

In the USA, Muntaner *et al*,[16 17] Schwalbe and Staples,[18] and Krieger *et al*[11] have used Wright's classification in epidemiological research. Among others, Wright's social class scheme has also been used in studies conducted in Spain[12] and in Israel.[19 20] Macleod *et al*, in the UK, have applied Wright's notion of contradictory class location to investigate the role of material circumstances versus perceived social status on health.[21]

(b) Lombardi *et al* social class classification

The other social class indicator based on Marx's theories originated in Brazil.[22 23] Similar to Wright's classification, it highlights new contradictory categories of skilled people working for a salary but being in the position to exploit other workers, as well as the increasing proportion of people working in the commerce or service sector who may also be both exploiters and exploited. It classifies occupations into six groups (table 1).

Other occupation based classifications

There are a number of country specific occupation based classifications based on combinations of occupation, education and/or income information, or of adaptations of the UK registrar social class classification.[24] They have often been developed in national statistical offices and are used in census and survey information originating within each country.[25–27] As an example, the Edwards' socioeconomic scheme is used in the US census and in North American studies.[28] It is based on the educational and income level required for each occupation and is thus similar (at least in terms of interpretation) to the British registrar general's scale (table 1). It classifies occupations into 13 categories that are often collapsed into a smaller number of major socioeconomic groups.[29 30]

In addition, readers are directed to earlier reviews for more complete descriptions of measures that are less commonly used in contemporary epidemiological research, for example, the Nam-Powers classification, Siegel's prestige scale, and Treiman's standard international occupational prestige scale.[28]

UK National Statistics socioeconomic classification (NS-SEC)

From 2000 the UK NS-SEC has replaced the registrar general's social class and another official classification, socioeconomic groups SEG (for details on the history, process, and conversion between these schemes consult the UK National Statistics web page http://www.statistics.gov.uk/methods_quality/ns_sec/default.asp). The NS-SEC is now used in all official statistics and surveys in the UK.

Theoretical basis

The NS-SEC is explicitly based on differences between employment conditions and relations, similar to the Erikson and Goldthorpe class schema.[31] People are placed in groups according to occupations with different employment relations and conditions—such as whether they have a wage rather than a salary, their prospects for promotion, and levels of autonomy.

Measurement

Occupations are usually grouped into 7, 5, or 3 (plus an additional category of ''never worked and long term unemployed'') (table 1). Only the grouping that collapses into three categories can be considered as hierarchical.

Interpretation

The direct interpretation of this association would be that the conditions and relations of employment have an effect upon health; although, again, differences in material resources will exist between the groups. This classification is related to health outcomes and life expectancy.[32]

Strengths and limitations

Similar to the Erikson and Goldthorpe classification (see above)

PROXY INDICATORS

Theoretical basis

When direct measures of SEP are not available, some researchers use proxy indicators. These indicators can be strongly correlated with SEP and in some cases may provide insight into the mechanism that explains the underlying association of SEP and a particular health outcome (for example the association of number of siblings and respiratory infection).

Measurement

Number of siblings has been used on the basis that in some contemporary industrialised societies larger numbers of children are associated with poorer SEP.[33 34] This is not necessarily the case in other populations or societies. Number of siblings may have a direct effect on health outcomes as it may increase the risk of early life infection. However, it may also reflect other mechanisms through which family size can affect health outcomes in individuals and family members. For example, the positive association between parity and coronary heart disease among women may in part reflect family lifestyle resulting in obesity in all family members and in part reflect pathophysiological processes related to large numbers of pregnancies.[35]

Infant and *maternal mortality* rates have been used as ecological measures of an area or country SEP.[36] Other characteristics such as *maternal marital status*, having a *single mother* or being an *orphan*, *illegitimacy*, *broken family*, and *death of father or mother* at an early age, are circumstances that often result in low SEP (for example, unemployment due to the inability of obtaining a flexible job and economic hardship can be associated with single motherhood). Several studies report worse health in these subgroups.[37–40] However, adverse health outcomes could also be caused by other factors associated with these circumstances but unrelated to SEP. For example, infant and maternal mortality may reflect climate factors leading to infection diseases (for example, malaria infection) in addition to reflecting SEP; broken family, or death of mother/father at an early age, could lead to ill health due to depression.

Strength and limitations

These are not indicators of SEP in itself but because of their strong correlation they may provide valuable information when direct measures are not available. It is important to always consider alternative explanations of their association with health outcomes. In addition, their association with socioeconomic circumstances can differ depending on the context. For example, number of siblings may be a marker of lower SEP in some, although not all, industrialised societies and may not be related at all with SEP in other settings.

WEALTH

Wealth is a continuous measure that combines total assets and income (see housing and income in part 1 of the glossary). Its relation to health assumes that income in combination with total assets is a better measure of someone's socioeconomic circumstances and therefore a better predictor of health than income alone. In addition to income, wealth includes financial and physical assets such as the value of housing, cars, investments, inheritance or pension rights.[16] The relative importance of wealth compared with income may change over the life course (wealth being more important in older age due to the accumulation of wealth and the impact of retirement on income[41]) or in population subgroups (for example, for a given level of income, African American and Hispanic households have less wealth than white households[42]).

WORKING LIFE INDICATORS AND EXCLUSION FROM THE LABOUR MARKET

People that cannot be classified in occupation based classifications can constitute a separate category. *Unemployment* can be used as an indicator based on exclusion from the workforce. Other work related indicators that can be used to measure SEP are *job insecurity* and *type of employement*.[43] These conditions are associated with worse objective and subjective health through a variety of mechanisms, for example, lack of material resources for those who are unemployed, as well as social isolation, loss of self esteem, and the stress of potential job loss in conditions of job insecurity.

COMPOSITE INDICATORS

A number of composite measures have been used to assess SEP at the individual level. However, the increasing interest in determining more specific mechanisms for—rather than merely describing—socioeconomic inequalities in health, has lead to these measures being less frequently used.[28 44] On the other hand, composite indicators may be efficient when SEP is measured as a confounding factor rather than as the main exposure of interest, as these composite measures incorporate, and therefore, adjust for different aspects of SEP.

Individual studies have designed and used specific composite indices, often dependent on the data available to that particular study. This is most appropriate when SEP is a confounding variable of the association of interest or when the specific mechanisms determining inequalities are not the main focus of the study. Standard composite indicators are the following: *Hollingshead index of social position*,[45] *Duncan index, Nam-Powers socioeconomic status, Warner's index of status characteristics*.[28] They have not been updated with current changes in the occupational structure and have not often been used in recent years. For more detailed explanations of these indicators we refer the reader to earlier reviews.[28]

AREA LEVEL MEASURES (INDICES OF DEPRIVATION)

Ecological, or area level, indicators are also used as measures of SEP. Most commonly these are aggregated from individual level or small area data, usually from census or other administrative databases. They can be used to characterise areas on a continuum from deprived to affluent (and are important for the allocation of public resources to areas) as well as a proxy for the SEP of the people living in those areas. In many studies one or more aggregate area measures, for example proportion of unemployed, proportion in blue collar or manual occupations, proportion with higher education in an area, are used with no attempt to combine measures into a composite score. In Britain a number of composite area level measures of SEP (referred to as indicators or indices of deprivation) have been developed for use in health related research and are increasingly used in other countries. The *Townsend deprivation index* is a measure of multiple deprivation using four variables from the (British) 1991 census: unemployment (defined as the proportion of economically active residents aged 16–64 who are unemployed), the proportion of households with no car, the proportion of households that are not owner occupied, and the proportion of households with overcrowding (>1 person per room).[46] The Townsend score for each area is a summation of the standardised scores (z scores) for each variable; a greater score indicates higher levels of material deprivation. Other similar indices are the *Carstairs deprivation index*[47] and the *Jarman or underprivileged area (UPA)* score.[48]

The *Breadline Britain index* has different conceptual origins.[49] This is a consensual measure of poverty, based on what people themselves understand and experience as the minimum acceptable standard of living in contemporary Britain. Combining survey data with census data, and using weights to account for the different probability subgroups in the population have of suffering from a particular type of deprivation,[50] this indicator is based on the proportions of: unemployment, people with no car, households non-owner occupied, lone parent households, households with persons with long term illness, unskilled and semi-skilled manual occupations (social class IV and V) in an area.[11] The Breadline Britain index thus includes a measure of health, and explorations of associations with health must take this into

account (a version of the index without this component can be derived). The Breadline Britain index (modified version) has been found to have a close relation with the geography of mortality in Britain.[51]

Recently, Krieger and colleagues evaluated the performance of different area socioeconomic measures in capturing the association with cause specific mortality and cancer incidence in the USA.[52] Interestingly, this work showed that among 11 single variable and eight composite measures it was ''percentage of persons living below the US poverty line'' that was best for use in surveillance of US socioeconomic differentials in mortality and cancer incidence.[52] The authors reached similar conclusions regarding other health outcomes such as low birth weight, childhood lead poisoning,[53] incidence of sexually transmitted diseases, tuberculosis, and non-fatal weapon related injuries.[54]

Area based indicators can be theorized as measures of the socioeconomic conditions of an area, and as such can have an independent influence on health. This idea is not new and in Britain has existed at least since Chadwick's time in the mid-1800s.[55] Increasing attention has been paid to the possibility that over and above individual characteristics, the place where a person lives can affect their health; ''where'' a person lives can be categorised as a neighbourhood, city, higher administrative areas (for example, health authority in the UK), region, or country.[56 57] Various indicators presented in this glossary can be used to capture the characteristics of these different levels. Studies investigating ''area effects'' tend to find small associations relative to the size of individual SEP effects, and it remains unclear whether the associations between area level measures of socioeconomic circumstances and health outcomes are related to the socioeconomic characteristics of where people live, independently of the (lifetime) characteristics of the people living in these areas.[57–60] This conceptual and empirical problem is especially pertinent when SEP is considered within a life course framework (see life course socioeconomic position below) and suggests historical information on both areas and individuals is required. The argument here is that adjustment for one single measure, which captures SEP at one point in time, is insufficient for capturing the full extent of individual effects.[61] An additional problem is that few area level indicators were conceptualised to measure area characteristics, and as we have noted above, they are usually formed from aggregates of individual level data.

Area measures are also used as proxies for individual level indicators when these are not available. In this case, given the misclassification of individual socioeconomic circumstances when measured by area characteristics, the association with health outcomes is likely to be underestimated.[62] The larger the areas the greater the misclassification will be. In addition, the variability in SEP picked up by the area level indicators will always be smaller than that of the individual level indicator, that is, the lowest value in area income will always be higher than the lowest individual income, and the other way around for the highest income.[63] However, if area characteristics have an independent effect on health outcomes, the association of individual SEP will be overestimated when area level indicators are used instead to predict individual level effects. Whether under or overestimation affects a given study will depend on the health outcomes under study, the area measures, and area size of every specific context.[44 62]

LIFE COURSE SOCIOECONOMIC POSITION

Socioeconomic circumstances are a changing but ever present backdrop to all stages of the life course and thus it is important to think about SEP as a time varying exposure. There is increasing evidence that adverse SEP in early life, independently of adult SEP, is a strong predictor of adult illness.[61 64 65] The indicators presented in the first part of this glossary, in addition to measuring different conceptual dimensions of SEP, can also capture information on SEP at different points in a person's life.[66] Therefore, a combination of these can be used to measure SEP at different times over the life course (see figure 1 in the first part of the glossary).

Several prospective studies report higher mortality among those who experience adverse socioeconomic position at different periods of the life course. A variety of mechanisms may explain these associations.[67] For example, infection with *Helicobacter pylori* during childhood plausibly explains the association between childhood deprivation and stomach cancer,[68] and suggests a critical period model for this health outcome.[67] On the other hand, coronary heart disease, ischaemic stroke, and chronic obstructive pulmonary disease seem to be influenced by factors acting across the entire life course and therefore may conform more to a cumulative risk model.[69–73] There is however an intrinsic problem in disentangling different life course processes (similar to differentiating age, cohort, and period effects).[74] Whether critical period, social mobility, accumulation of risks or combinations of these underlie the association between SEP and a given health outcome requires prior knowledge of the specific causal mechanisms.[74]

As the cumulative life course effect of adverse SEP on adult disease outcomes become more apparent, the need to adjust for different measures of SEP from across the life course in observational studies of exposures and outcomes that are strongly socially patterned is increasingly acknowledged.[75] It is unlikely that residual socioeconomic confounding can be ruled out by simple adjustment for one or perhaps two measures of SEP at a single point in time.[76]

CONCLUDING REMARKS

SEP is key to understanding inequalities in health and is best considered as an umbrella term for a range of indicators and interconnected concepts. Individually and in aggregate, across the life course, time and place, a vast number of studies have shown how socioeconomic disadvantage is related to poorer health. A descriptive approach to considering this body of research emphasises the consistency of the associations and invokes ideas of ''fundamental cause''[77 78] and the ''general susceptibility''[79] of the disadvantaged. However, an aetiological framework needs to focus on the specificity of these associations.[73] The departure point for a more complete aetiological understanding of socioeconomic health differentials should be based on mechanistic specificity of links between particular SEP indicators (as described above) and different health outcomes. This approach seems fruitful in developing greater insights into the mechanisms that generate socioeconomic inequalities in health, in different places and times.[73 80]

Authors' affiliations

B Galobardes, M Shaw, D A Lawlor, G Davey Smith, Department of Social Medicine, University of Bristol, Bristol, UK
M Shaw, South West Public Health Observatory, UK
J W Lynch, Department of Epidemiology, School of Public Health and Center for Social, Epidemiology and Population Health, University of Michigan, USA

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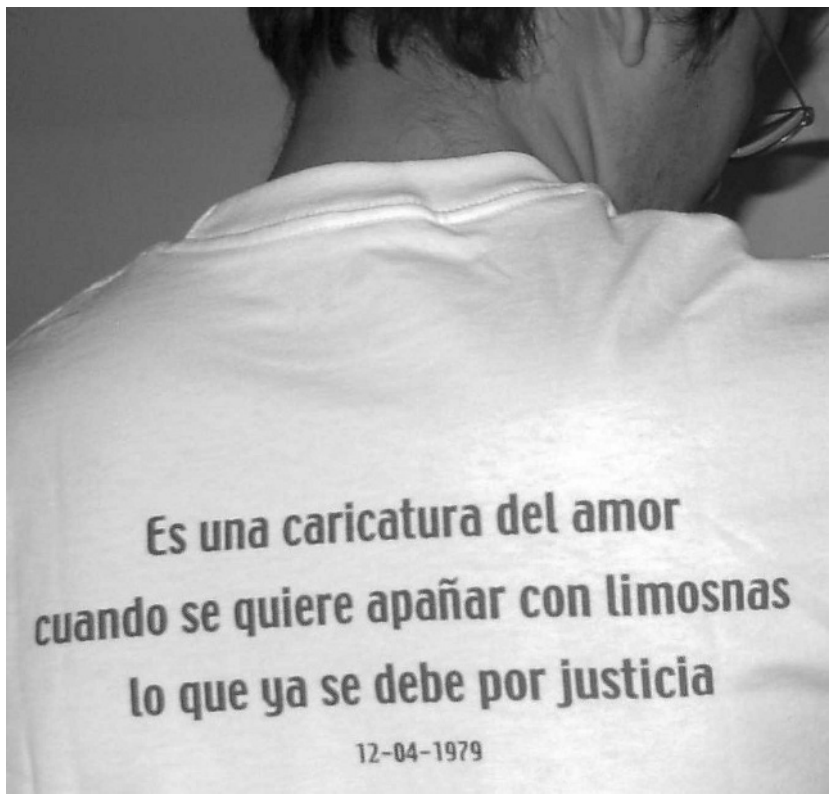
THE *JECH* GALLERY

Love pounds, tons of inequities

News[1] alerted to El Salvador in 2004: in four decades young people died for the first time by hunger. It was an announced death: the undernutrition, re-emergent disease is a direct consequence of the neoliberal era, and has deepened. The suppression of the agricultural subsidies annihilated food security and the subsistence cultures of poor farmers. The minimum wage was frozen to compete with low production costs, in the globalised market of the textile manufacturing. An economy dominated by dollars and an increasing cost of the basic basket, especially foods, completed the picture. These factors featured heavily in a report of the Office of the Judge Advocate General for the Defence of the Human Rights.[2] The answer: an assisted programme of nutritional consultation and food distribution called ''Pounds of love''.[3] But the inequities, exacerbated by unequal international trade relations, unjust distribution of the wealth, unemployment, payments in the public health system, and poor social investment continue to grow and generate poverty, social violence, and insanity to a rate that soon will end in the inability to govern.

Correspondence to: Dr E Espinoza, Final 25 Avenida Norte y Boulevard de Los Héroes Edificio de la Rectoría, San Salvador, El Salvador; espinoza@telesal.net



A tee shirt legend on the 25 year anniversary of the murder of Archbishop Oscar Romero—''It is a cartoon of love when it is wanted to patch up with gifts that which is already owed by justice''. (Taken from the 12 April 1979 homily of the Archbishop Romero whose assassination in 1980 unleashed a civil war of 12 years in El Salvador).

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A Tale of Two Cities: Effects of Air Pollution on Hospital Admissions in Hong Kong and London Compared

Chit-Ming Wong,[1] Richard W Atkinson,[2] H. Ross Anderson,[2] Anthony Johnson Hedley,[1] Stefan Ma,[1] Patsy Yuen-Kwan Chau,[1] and Tai-Hing Lam[1]

[1]Department of Community Medicine, The University of Hong Kong, Hong Kong, China; [2]Department of Public Health Sciences, St. George's Hospital Medical School, London, United Kingdom

The causal interpretation of reported associations between daily air pollution and daily admissions requires consideration of residual confounding, correlation between pollutants, and effect modification. If results obtained in Hong Kong and London—which differ in climate, lifestyle, and many other respects—were similar, a causal association would be supported. We used identical statistical methods for the analysis in each city. Associations between daily admissions and pollutant levels were estimated using Poisson regression. Nonparametric smoothing methods were used to model seasonality and the nonlinear dependence of admissions on temperature, humidity, and influenza admissions. For respiratory admissions (≥ 65 years of age), significant positive associations were observed with particulate matter < 10 μm in aerodynamic diameter (PM_{10}), nitrogen dioxide, sulfur dioxide, and ozone in both cities. These associations tended to be stronger at shorter lags in Hong Kong and at longer lags in London. Associations were stronger in the cool season in Hong Kong and in the warm season in London, periods during which levels of humidity are at their lowest in each city. For cardiac admissions (all ages) in both cities, significant positive associations were observed for PM_{10}, NO_2, and SO_2 with similar lag patterns. Associations tended to be stronger in the cool season. The associations with NO_2 and SO_2 were the most robust in two-pollutant models. Patterns of association for pollutants with ischemic heart disease were similar in the two cities. The associations between O_3 and cardiac admissions were negative in London but positive in Hong Kong. We conclude that air pollution has remarkably similar associations with daily cardiorespiratory admissions in both cities, in spite of considerable differences between cities in social, lifestyle, and environmental factors. The results strengthen the argument that air pollution causes detrimental short-term health effects.
***Key words*: air pollution, cardiac and respiratory hospital admissions, daily time-series, Hong Kong, London. *Environ Health Perspect* 110:67–77 (2002). [Online 18 December 2001]**
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There is now considerable evidence that daily hospital admissions for cardiorespiratory diseases are linked to levels of particulate and gaseous ambient air pollution on the same or previous days (*1–3*). This is consistent with even more substantial evidence concerning daily mortality. In the formulation of public health policy it has been assumed that these associations have a causal basis, but at the scientific level there remain important questions concerning residual confounding, the effects of individual pollutants or mixtures, and other factors that may modify health effects. Further evidence on these issues will have an important bearing on conclusions about the cause and mechanisms of the health effects of air pollution.

Because populations are exposed to mixtures rather than to individual pollutants, multicity studies have the potential to create added insights into some of these issues. Those that have been established so far, using the approaches of APHEA (Air Pollution and Health: a European Approach) Phase I (*4*) and Phase II (*5*) and NMMAPS (National Mortality and Morbidity Air Pollution Study) (*6,7*), are confined to the temperate climatic zones. Hong Kong is a large city in a subtropical region where there is evidence of adverse effects of air pollution (*8,9*). London, United Kingdom, is a city of similar size for which adverse health effects of air pollution have also been reported (*10,11*). On one hand, there are similarities between the two cities in terms of their main sources and levels of pollutants and patterns of the respiratory and cardiac diseases. On the other hand, there are differences between the two cities in terms of a number of factors that might influence confounding or effect modification; these include demography, climate, housing, lifestyle, patterns of disease, the health care system, and seasonal cycles of both weather and pollution variables.

We have conducted parallel analyses of the short-term associations between air pollution and daily hospital admissions in Hong Kong and London to compare and contrast the health effects of air pollution in the two cities. This comparison has relevance to the understanding of the short-term health effects of air pollution, their consistency, and the factors that may modify their effects.

Methods

Daily emergency hospital admissions for respiratory and cardiac diseases were obtained from routine hospital information systems for Hong Kong (1995–1997) and London (1992–1994). The data included in this study are from patients admitted to hospitals immediately either through the accident and emergency departments, general outpatient departments, or directly to the inpatient wards on the grounds of urgency. The series that we chose for comparison were those selected by the APHEA-2 collaboration; these included asthma [*International Classification of Diseases, Revision 9* (ICD-9) code 493] (*12*) for ages 15–64 years, respiratory disease (ICD-9 460–519) for ages 65 and over, cardiac diseases (ICD-9 396–429) for all ages, and ischemic heart disease (IHD; ICD-9 410–414) for all ages.

Daily average 24-hr concentrations of PM_{10} (particles with median aerodynamic diameter < 10 μm), nitrogen dioxide, and sulfur dioxide and average 8-hr concentrations of ozone were collected from background monitoring stations in each city. Only stations able to provide data for 75% or more days during the study periods were used. A daily concentration was accepted as valid if more than 17/24 or 5/8 (in the case of O_3) hourly measurements were made. When data were available from more than one monitoring station, we used a simple filling-in procedure to improve data completeness. Missing values were replaced with the mean of values from those stations with available data. The pollutant measures from

Address correspondence to A.J. Hedley, Department of Community Medicine, The University of Hong Kong, Patrick Manson Building South Wing, 7 Sassoon Road, Pokfulam, Hong Kong, China. Telephone: (852) 2819-9282. Fax: (852) 2855-9528. E-mail: commed@hkucc.hku.hk

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Table 1. Comparison of environmental factors of Hong Kong and London.

Environmental factor	Hong Kong	London
Population (millions)	6.2 (1995)[a]	6.9 (1992)[b]
Area (km^2)	1,092	1,580
Climate	Subtropical, with rain and tropical cyclones in the summer months	Maritime, with mild winters and temperate summers
Mean January/July temperatures (°C)	16/29	3/23
Rainfall	224 cm, most falling in the summer months	58 cm, evenly distributed through the year
Topography	Peninsula with offshore islands	Estuarine river basin
Lifestyle		
Smoking rates (≥ 15 years of age)	Male 26.7%; female 3.1%[c]	Male 28%; female 27%[d]
Regular alcohol consumers	Male 20.0%; female 2.0%[e]	Male 27%; female 11%[d]
Health care system	Primary care services provided mainly by private sector (85%) Hospital services provided mainly by public sector (86%)	National Health Service
Median size of private dwellings	40.0–69.9 m^2[a]	85 m^2[f]
GDP per capita (with adjustment for purchasing power parity)	U.S. $20,458[g]	U.S. $20,890[g]
Leading causes of death	(1996 data)[h]	(1996 data)[i]
	1. Malignant neoplasms, 31.3%	1. Circulatory diseases, 42.6%
	2. Heart diseases, 15.8%	2. Malignant neoplasms, 25.0%
	3. Cerebrovascular disease, 10.7%	3. Respiratory diseases, 15.9%
	4. Pneumonia (all forms), 10.6%	4. Digestive diseases, 3.6%
	5. Injury and poisoning, 5.1%	5. Injury and poisoning, 2.9%

GDP, gross domestic product.
[a]Data from the Hong Kong Annual Digest of Statistics (*17*). [b]Data from the Office of Population and Censuses Surveys (*18*). [c]Data from the Census and Statistics Department (*19*). [d]Data from Statistics on Smoking: England, 1976 to 1996 (*20*). [e]Data from Janus et al. (*21*); alcohol consumption at least once per week (25–74 years of age). [f]Data from the Office of National Statistics (*22*). [g]Data from Asia Week (*23*). [h]Department of Health. Department of Health Annual Report (*24*). [i]Data from the Office of National Statistics (*25*).

Table 2. Comparison of selected health and air pollution statistics between Hong Kong and London.

Health variable	Hong Kong	London
Population < 15/> 65 years of age (%)	18.9/10.0 (1996)[a]	18.8/13.9 (1992)[b]
Infant mortality rate (per 1,000 live births)	4.0	7.2
Age-standardized mortality[c] (per 1,000 population)		
From all causes	3.7	4.5
From respiratory diseases	0.7	0.5
From cardiovascular diseases	0.9	1.9
Emergency admissions for respiratory disease		
Respiratory (% of all causes)	10.0 (1996)	5.1 (1992/1993)
Age standardized rate[c] (per 1,000 population)	12.9	8.0 (1992–1994)
Age distribution (%)		
0–14 years	33	35
15–64 years	22	26
≥ 65 years	45	39
Subcategories (%)		
Lower respiratory infections (ICD-9 466, 480–487)	23	22
Asthma (ICD-9 493)	13	25
COPD (ICD-9 490–496, excluding 493)	24	15
Emergency admissions for cardiovascular disease		
Cardiovascular (% of all causes)	7.6 (1996)	5.9 (1992/1993)
Age standardized rate (per 1,000 population)	5.8	5.5 (1992–1994)
Age distribution (%)		
0–14 years	2	0
15–64 years	37	32
≥ 65 years	61	68
Subcategories (%)		
Stroke (ICD-9 430–438)	22	19
Cardiac (ICD-9 390–429)	63	70
[Ischemic heart disease (ICD-9 410–414)]	37	30
[Arrhythmias (ICD-9 427)]	20	9
[Cardiac failure (ICD-9 428)]	22	18
Sources of pollutant emissions	(1997)[d] (TSP including PM_{10})	(1997)[e]
PM_{10} (%)		
Traffic (vehicle, marine vessel, aircraft)	61	83
Industry	6	11
Power generation (and heating for London)	33	6
NO_x (%)		
Traffic (vehicle, marine vessel, aircraft)	41	83
Industry	8	5
Power generation (and heating for London)	45	13
SO_2 (%)		
Traffic (vehicle, marine vessel, aircraft)	14	28
Industry	21	34
Power generation (and heating for London)	65	38

TSP, total suspended particulate.
[a]Data from the Hong Kong Department of Health (*24*). [b]Data from the Office of Population and Censuses Surveys (*18*). [c]The standard population was adopted from Segi (*26*). [d]Data from the Planning, Environment and Lands Bureau (*27*). [e]Data from the London Research Centre (*28*).

all stations providing data were then averaged to provide city-wide daily estimates.

We used a statistical approach that closely followed the one adopted by the APHEA-2 study. Poisson regression was used to model the associations between the dependent variable, daily admission counts, and independent variables including nonparametric smooth functions of time, temperature, humidity, and influenza. We used loess functions (*13*) of time with a minimum span of 60 days to model seasonal fluctuations in admission counts. Temperature and humidity recorded on the day of admission and up to 3 days before admission were investigated and modeled using nonparametric smooth functions, with the degree of smoothing determined by the exposure–response curves and the Akaike's Information Criteria (*14*). In addition, dummy variables for days of the week, holidays, and unusual events such as thunderstorms and influenza epidemics were included as other independent variables. Daily admission counts for influenza at the 4th quartile (for each week) were used as indicators of influenza epidemics. Models were fitted using a quasi-likelihood method assuming constant over-dispersion over time. This modeling procedure was carried out for each series studied, and the core models were assessed using plots of model residuals and fitted values and plots of the estimated partial autocorrelation functions. Pollution measures were then added in turn, and if necessary, both overdispersion and autocorrelation were further adjusted for using statistical procedures implemented in S-PLUS (Insightful Corporation, Seattle, WA, USA) (*15*). We examined concentrations on the day of admission and on the previous 3

days, and the means of the current day and the previous day (lag 0–1).

Any linear effect of the pollutant could be assessed by adding a pollutant measure into the model described above. A possible nonlinear effect of the pollutant was further assessed by an exposure–response relationship generated by generalized additive modeling (*16*). The procedure involved symmetrical application of a loess smoothing function on a number of pollutant measures around a specific point and estimation of the risk at that specific point. A plot of risk against all the specific points along the *x*-axis produced an exposure–response curve.

To investigate seasonal differences in the pollution effects, dummy variables were added to the models to indicate season and pollutant-season interaction terms. The warm season was defined as April–September and the cool season was October–March. We derived estimates of the pollutant effects in each season from the models together with *p*-values for the interaction terms, which indicated whether or not the observed seasonal differences were statistically significant.

We used two-pollutant models to estimate the effects of one pollutant at mean cumulative lag 0–1 days after controlling for another pollutant also at mean cumulative lag 0–1 days.

Results

Background demographic, health, and environmental data. The background characteristics of the two cities have been summarized (Table 1). Hong Kong has a population of over 6 million and occupies an area of approximately 1,000 km^2, comprising two major islands, some smaller outer islands, a peninsula, the lands adjacent to the mainland, and some reclaimed areas. It is situated at 22.5°N latitude at the mouth of the Pearl River, which opens into the South China sea. Hong Kong has a subtropical climate that tends toward the temperate for nearly half the year. The average annual rainfall is 224 cm, most of which falls in the summer months.

Greater London has a population of about 7 million people and occupies a roughly circular basin of 1,600 km^2, which is bisected east to west by the River Thames and bounded to the north and south by low hills. It lies at a latitude of 45°N and has a temperate maritime climate. The average annual rainfall is 58 cm, which falls throughout the year.

Table 2 shows a comparison of relevant demographic, health, and environmental characteristics for Hong Kong and London. The age distributions of the two cities are similar, but age-standardized annual mortality rates are lower in Hong Kong than in London for deaths from all causes and from cardiovascular diseases. Standardized annual rates for admission to public hospitals are higher in Hong Kong than in London for respiratory disease (12.9 vs. 8.0 per 1,000) and for cardiovascular disease (5.8 vs. 5.5 per 1,000). Among respiratory hospital admissions, the proportions due to respiratory infections are similar, but admissions due to chronic obstructive pulmonary disease are greater in Hong Kong and those due to asthma are higher in London. The relative distributions of subcategories of cardiac diseases were similar except that arrhythmias were more common in Hong Kong.

PM_{10} and NO_2 emissions in London were both predominantly from traffic (83% and 83%, respectively); in Hong Kong they were from both traffic (61% and 41%, respectively) and power generation (33% and 45%, respectively). SO_2 in London was almost equally derived from traffic, industry, and power generation (28%, 34%, and 38%, respectively), but in Hong Kong they were mainly from power generation (65%) and industry (21%).

Daily time-series data. Summary statistics for daily counts of admissions, by cause and age, pollutant concentrations, and meteorologic variables are shown in Table 3. Correlations between these variables are shown in Table 4. London had almost twice the median daily count of admissions for asthma as Hong Kong but only two-thirds the median number of admissions for respiratory disease. The numbers of cardiac admissions were more comparable, but London had almost 50% more emergency admissions for IHD than Hong Kong.

The concentrations of NO_2, SO_2, and O_3 were higher in London, whereas PM_{10} levels in Hong Kong were almost double those in London (46.8 vs. 24.8 μg/m^3) (Table 3). In Hong Kong, there was a marked seasonal variation in ambient concentrations of NO_2, O_3, and PM_{10}, all of which were lowest in the warm season and highest in the cool season. In contrast, SO_2 tended to show less seasonal variation and was highest in the warm season. In London, there was little seasonal variation in NO_2,

Table 3. Summary statistics for daily hospital admissions, pollutant concentrations, and meteorologic measurements in Hong Kong (1995–1997) and London (1992–1994); n = 1,096 days.

				Percentile				
Variable, city	Mean	(Warm/cool)	SD	Min	10th	50th	90th	Max
Emergency hospital admission (no./day)								
Asthma (ICD-9 493), 15–64 years								
Hong Kong	7.8	(7.0/8.6)	3.4	0.0	4.0	7.0	12.0	24.0
London	14.1	(13.0/15.1)	5.8	2.0	8.0	13.0	21.0	85.0
Respiratory (ICD-9 460–519), ≥ 65 years								
Hong Kong	91.3	(86.7/96.1)	22.5	45.0	64.0	88.0	122.0	174.0
London	58.3	(49.5/67.4)	19.4	13.0	37.0	55.0	82.0	150.0
Cardiac (ICD-9 390–429), all ages								
Hong Kong	98.7	(94.0/103.4)	23.3	40.0	67.0	101.0	127.5	176.0
London	121.1	(118.3/124.0)	23.4	50.0	89.0	121.0	152.0	196.0
IHD (ICD-9 410–414), all ages								
Hong Kong	36.0	(35.3/36.7)	10.3	8.0	23.0	35.0	49.0	76.0
London	51.3	(50.5/52.0)	10.0	22.0	39.0	51.0	64.0	86.0
Pollutant concentration (daily μg/m^3)								
NO_2 (24 hr)								
Hong Kong[a]	55.9	(48.1/63.8)	19.4	15.3	31.8	53.5	81.8	151.5
London[b]	64.3	(62.6/66.1)	20.4	23.7	42.3	61.2	88.8	255.8
O_3 (8 hr)								
Hong Kong[c]	33.5	(32.0/35.1)	23.0	0	7.9	28.3	64.0	168.9
London[d]	34.9	(45.3/24.0)	23.1	2.4	8.6	32.0	60.1	159.8
PM_{10} (24 hr)								
Hong Kong[e]	51.8	(42.2/61.6)	25.0	14.1	24.7	46.8	87.2	163.8
London[f]	28.5	(28.2/28.8)	13.7	6.8	15.8	24.8	46.4	99.8
SO_2 (24 hr)								
Hong Kong[g]	17.7	(18.3/17.2)	12.3	1.1	6.2	14.5	32.8	90.0
London[h]	23.7	(22.2/25.3)	12.3	6.2	13.2	20.6	38.1	113.6
Meteorologic measurements (daily)								
Temperature (°C)								
Hong Kong	23.2	(27.2/19.0)	5.0	6.9	16.0	24.3	29.1	30.9
London	11.9	(15.5/8.3)	5.0	–0.8	5.6	11.8	18.6	25.5
Humidity (%)								
Hong Kong	77.7	(80.7/74.7)	10.6	31.0	64.0	79.0	90.0	97.0
London	70.6	(67.5/73.7)	10.9	41.0	56.0	70.0	85.0	97.0

Abbreviations: Max, maximum; Min, minimum.
[a] r = 0.65–0.90 between seven stations. [b] r = around 0.8 between three stations. [c] r = 0.79 between two stations. [d] r = 0.95 between two stations. [e] r = 0.92–0.97 between five stations. [f] Only one station involved. [g] r = 0.44–0.81 between five stations. [h] r = –0.1 to 0.8 (median 0.5) in six stations.

SO_2, or PM_{10}, but there was marked seasonal variation in O_3, which was highest in the warm season. Thus, the only pollutant with a similar seasonal pattern in both cities was SO_2. Mean daily temperature was twice as high in Hong Kong as in London (23°C vs. 12°C), and the mean relative humidity was also higher in Hong Kong. The two cities have similar cycles of temperature, but their seasonal patterns for humidity differ markedly; humidity in Hong Kong is highest in the warm season, but in London it is highest in the cool season (Table 3).

Single-pollutant models. The associations between pollutants (*a priori* mean lag 0–1 days) and the four admission outcomes are shown in Table 5. We found no statistically significant associations between asthma admissions and any of the four pollutants in either of the cities. For respiratory admissions, we found small, positive, and statistically significant associations with all four pollutants in Hong Kong. By contrast, only O_3 was significantly associated with respiratory admissions in London. For cardiac diseases, both cities showed significant positive associations of comparable size with NO_2, PM_{10}, and SO_2. There were no significant positive associations with O_3 in Hong Kong, whereas in London it was significantly negative. The direction of effects for IHD was the same as for all cardiac diseases in both cities, but the estimates were lower in Hong Kong than in London (except O_3) and none were significant. In London, the relative risks for IHD were similar to those for all cardiac diseases and all were significant; the association with O_3 was negative.

Results for the most significant single day lag from lags 0 to 3 are shown in Table 6 and illustrated along with the other single day lags in Figure 1. Generally, these results are similar in terms of direction and magnitude to the *a priori* choice of mean lags 0 and 1. One difference was that in London, the associations between admissions for asthmatic attacks in the 15–64 age group, as well as respiratory disease in the ≥ 65 age group and NO_2, PM_{10}, and SO_2 in the best single lag days, were larger than the *a priori* (lag 0–1) choice and are statistically significant.

Table 4. Matrix of Spearman's rank correlation coefficient (*r*) between mean daily concentration of pollutants and meteorologic data (1995–1997).

	SO_2	PM_{10}	O_3	Temperature	Humidity
Hong Kong					
Whole year					
NO_2	0.37	0.82	0.43	–0.45	–0.35
SO_2		0.30	–0.18	0.17	–0.16
PM_{10}			0.54	–0.42	–0.53
O_3				–0.14	–0.59
Temperature					0.19
Warm season					
NO_2	0.28	0.80	0.54	–0.43	–0.18
SO_2		0.22	–0.14	0.37	–0.16
PM_{10}			0.65	–0.25	–0.40
O_3				–0.17	–0.57
Temperature					–0.26
Cool season					
NO_2	0.61	0.72	0.23	0.10	–0.36
SO_2		0.53	–0.21	0.13	–0.20
PM_{10}			0.36	0.01	0.55
O_3				0.05	–0.60
Temperature					0.21

	SO_2	PM_{10}	O_3	Temperature	Humidity
London					
Whole year					
NO_2	0.71	0.68	–0.29	–0.16	0.01
SO_2		0.64	–0.25	–0.13	–0.15
PM_{10}			0.17	0.02	–0.05
O_3				0.47	–0.52
Temperature					–0.27
Warm season					
NO_2	0.66	0.68	0.05	0.08	–0.09
SO_2		0.56	0.14	0.26	–0.33
PM_{10}			0.27	0.32	–0.14
O_3				0.26	–0.53
Temperature					0.26
Cool season					
NO_2	0.76	0.68	–0.61	–0.36	0.01
SO_2		0.70	–0.58	–0.46	–0.05
PM_{10}			–0.56	0.23	0.01
O_3				0.29	–0.37
Temperature					0.05

Table 5. Summary of single-pollutant excess risk (ER) and 95% confidence interval (CI) for a 10 μg/m^3 change in pollutant concentration for mean lag 0–1 day: comparison between Hong Kong and London.

Emergency admission complaints, age	Hong Kong ER (95% CI)	London ER (95% CI)
Asthma, 15–64 years		
NO_2	−0.6 (−2.1–1.0)	1.0 (0.0–2.1)
O_3	0.0 (−1.3–1.4)	−0.7 (−1.8–0.4)
PM_{10}	−1.1 (−2.4–0.1)	1.4 (−0.1–3.0)
SO_2	−0.1 (−2.4–2.2)	0.7 (−1.0–2.5)
Respiratory, ≥ 65 years		
NO_2	1.8 (1.2– 2.4)	−0.1 (−0.6–0.5)
O_3	0.8 (0.3–1.3)	0.8 (0.2–1.4)
PM_{10}	1.0 (0.5–1.5)	0.4 (−0.3–1.2)
SO_2	1.8 (0.9–2.6)	0.2 (−0.6–1.1)
Cardiac, all ages		
NO_2	1.4 (0.9–2.0)	0.7 (0.3–1.0)
O_3	0.3 (−0.2–0.7)	−0.6 (−1.0–−0.1)
PM_{10}	0.7 (0.3–1.1)	0.8 (0.3–1.4)
SO_2	2.1 (1.3–2.8)	1.6 (1.0–2.2)
IHD, all ages		
NO_2	0.6 (−0.2–1.4)	0.7 (0.2–1.2)
O_3	0.4 (−0.3–1.1)	−0.8 (−1.4–−0.2)
PM_{10}	0.5 (−0.1–1.1)	0.9 (0.1–1.6)
SO_2	0.1 (−1.1–1.2)	1.7 (0.8–2.6)

Table 6. Summary of single-pollutant excess risk (ER) and 95% confidence interval (CI) for a 10 μg/m^3 change in pollutant concentration for the best single lag day: comparison between Hong Kong and London.

Emergency admission complaints, age	Hong Kong Lag	Hong Kong ER (95% CI)	London Lag	London ER (95% CI)
Asthma, 15–64 years				
NO_2	1	−1.3 (−2.6–0.1)	2	1.1 (0.2–2.0)
O_3	2	1.2 (0.0–2.4)	0	−0.7 (−1.7–0.3)
PM_{10}	0	−1.1 (−2.1–0.0)	2	2.2 (0.8–3.6)
SO_2	2	−1.5 (−3.4–0.5)	3	2.1 (0.7–3.6)
Respiratory, ≥ 65 years				
NO_2	0	1.3 (0.8–1.8)	3	0.9 (0.5–1.3)
O_3	1	0.6 (0.2–1.0)	0	0.6 (0.1–1.2)
PM_{10}	0	0.7 (0.3–1.0)	3	1.5 (0.8–2.2)
SO_2	0	1.7 (1.0–2.4)	3	1.2 (0.5–2.0)
Cardiac, all ages				
NO_2	0	1.2 (0.7–1.7)	0	0.7 (0.4–1.0)
O_3	2	0.5 (0.1–0.8)	0	−0.8 (−1.2–−0.4)
PM_{10}	0	0.5 (0.2–0.9)	0	1.1 (0.5–1.5)
SO_2	0	1.6 (1.0–2.2)	0	1.4 (0.9–1.9)
IHD, all ages				
NO_2	3	0.7 (0.1–1.4)	0	0.7 (0.2–1.1)
O_3	3	0.5 (0.0–1.0)	0	−0.9 (−1.4–−0.3)
PM_{10}	2	0.5 (−0.1–1.0)	3	0.3 (−0.5–1.0)
SO_2	2	0.4 (−0.5–1.4)	0	1.4 (0.7–2.2)

These stronger associations all occur with longer lag 3 except once with lag 2. Another clear difference between the two cities was for admissions for IHD. In Hong Kong the most significant associations occurred at lag 2 or 3 days for the four pollutants, whereas in London they were at lag 0 days for NO_2, O_3, and SO_2. PM_{10} was the exception in London, with the most significant lag occurring at lag 3 days. In both cities however the magnitude of the effects were similar whether at mean lag 0–1 days or the most significant day.

Estimates of pollution effects by season (Table 7) showed contrasting patterns between the two cities for respiratory disease and similar patterns for cardiac disease (Figure 2). In Hong Kong, pollution effects on respiratory disease tended to be greater in the cool season and significantly so for NO_2 and SO_2 (Table 7). In London, the pattern was reversed with greater effects in the warm season, significantly so for NO_2 and PM_{10} (Table 7). The two cities were similar in having larger estimates of cardiac admissions in the cool season (with the exception of O_3 for London); all of these seasonal interactions were significant for Hong Kong, but only one (PM_{10}) was significant for London (Table 7).

Two-pollutant models. In Hong Kong, associations between respiratory admissions and each of the four pollutants studied tended to be robust to inclusion of a second pollutant into the models (Table 8). There were two exceptions: the PM_{10} and SO_2 associations were substantially reduced after NO_2 was added to the models. In London, associations between respiratory admissions and NO_2, PM_{10}, and SO_2 were nonsignificant and remained unchanged after the addition of a second pollutant. The significant O_3 associations found in London were robust to the inclusion of an additional pollutant.

For cardiac admissions in Hong Kong, the addition of NO_2 or SO_2 reduced the magnitude and statistical significance of NO_2, SO_2, and PM_{10} associations (O_3 was not found to be significant in single-pollutant models). These results were largely replicated in the London analyses, although in a model containing NO_2 and SO_2, SO_2 was clearly the "most robust" pollutant, retaining both the magnitude and statistical significance of its association after the inclusion of NO_2.

Exposure–response relationships. For respiratory admissions in Hong Kong, a negative

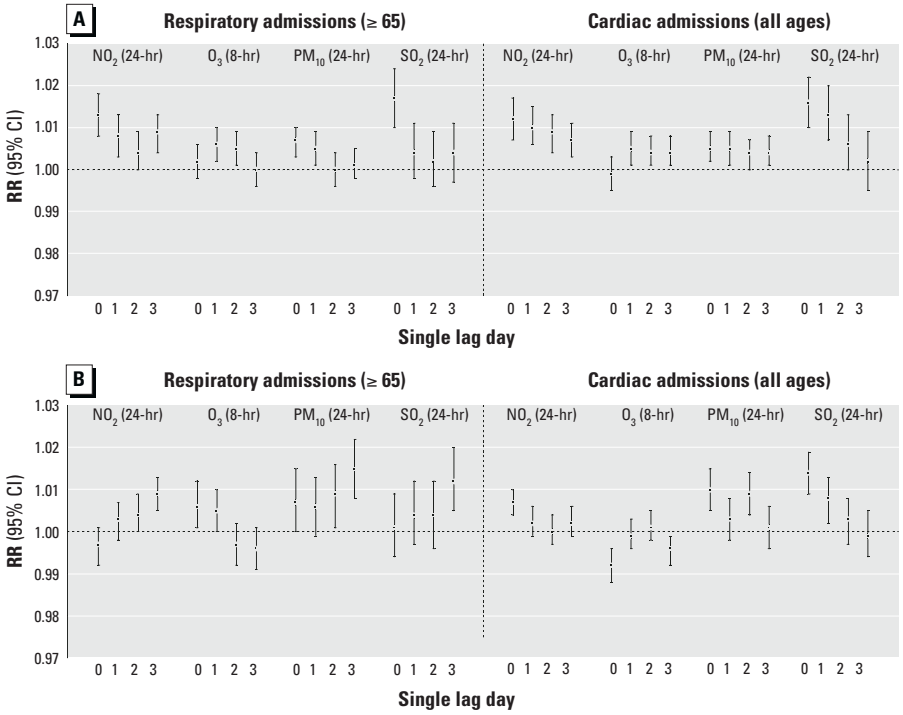

Figure 1. Effect of pollutants at a single lag day on hospital admissions due to cardiac and respiratory disease in (*A*) Hong Kong and (*B*) London. Values shown are relative risk (RR) and 95% confidence interval (CI) for a 10 μg/m^3 increase in concentration.

Table 7. Summary of single-pollutant results in excess risk (ER) and 95% confidence interval (CI) for a 10 μg/m^3 change in concentration at mean lag 0–1 day in warm and cool seasons.

Emergency admission complaints, age	Warm ER (95% CI)	Cool ER (95% CI)	Significance for pollutant by season interaction
Hong Kong			
Asthma, 15–64 years			
NO_2	−0.5 (−2.7–1.6)	−0.6 (−2.8–1.6)	
O_3	−0.3 (−2.0–1.3)	0.6 (−1.4–2.6)	
PM_{10}	−1.0 (−2.8–0.8)	−1.2 (−2.8–0.4)	
SO_2	1.5 (−1.5–4.6)	−2.0 (−5.4–1.4)	
Respiratory, ≥ 65 years			
NO_2	0.8 (0.1–1.6)	3.0 (2.1–3.9)	$p \leq 0.001$
O_3	0.8 (0.2–1.4)	1.0 (0.2–1.7)	
PM_{10}	0.8 (0.1–1.4)	1.2 (0.6–1.9)	
SO_2	1.1 (0.0–2.2)	2.7 (1.4–4.0)	$p \leq 0.05$
Cardiac, all ages			
NO_2	0.3 (−0.4–1.0)	2.6 (1.9–3.3)	$p \leq 0.001$
O_3	0.0 (−0.5–0.6)	0.9 (0.2–1.6)	$p \leq 0.05$
PM_{10}	0.0 (−0.6–0.6)	1.3 (0.8–1.9)	$p \leq 0.001$
SO_2	1.0 (0.0–2.0)	3.3 (2.1–4.4)	$p \leq 0.01$
IHD, all ages			
NO_2	0.1 (−0.9–1.2)	1.2 (0.0–2.3)	
O_3	0.4 (−0.4–1.2)	0.6 (−0.5–1.6)	
PM_{10}	0.2 (−0.7–1.0)	0.8 (−0.1–1.6)	
SO_2	−0.6 (−2.0–0.8)	1.0 (−0.8–2.8)	

Emergency admission complaints, age	Warm ER (95% CI)	Cool ER (95% CI)	Significance for pollutant by season interaction
London			
Asthma, 15–64 years			
NO_2	0.6 (−0.8–2.0)	1.3 (−0.1–2.8)	
O_3	−0.1 (−1.4–1.2)	−2.6 (−4.6–−0.5)	$p \leq 0.05$
PM_{10}	0.6 (−1.9–3.1)	1.6 (−0.3–3.6)	
SO_2	−1.4 (−4.7–1.9)	1.6 (−0.5–3.8)	
Respiratory, ≥ 65 years			
NO_2	0.6 (−0.2–1.4)	−0.7 (−1.4–0.0)	$p \leq 0.01$
O_3	1.0 (0.3–1.7)	0.2 (−0.7–1.2)	
PM_{10}	1.8 (0.5–3.1)	−0.5 (−1.5–0.5)	$p \leq 0.01$
SO_2	1.3 (−0.5–3.1)	−0.3 (−1.3–0.8)	
Cardiac, all ages			
NO_2	0.4 (−0.1–0.9)	0.8 (0.3–1.4)	
O_3	−0.2 (−0.7–0.3)	−1.1 (−1.8–−0.4)	
PM_{10}	0.1 (−0.7–1.0)	1.2 (0.5–2.0)	$p \leq 0.01$
SO_2	0.6 (−0.6–1.7)	1.9 (1.2–2.7)	
IHD, all ages			
NO_2	0.4 (−0.3–1.1)	1.0 (0.2–1.7)	
O_3	−0.5 (−1.2–0.2)	−1.3 (−2.3–−0.3)	
PM_{10}	0.1 (−1.1–1.4)	1.3 (0.3–2.3)	
SO_2	1.0 (−0.6–2.6)	2.0 (0.9–3.1)	

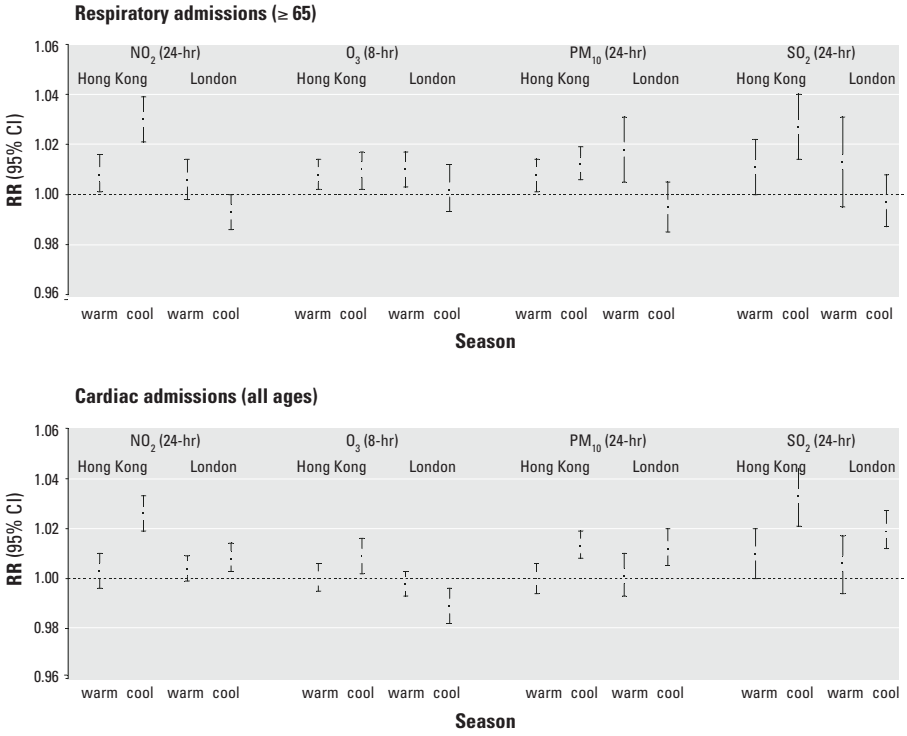

Figure 2. Comparison of pollutant effects in cool and warm seasons on hospital admissions due to respiratory and cardiac diseases. Values shown are relative risk (RR) and 95% confidence interval (CI) for a 10 μg/m^3 increase in concentration in mean lag 0–1 days.

Table 8. Excess risk (ER) and 95% confidence interval (CI) for a 10 μg/m^3 change in mean concentration of lag 0–1 day in each air pollutant from a single- and co-pollutant model.

Emergency admission	After adjusting for co-pollutant: NO_2 ER (95% CI)	O_3 ER (95% CI)	PM_{10} ER (95% CI)	SO_2 ER (95% CI)
Respiratory				
NO_2				
Hong Kong	1.8 (1.2–2.4)[a]	1.6 (1.0–2.3)	1.7 (0.8–2.7)	1.6 (0.8–2.4)
London	−0.1 (−0.6–0.5)[a]	0.1 (−0.5–0.6)	−0.4 (−1.2–0.4)	−0.2 (−0.9–0.5)
O_3				
Hong Kong	0.5 (0.0–1.0)	0.8 (0.3–1.3)[a]	0.5 (0.0–1.1)	1.0 (0.5–1.5)
London	0.8 (0.2–1.4)	0.8 (0.2–1.4)[a]	1.1 (0.5–1.7)	0.9 (0.3–1.5)
PM_{10}				
Hong Kong	0.0 (−0.7–0.7)	0.8 (0.3–1.3)	1.0 (0.5–1.5)[a]	0.6 (0.1–1.1)
London	0.9 (−0.3–2.0)	0.4 (−0.3–1.2)	0.4 (−0.3–1.2)[a]	0.7 (−0.5–1.8)
SO_2				
Hong Kong	0.3 (−0.7–1.4)	1.9 (1.1–2.8)	1.2 (0.3–2.2)	1.8 (0.9–2.6)[a]
London	0.5 (−0.7–1.7)	0.5 (−0.4–1.5)	−0.4 (−1.8–1.0)	0.2 (−0.6–1.1)[a]
Cardiac				
NO_2				
Hong Kong	1.4 (0.9–2.0)[a]	1.5 (0.9–2.0)	1.7 (0.9–2.5)	0.7 (0.1–1.4)
London	0.7 (0.3–1.0)[a]	0.7 (0.3–1.1)	0.6 (0.0–1.2)	0.1 (−0.3–0.6)
O_3				
Hong Kong	−0.1 (−0.6–0.4)	0.3 (−0.2–0.7)[a]	0.0 (−0.5–0.5)	0.4 (−0.1–0.9)
London	−0.5 (−0.9–0.0)	−0.6 (−1.0–−0.1)[a]	−0.6 (−1.0–−0.1)	−0.3 (−0.8–0.1)
PM_{10}				
Hong Kong	−0.3 (−0.9–0.4)	0.7 (0.3–1.2)	0.7 (0.3–1.1)[a]	0.1 (−0.4–0.6)
London	0.2 (−0.6–1.0)	0.8 (0.3–1.3)	0.8 (0.3–1.4)[a]	−0.3 (−1.1–0.4)
SO_2				
Hong Kong	1.4 (0.4–2.3)	2.1 (1.4–2.9)	2.0 (1.1–2.8)	2.1 (1.3–2.8)[a]
London	1.4 (0.6–2.3)	1.6 (0.9–2.2)	2.2 (1.2–3.2)	1.6 (1.0–2.2)[a]

[a]Estimates from the single-pollutant model.

exposure–response relationship was observed for concentrations of O_3 < 20 μg/m^3 (mainly in the warm season); in London (mainly in the cool season), a neutral relationship was found. For levels of O_3 > 20 μg/m^3, there were similar positive linear relationships in both cities (Figure 3).

For cardiac admissions and PM_{10} between the 10th and 90th percentiles (i.e., 25–87 μg/m^3 in Hong Kong and 16–46 μg/m^3 in London), both cities showed positive exposure–response relationships (Figure 3). We observed a negative linear association for O_3 across the range of the pollutant in London, whereas in Hong Kong we observed a "J"-shaped exposure–response relationship, indicating a positive association between cardiac admissions and the higher levels of O_3 (data not shown).

For the other exposure–response relationship, there were similarities as well as dissimilarities between the two cities (Figures 4–7), which was quite in agreement with those results presented in Table 5 for the same lag 0–1 day effects.

Discussion

Validity of results. The analytic method was the same in each city and followed the approach adopted by the APHEA collaboration. One of the present authors (R.W.A.) was responsible for analyzing the APHEA 2 respiratory admissions data and worked closely with researchers in Hong Kong to ensure that the application of methods was the same in each city. One feature of this method of Poisson regression is that seasonal, long-term trends and weather factors were modeled using nonparametric methods. This method is widely accepted and has been found to yield comparable results to the earlier method, which uses sinusoidal models for seasonal control (*29*). It also gives similar results to methods that use a synoptic approach to control for weather factors (*30*). In a sensitivity analysis, the method of parametric seasonal control was applied to selected series in both London (*11*) and Hong Kong; results were similar to those observed using the current method, which used generalized additive models (data not shown). The data on air pollution, weather, and outcomes were defined in an identical manner. We did not validate the consistency of hospital diagnosis, but since medical practice and the death certification procedure in Hong Kong has been strongly influenced by British and Commonwealth medical education, it is unlikely that there were major differences. In any case, the adoption of some broad categories (lower respiratory disease and cardiac disease) should have absorbed diagnostic transfer within those groups. The lower level of asthma admissions corresponds to the

known lower prevalence of asthma in Hong Kong (*31,32*). The lack of statistically significant association in asthmatic admissions may be due to the small numbers, relative to the other categories, and low statistical power to detect a significant association.

Respiratory admissions. The results for respiratory admissions were similar when the best single day lag was chosen, with all pollutants showing significant effects in both cities. These results are in line with many other studies (*33*). However, when the 0–1 day lag was compared, the cities were similar only for O_3, with only Hong Kong showing significant effects of the other pollutants. This may be explained by the fact that in Hong Kong the effects of PM_{10}, NO_2, and SO_2 were greatest at early lags, whereas in London the effects were greater with later lags. We have considered whether this difference in lags could be explained by the different primary health care systems. In Hong Kong this is a combination of private practitioners (the great majority) and public out-patient clinics, and heavy use of hospital accident and emergency departments. Perhaps this results in more rapid referral to hospital of persons with severe lower respiratory disease than in London, where the state-provided primary care system takes more responsibility for treating moderately severe disease at home and for controlling access to hospital facilities. We observed that the lag patterns for respiratory mortality associated with NO_2, PM_{10}, and SO_2 (Figure 8) (*34,35*) also followed the respective patterns for respiratory admissions (Figure 1). The other difference in the effects of NO_2, PM_{10}, and SO_2 was that in Hong Kong, the effects were stronger in the cool season, whereas they were stronger in the warm season in London. One common factor here is that the humidity is lower in the season showing the largest effects. It may also be relevant that the average levels of all pollutants apart from SO_2 are highest during the cool season in Hong Kong.

The strong associations between respiratory admissions and NO_2 and PM_{10} suggest that traffic may be an important source of toxic pollution. In both cities, it has been estimated that only a minority (about 20–40%) of PM_{10} particles in the ambient air (not just for emissions from various sources) is derived from local traffic (*36,37*). This is consistent with the finding that NO_2 retains its strong association in two pollutant models while PM_{10} does not.

O_3 showed consistent significant effects on respiratory admissions, irrespective of whether the mean lag 0–1 days or best single day lag was chosen. The exposure–response relationships with O_3 were linear in both cities when concentrations were > 20 μg/m^3, but in Hong Kong, a negative relationship was observed below this level. It could be postulated that the Hong Kong population would be more resistant to O_3 because the diet is higher in antioxidants and because air conditioning is used in most closed spaces, but our data suggest that both populations are equally susceptible. It is relevant to note that O_3 also shows associations with respiratory admissions in a range of European cities, with little heterogeneity (*33,38*). In both London and Hong Kong, the association with O_3 was very robust to the inclusion of other pollutants in the model.

Cardiac admissions. The results for cardiac admissions were similar for both cities in respect to NO_2, PM_{10}, and SO_2. This was irrespective of whether the mean lag 0–1 or the best lag was chosen, because in contrast to respiratory admissions, both cities displayed the same lag patterns, with lower risks at longer lags. These results add to the accumulating evidence worldwide that air pollution has short-term effects on cardiac admissions. Our evidence indicates that within the cardiac group of diagnoses, there are also effects on ischemic heart disease, but we do not know from this study if the same applies to other diagnoses such as cardiac failure or cardiac arrhythmias. However, we previously demonstrated an effect of O_3 in the cool season on admissions for these cardiac events in the elderly in Hong Kong (*8*). The exposure–response relationships with NO_2, PM_{10}, and SO_2 were linear in both cities, and there were similar seasonal associations, with both cities having larger effects in the cool season. The two-pollutant models also showed considerable similarities, with NO_2 being robust to the inclusion of PM_{10} in the models but affected to some extent by SO_2. In both cities, the effect of SO_2 retained its statistical significance in the presence of all the other pollutants.

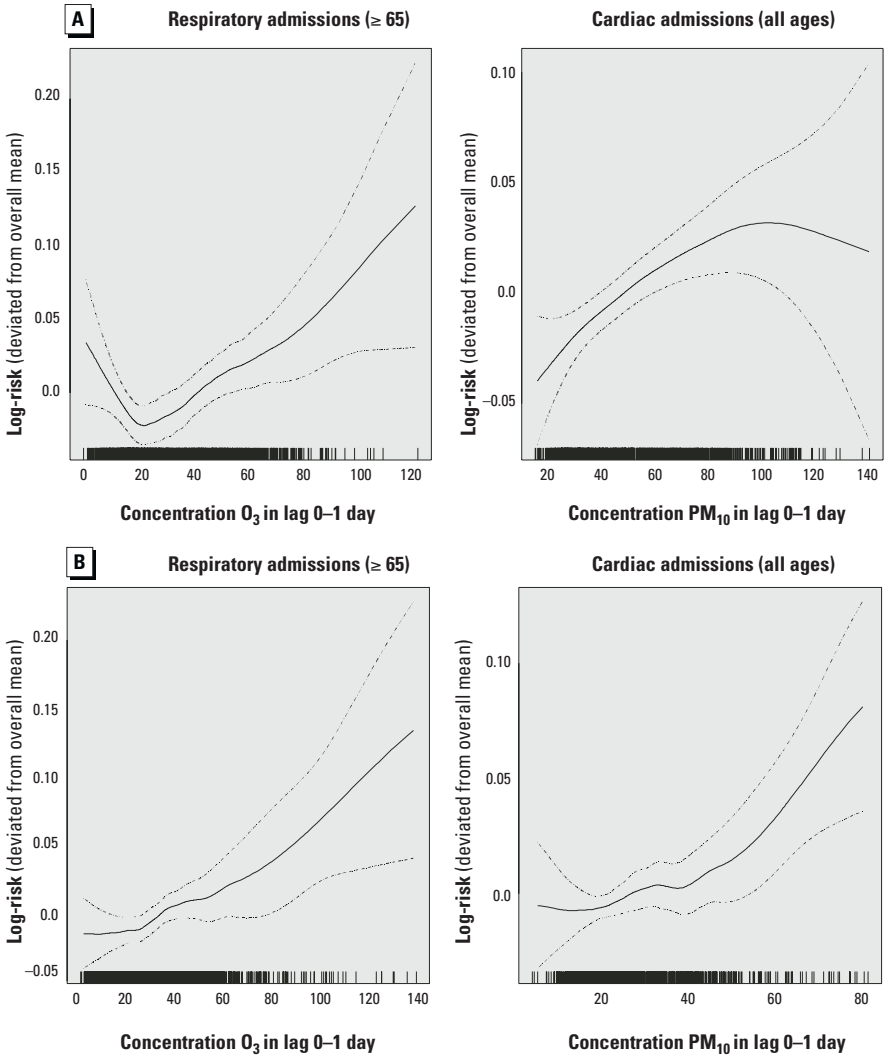

Figure 3. Exposure (μg/m^3) and response relationships for O_3 and respiratory admissions and for PM_{10} and cardiac admissions in (*A*) Hong Kong and (*B*) London. The density of the vertical bars on the *x*-axis shows the distribution of the pollutant concentration data.

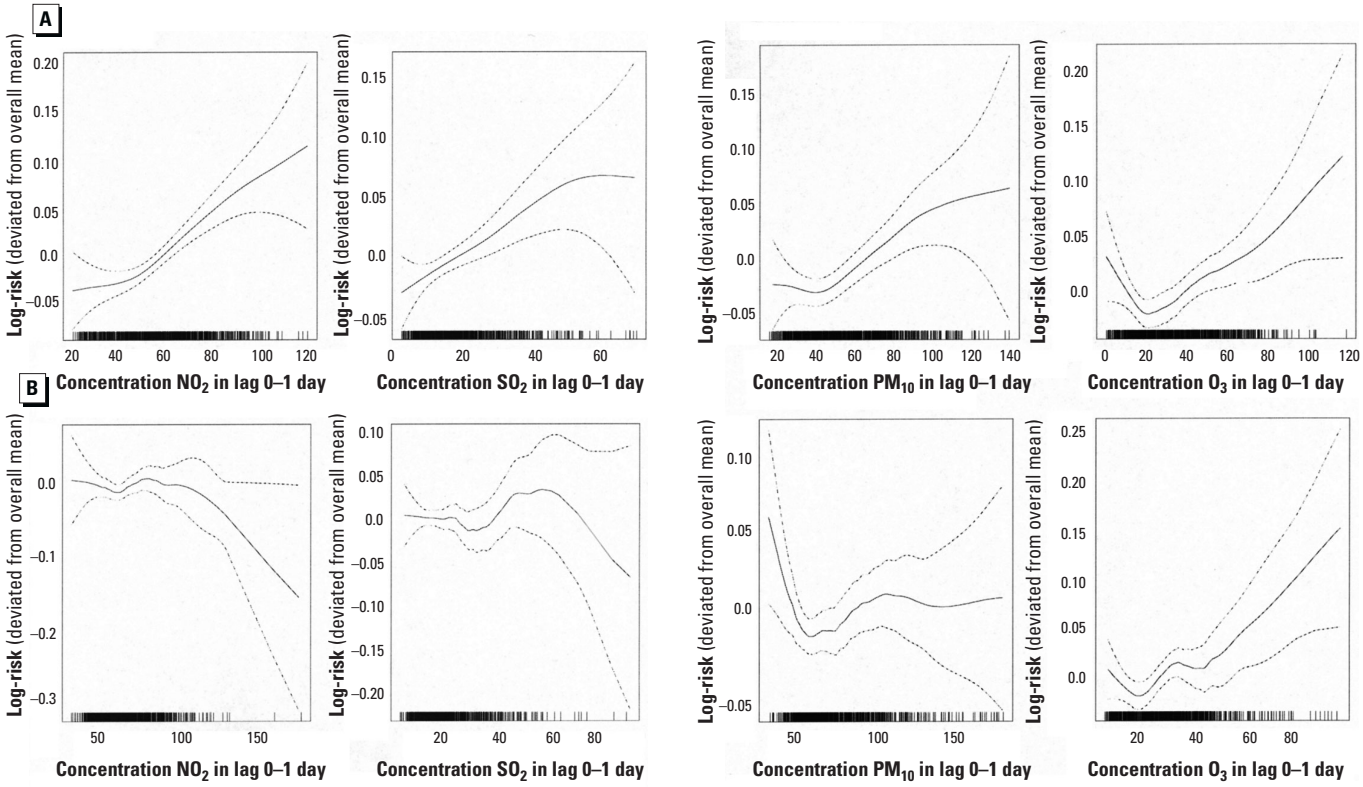

Figure 4. Exposure response curves for respiratory admissions (≥ 65 years of age) in (*A*) Hong Kong and (*B*) London for all pollutants under study.

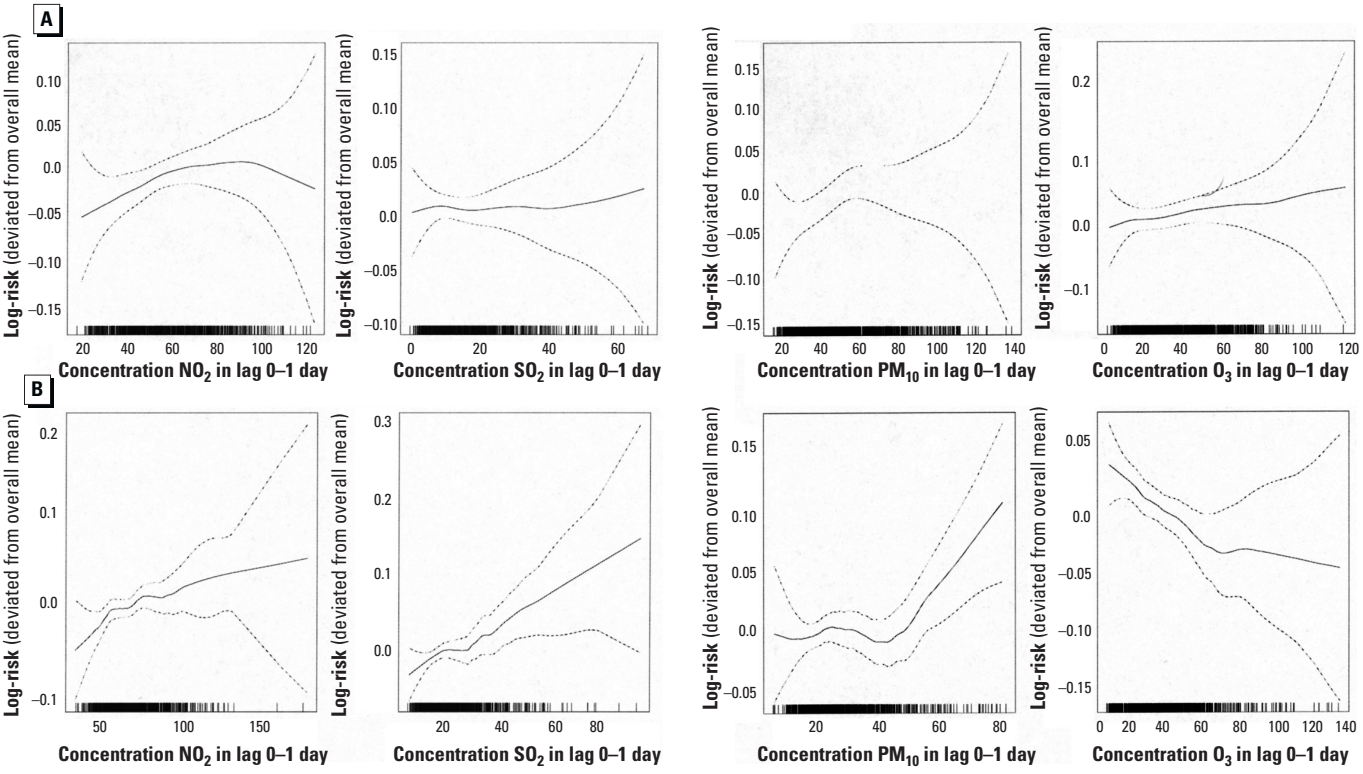

Figure 5. Exposure response curves for IHD (all ages) in (*A*) Hong Kong and (*B*) London for all pollutants under study.

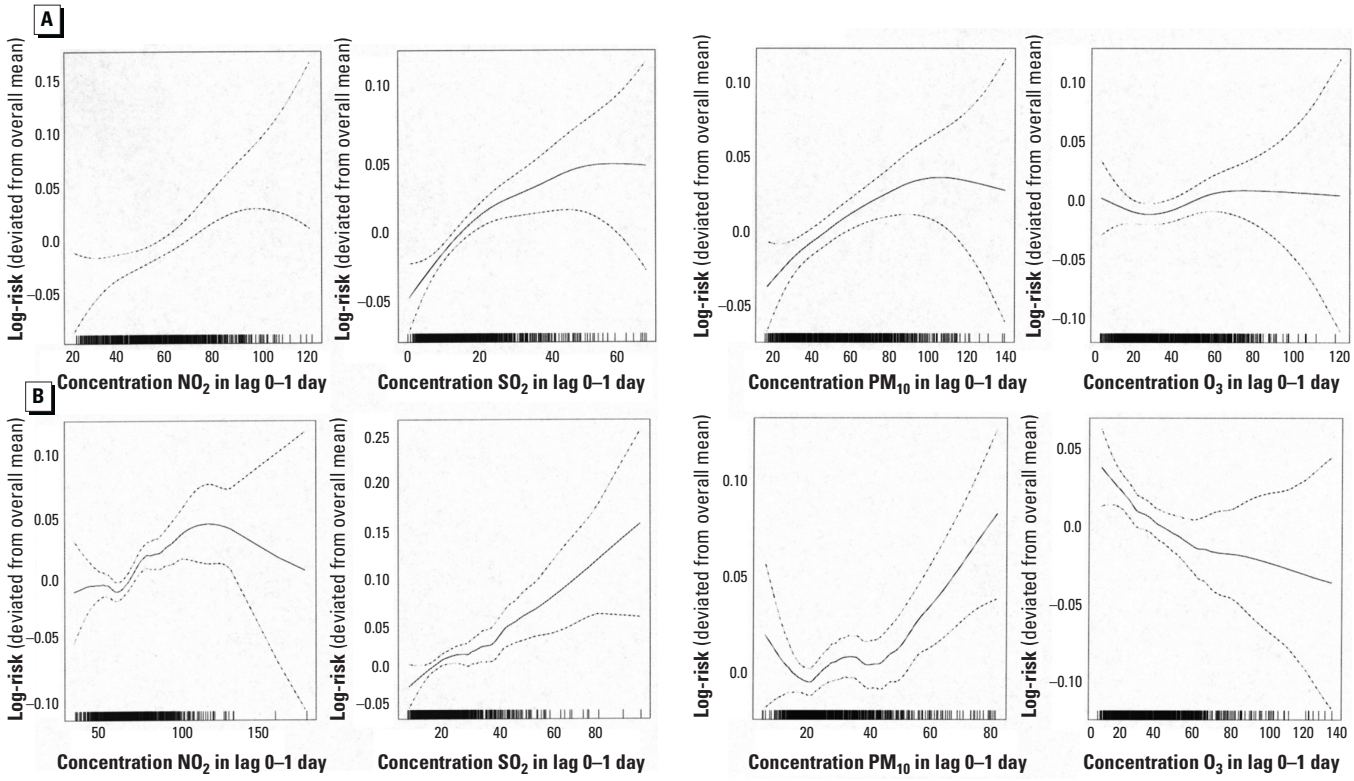

Figure 6. Exposure response curves for cardiac admissions (all ages) in (*A*) Hong Kong and (*B*) London for all pollutants under study.

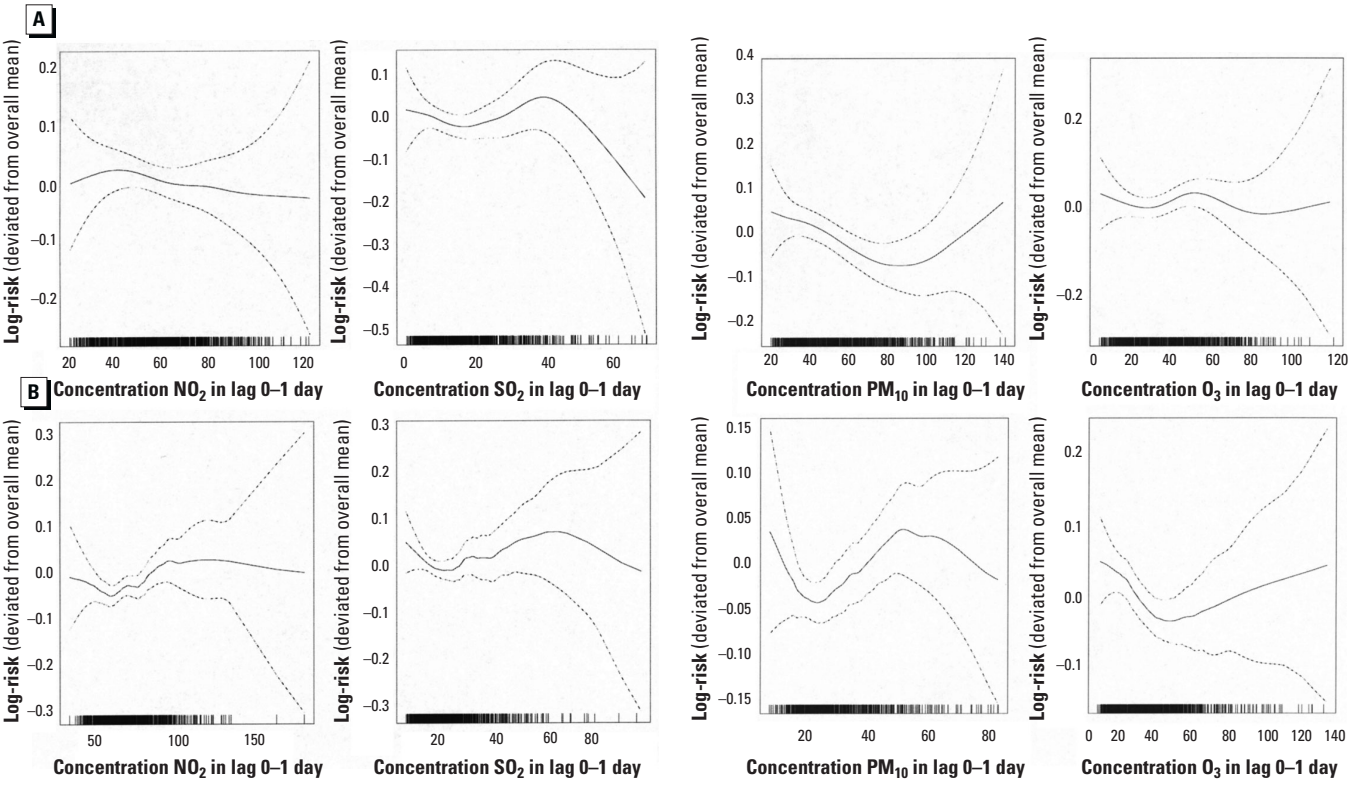

Figure 7. Exposure response curves for asthma (15–64 years of age) in (*A*) Hong Kong and (*B*) London for all pollutants under study.

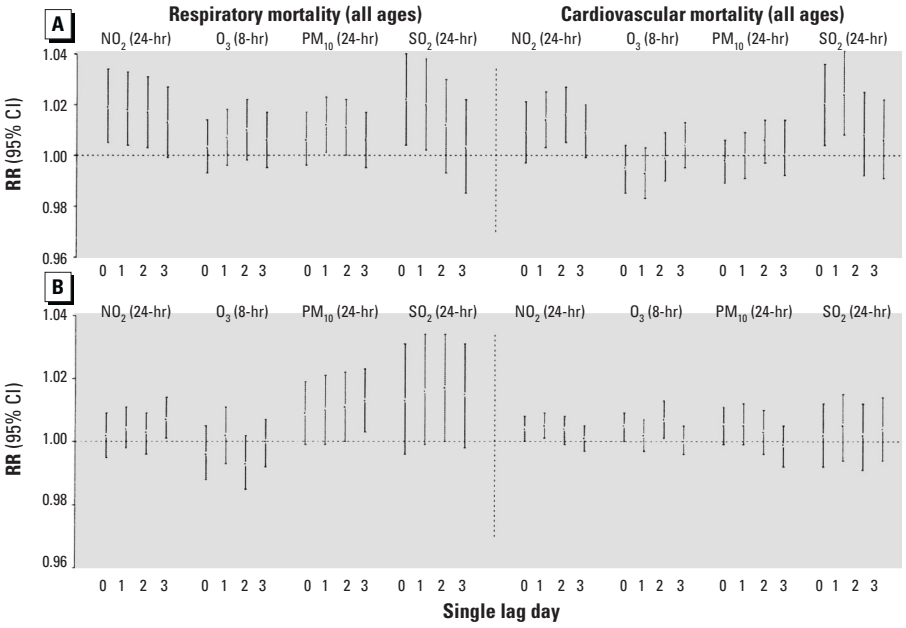

Figure 8. Effect of pollutants at a single day lag on mortality due to cardiovascular and respiratory diseases in (*A*) Hong Kong and (*B*) London. Values shown are relative risk (RR) and 95% confidence interval (CI) for a 10 μg/m^3 increase in concentration.

Relevance of results. The principal aim of this study was to determine if the effects of air pollution on daily hospital admissions are consistent between Hong Kong and London. An important component of causal thinking in observational studies is whether the associations are consistent in widely varying environments. This is one way in which concerns about unknown or inadequately controlled confounding can be addressed. In air pollution time-series studies, this is especially important because other components of causal reasoning such as size of effect, biological plausibility, and coherence are less convincing than many would wish. Hong Kong and London differ markedly in many respects that could affect confounding or effect modification, especially in climate and lifestyle. We have based our comparison on the size, significance, and direction of estimates of effect, lag pattern, exposure–response relationship, and seasonal effects. We conclude overall that there are considerable similarities in the effects of each pollutant, although the explanations for some differences, including a lack of association with asthma admissions in adults in Hong Kong, differences in the lag pattern for all respiratory admissions, and opposite directions of effect for O_3 and cardiac admissions, remain uncertain. Overall, we consider the similarities to outweigh the differences; thus, we conclude that our study strengthens the argument for the causality of air pollution associations with hospital admissions.

The comparison has done less to clarify which component of the pollution mixture is important. The O_3 associations with respiratory disease are at least independent of other pollutants and in line with studies elsewhere. There is also evidence that O_3 is potentially toxic at near ambient levels (*2*). For cardiac admissions, the PM_{10} associations were less independent of NO_2 (and in some cases SO_2) than the reverse. Toxicologic evidence suggests that NO_2 and SO_2 are unlikely to have effects at this level, which points toward them being surrogates for some other toxic component. PM_{10} is widely regarded as important in spite of meagre human toxicologic corroboration. The cities were similar in the proportion of fine particles comprising PM_{10} and in other components such as sulfate (as an indicator of secondary particles) and carbon (as an indicator of primary particles) (*36,39–41*). Our study, like many others, suggests that traffic sources are important but cannot be more specific. Analysis using many, rather than only two, cities may be one way of learning more about the effects of different pollution mixtures (*42*).

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Referencias adicionales de estudios en salud

A continuación se listan referencias adicionales en salud relacionados con el dióxido de azufre:

1. Pope CA *et al.* (2002). Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. Journal of the American Medical Association, 287:1132–1141.

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Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD
Richard T. Burnett, PhD
Michael J. Thun, MD
Eugenia E. Calle, PhD
Daniel Krewski, PhD
Kazuhiko Ito, PhD
George D. Thurston, ScD

Context Associations have been found between day-to-day particulate air pollution and increased risk of various adverse health outcomes, including cardiopulmonary mortality. However, studies of health effects of long-term particulate air pollution have been less conclusive.

Objective To assess the relationship between long-term exposure to fine particulate air pollution and all-cause, lung cancer, and cardiopulmonary mortality.

Design, Setting, and Participants Vital status and cause of death data were collected by the American Cancer Society as part of the Cancer Prevention II study, an ongoing prospective mortality study, which enrolled approximately 1.2 million adults in 1982. Participants completed a questionnaire detailing individual risk factor data (age, sex, race, weight, height, smoking history, education, marital status, diet, alcohol consumption, and occupational exposures). The risk factor data for approximately 500 000 adults were linked with air pollution data for metropolitan areas throughout the United States and combined with vital status and cause of death data through December 31, 1998.

Main Outcome Measure All-cause, lung cancer, and cardiopulmonary mortality.

Results Fine particulate and sulfur oxide–related pollution were associated with all-cause, lung cancer, and cardiopulmonary mortality. Each 10-μg/m^3 elevation in fine particulate air pollution was associated with approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively. Measures of coarse particle fraction and total suspended particles were not consistently associated with mortality.

Conclusion Long-term exposure to combustion-related fine particulate air pollution is an important environmental risk factor for cardiopulmonary and lung cancer mortality.

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Based on several severe air pollution events,[1-3] a temporal correlation between extremely high concentrations of particulate and sulfur oxide air pollution and acute increases in mortality was well established by the 1970s. Subsequently, epidemiological studies published between 1989 and 1996 reported health effects at unexpectedly low concentrations of particulate air pollution.[4] The convergence of data from these studies, while controversial,[5] prompted serious reconsideration of standards and health guidelines[6-10] and led to a long-term research program designed to analyze health-related effects due to particulate pollution.[11-13] In 1997, the Environmental Protection Agency adopted new ambient air quality standards that would impose regulatory limits on fine particles measuring less than 2.5 μm in diameter ($PM_{2.5}$). These new standards were challenged by industry groups, blocked by a federal appeals court, but ultimately upheld by the US Supreme Court.[14]

Although most of the recent epidemiological research has focused on effects of short-term exposures, several studies suggest that long-term exposure may be more important in terms of overall public health.[4] The new standards for long-term exposure to $PM_{2.5}$ were originally based primarily on 2 prospective cohort studies,[15,16] which evaluated the effects of long-term pollution exposure on mortality. Both of these studies have been subjected to much scrutiny,[5] including an extensive independent audit and reanalysis of the original data.[17] The larger of these 2 studies linked individual risk factor and vital status data with national ambient air pollution data.[16] Our analysis uses data from the larger study and

Author Affiliations: Brigham Young University, Provo, Utah (Dr Pope); Health Canada, Ottawa, Ontario (Dr Burnett); University of Ottawa, Ottawa, Ontario (Drs Burnett and Krewski); American Cancer Society, Atlanta, Ga (Drs Thun and Calle); and New York University School of Medicine, Tuxedo, NY (Drs Ito and Thurston).
Corresponding Author and Reprints: C. Arden Pope III, PhD, Department of Economics, Brigham Young University, 142 FOB, Provo, UT 84602 (e-mail: cap3@email.byu.edu).

(1) doubles the follow-up time to more than 16 years and triples the number of deaths; (2) substantially expands exposure data, including gaseous copollutant data and new $PM_{2.5}$ data, which have been collected since the promulgation of the new air quality standards; (3) improves control of occupational exposures; (4) incorporates dietary variables that account for total fat consumption, and consumption of vegetables, citrus, and high-fiber grains; and (5) uses recent advances in statistical modeling, including the incorporation of random effects and nonparametric spatial smoothing components in the Cox proportional hazards model.

METHODS

Study Population

The analysis is based on data collected by the American Cancer Society (ACS) as part of the Cancer Prevention Study II (CPS-II), an ongoing prospective mortality study of approximately 1.2 million adults.[18,19] Individual participants were enrolled by ACS volunteers in the fall of 1982. Participants resided in all 50 states, the District of Columbia, and Puerto Rico, and were generally friends, neighbors, or acquaintances of ACS volunteers. Enrollment was restricted to persons who were aged 30 years or older and who were members of households with at least 1 individual aged 45 years or older. Participants completed a confidential questionnaire, which included questions about age, sex, weight, height, smoking history, alcohol use, occupational exposures, diet, education, marital status, and other characteristics.

Vital status of study participants was ascertained by ACS volunteers in September of the following years: 1984, 1986, and 1988. Reported deaths were verified with death certificates. Subsequently, through December 31, 1998, vital status was ascertained through automated linkage of the CPS-II study population with the National Death Index.[19] Ascertainment of deaths was more than 98% complete for the period of 1982-1988 and 93% complete after 1988.[19] Death certificates or codes for cause of death were obtained for more than 98% of all known deaths. Cause of death was coded according to the *International Classification of Diseases, Ninth Revision (ICD-9)*. Although the CPS-II cohort included approximately 1.2 million participants with adequate questionnaire and cause-of-death data, our analysis was restricted to those participants who resided in US metropolitan areas with available pollution data. The actual size of the analytic cohort varied depending on the number of metropolitan areas for which pollution data were available. TABLE 1 provides the number of metropolitan areas and participants available for each source of pollution data.

Air Pollution Exposure Estimates

Each participant was assigned a metropolitan area of residence based on address at time of enrollment and 3-digit ZIP code area.[20] Mean (SD) concentrations of air pollution for the metropolitan areas were compiled from various primary data sources (Table 1). Many of the particulate pollution indices, including $PM_{2.5}$, were available from data from the Inhalable Particle Monitoring Network for 1979-1983 and data from the National Aerometric Database for 1980-1981, periods just prior to or at the beginning of the follow-up period. An additional data source was the Environmental Protection Agency Aerometric Information Retrieval System (AIRS). The mean concentration of each pollutant from all available monitoring sites was calculated for each metropolitan area during the 1 to 2 years prior to enrollment.[17]

Additional information on ambient pollution during the follow-up period was extracted from the AIRS database as quarterly mean values for each routinely monitored pollutant for 1982 through 1998. All quarterly averages met summary criteria imposed by the Environmental Protection Agency and were based on observations made on at least 50% of the scheduled sampling days at each site. The quarterly mean values for all stations in each metropolitan area were calculated across the study years using daily average values for each pollutant except ozone. For ozone, daily 1-hour maximums were used and were calculated for the full year and for the third quarter only (ie, July, August, September). While gaseous pollutants generally had recorded data throughout the entire follow-up period of interest, the particulate matter monitoring protocol changed in the late 1980s from total suspended particles to particles measuring less than 10 μm in diameter (PM_{10}), resulting in the majority of total suspended particle data being available in the early to mid-1980s and PM_{10} data being mostly available in the early to mid-1990s.

As a consequence of the new $PM_{2.5}$ standard, a large number of sites began collecting $PM_{2.5}$ data in 1999. Daily $PM_{2.5}$ data were extracted from the AIRS database for 1999 and the first 3 quarters of 2000. For each site, quarterly averages for each of the 2 years were computed. The 4 quarters were averaged when at least 1 of the 2 corresponding quarters for each year had at least 50% of the sixth-day samples and at least 45 total sampling days available. Measurements were averaged first by site and then by metropolitan area. Although no network of $PM_{2.5}$ monitoring existed in the United States between the early 1980s and the late 1990s, the integrated average of $PM_{2.5}$ concentrations during the period was estimated by averaging the $PM_{2.5}$ concentration for early and later periods.

Mean sulfate concentrations for 1980-1981 were available for many cities based on data from the Inhalable Particle Monitoring Network and the National Aerometric Database. Recognizing that sulfate was artifactually overestimated due to glass fiber filters used at that time, season and region-specific adjustments were made.[17] Since few states analyzed particulate samples for sulfates after the early 1980s, individual states were directly contacted for data regarding filter use. Ion chromatography was used to analyze PM_{10} filters and this data could be obtained from metropolitan areas across the

United States. Filters were collected for a single reference year (1990) in the middle of the 1982-1998 study period. The use of quartz filters virtually eliminated the historical overestimation of sulfate. Mean sulfate concentrations for 1990 were estimated using sulfate from AIRS, data reported directly from individual states, and analysis of archived filters.

Statistical Analysis

The basic statistical approach used in this analysis is an extension of the standard Cox proportional hazards survival model,[21] which has been used for risk estimates of pollution-related mortality in previous longitudinal cohort studies.[15,16] The standard Cox model implicitly assumes that observations are statistically independent after controlling for available risk factors, resulting in 2 concerns with regard to risk estimates of pollution-related mortality.[22] First, if the assumption of statistical independence is not valid, the uncertainty in the risk estimates of pollution-related mortality may be misstated. Second, even after controlling for available risk factors, survival times of participants living in communities closer together may be more similar than participants living in communities farther apart, which results in spatial autocorrelation. If this spatial autocorrelation is due to missing or systematically mismeasured risk factors that are spatially correlated with air pollution, then the risk estimates of pollution-related mortality may be biased due to inadequate control of these factors. Therefore, in this analysis, the Cox proportional hazards model was extended by incorporating a spatial random-effects component, which provided accurate es-

Table 1. Summary of Alternative Pollution Indices*

Pollutant (Years of Data Collection)	Units	Source of Data	Data Compilation Team†	No. of Metropolitan Areas	No. of Participants, in Thousands	Mean (SD)
$PM_{2.5}$	$\mu g/m^3$					
1979-1983		IPMN	HEI	61	359	21.1 (4.6)
1999-2000		AIRS	NYU	116	500	14.0 (3.0)
Average				51	319	17.7 (3.7)
PM_{10}	$\mu g/m^3$					
1982-1998		AIRS	NYU	102	415	28.8 (5.9)
PM_{15}	$\mu g/m^3$					
1979-1983		IPMN	HEI	63	359	40.3 (7.7)
$PM_{15-2.5}$	$\mu g/m^3$					
1979-1983		IPMN	HEI	63	359	19.2 (6.1)
Total suspended particles	$\mu g/m^3$					
1980-1981		NAD	HEI	156	590	68.0 (16.7)
1979-1983		IPMN	HEI	58	351	73.7 (14.3)
1982-1998		AIRS	NYU	150	573	56.7 (13.1)
Sulfate	$\mu g/m^3$					
1980-1981		IPMN and NAD, artifact adjusted	HEI	149	572	6.5 (2.8)
1990		Compilation and analysis of PM_{10} filters	NYU	53	269	6.2 (2.0)
Sulfur dioxide	ppb	AIRS				
1980			HEI	118	520	9.7 (4.9)
1982-1998			NYU	126	539	6.7 (3.0)
Nitrogen dioxide	ppb	AIRS				
1980			HEI	78	409	27.9 (9.2)
1982-1998			NYU	101	493	21.4 (7.1)
Carbon monoxide	ppm	AIRS				
1980			HEI	113	519	1.7 (0.7)
1982-1998			NYU	122	536	1.1 (0.4)
Ozone	ppb	AIRS				
1980			HEI	134	569	47.9 (11.0)
1982-1998			NYU	119	525	45.5 (7.3)
1982-1998‡			NYU	134	557	59.7 (12.8)

*$PM_{2.5}$ indicates particles measuring less than 2.5 μm in diameter; PM_{10}, particles measuring less than 10 μm in diameter; PM_{15}, particles measuring less than 15 μm in diameter; $PM_{15-2.5}$, particles measuring between 2.5 and 15 μm in diameter; $\mu g/m^3$, micrograms per cubic meter; ppb, parts per billion; ppm, parts per million; IPMN, Inhalable Particle Monitoring Network; AIRS, Aerometric Information Retrieval System [Environmental Protection Agency]; and NAD, National Aerometric Database.
†HEI indicates data were compiled by the Health Effects Institute reanalysis team, which was previously published.[17] NYU indicates data were compiled at the New York University School of Medicine, Nelson Institute of Environmental Medicine (K.I. and G.D.T.).
‡Daily 1-hour maximums were used. Values were calculated only for the third quarter (ie, July, August, September).

timates of the uncertainty of effect estimates. The model also evaluated spatial autocorrelation and incorporated a nonparametric spatial smooth component (to account for unexplained spatial structure). A more detailed description of this modeling approach is provided elsewhere.[22]

The baseline analysis in this study estimated adjusted relative risk (RR) ratios for mortality by using a Cox proportional hazards model with inclusion of a metropolitan-based random-effects component. Model fitting involved a 2-stage process. In the first stage, survival data were modeled using the standard Cox proportional hazards model, including individual level covariates and indicator variables for each metropolitan area (without pollution variables). Output from stage 1 provided estimates of the metropolitan-specific logarithm of the RRs of mortality (relative to an arbitrary reference community), which were adjusted for individual risk factors. The correlation between these values, which was induced by using the same reference community, was then removed.[23] In the second stage, the estimates of adjusted metropolitan-specific health responses were related to fine particulate air pollution using a linear random-effects regression model.[24] The time variable used in the models was survival time from the date of enrollment. Survival times of participants who did not die were censored at the end of the study period. To control for age, sex, and race, all of the models were stratified by 1-year age categories, sex, and race (white vs other), which allowed each category to have its own baseline hazard. Models were estimated for all-cause mortality and for 3 separate mortality categories: cardiopulmonary (*ICD-9* 401-440 and 460-519), lung cancer (*ICD-9* 162), and all others.

Models were estimated separately for each of the 3 fine particle variables, $PM_{2.5}$ (1979-1983), $PM_{2.5}$ (1999-2000), and $PM_{2.5}$ (average). Individual level covariates were included in the models to adjust for various important individual risk factors. All of these variables were classified as either indicator (ie, yes/no, binary, dummy) variables or continuous variables. Variables used to control for tobacco smoke, for example, included both indicator and continuous variables. The smoking indicator variables included: current cigarette smoker, former cigarette smoker, and a pipe or cigar smoker only (all vs never smoking) along with indicator variables for starting smoking before or after age 18 years. The continuous smoking variables included: current smoker's years of smoking, current smoker's years of smoking squared, current smoker's cigarettes per day, current smoker's cigarettes per day squared, former smoker's years of smoking, former smoker's years of smoking squared, former smoker's cigarettes per day, former smoker's cigarettes per day squared, and the number of hours per day exposed to passive cigarette smoke.

To control for education, 2 indicator variables, which indicated completion of high school or education beyond high school, were included. Marital status variables included indicator variables for single and other vs married. Both body mass index (BMI) values and BMI values squared were included as continuous variables. Indicator variables for beer, liquor, and wine drinkers and nonresponders vs nondrinkers were included to adjust for alcohol consumption. Occupational exposure was controlled for using various indicator variables: regular occupational exposure to asbestos, chemicals/acids/solvents, coal or stone dusts, coal tar/pitch/asphalt, diesel engine exhaust, or formaldehyde, and additional indicator variables that indicated 9 different rankings of an occupational dirtiness index that has been developed and described elsewhere.[17,25] Two diet indices that accounted for fat consumption and consumption of vegetables, citrus, and high-fiber grains were derived based on information given in the enrollment questionnaire.[18] Quintile indicator variables for each of these diet indices were also included in the models.[18]

In addition to the baseline analysis, several additional sets of analysis were conducted. First, to more fully evaluate the shape of the concentration-response function, a robust locally weighted regression smoother[26] (within the generalized additive model framework[27]) was used to estimate the relationship between particulate air pollution and mortality in the second stage of model fitting. Second, the sensitivity of the fine particle mortality risk estimates compared with alternative modeling approaches and assumptions was evaluated. Standard Cox proportional hazards models were fit to the data including particulate air pollution as a predictor of mortality and sequentially adding (in a controlled forward stepwise process) groups of variables to control for smoking, education, marital status, BMI, alcohol consumption, occupational exposures, and diet.

In addition, to evaluate the sensitivity of the estimated pollution effect while more aggressively controlling for spatial differences in mortality, a 2-dimensional term to account for spatial trends was added to the models and was estimated using a locally weighted regression smoother. The "span" parameter, which controls the complexity of the surface smooth, was set at 3 different settings to allow for increasingly aggressive fitting of the spatial structure. These included a default span of 50%, the span that resulted in the lowest unexplained variance in mortality rate between metropolitan areas, and the span that resulted in the strongest evidence (highest *P* value) to suggest no residual spatial structure. The risk estimates and SEs (and thus the confidence intervals) were estimated using generalized additive modeling[27] with S-Plus statistical software,[28] which provides unbiased effect estimates, but may underestimate SEs if there is significant spatial autocorrelation and significant correlations between air pollution and the smoothed surface of mortality. Therefore, evidence of spatial autocorrelation was carefully evaluated and tested using the Bartlett test.[29] The correlations of residual mortality

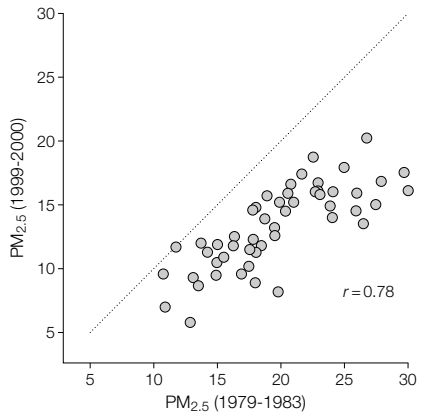
with distance between metropolitan areas were graphically examined.

Analyses were also conducted of effect modification by age, sex, smoking status, occupational exposure, and education. Finally, models were fit using a variety of alternative pollution indices, including gaseous pollutants. Specifically, models were estimated separately for each of the pollution variables listed in Table 1, while also including all of the other risk factor variables.

RESULTS

Fine particulate air pollution generally declined in the United States during the follow-up period of this study. FIGURE 1 plots mean $PM_{2.5}$ concentrations for 1999-2000 over mean $PM_{2.5}$ concentrations for 1979-1983 for the 51 cities in which paired data were available. The concentrations of $PM_{2.5}$ were lower in 1999-2000 than in 1979-1983 for most cities, with the largest reduction observed in the cities with the highest concentrations of pollution during 1979-1983. Mean $PM_{2.5}$ levels in the 2 periods were highly correlated (r=0.78). The rank ordering of cities by relative pollution levels remained nearly the same. Therefore, the relative levels of fine particle concentrations were similar whether based on measurements at the beginning of the study period, shortly following the study period, or an average of the 2.

Figure 1. Mean Fine Particles Measuring Less Than 2.5 µm in Diameter ($PM_{2.5}$)



Mean $PM_{2.5}$ concentrations in micrograms per meters cubed for 1999-2000 are plotted along with concentrations for 1979-1983 for the 51 metropolitan areas with paired pollution data. The dotted line is a reference 45°-equality line.

As reported in TABLE 2, all 3 indices of fine particulate air pollution were associated with all-cause, cardiopulmonary, and lung cancer mortality, but not mortality from all other causes combined. FIGURE 2 presents the nonparametric smoothed exposure response relationships between cause-specific mortality and $PM_{2.5}$ (average). The log RRs for all-cause, cardiopulmonary, and lung cancer mortality increased across the gradient of fine particulate matter. Goodness-of-fit tests indicated that the associations were not significantly different from linear associations (P>.20).

The fine particle mortality RR ratios from various alternative modeling approaches and assumptions are presented in FIGURE 3. After controlling for smoking, education, and marital status, the controlled forward stepwise inclusion of additional covariates had little influence on the estimated associations with fine particulate air pollution on cardiopulmonary and lung cancer mortality. As expected, cigarette smoking was highly significantly associated with elevated risk of all-cause, cardiopulmonary, and lung cancer mortality (P<.001). Estimated RRs for an average current smoker (men and women combined, 22 cigarettes/day for 33.5 years, with initiation before age 18 years) were equal to 2.58, 2.89, and 14.80 for all-cause, cardiopulmonary, and lung cancer mortality, respectively. Statistically significant, but substantially smaller and less robust associations, were also observed for education, marital status, BMI, alcohol consumption, occupational exposure, and diet variables. Although many of these covariates were also statistically associated with mortality, the risk estimates of pollution-related mortality were not highly sensitive to the inclusion of these additional covariates.

Figure 3 also demonstrates that the introduction of the random-effects component to the model resulted in larger SEs of the estimates and, therefore, somewhat wider 95% confidence intervals. There was no evidence of statistically significant spatial autocorrelation in the survival data based on the Bartlett test (P>.20) after controlling for fine particulate air pollution and the various individual risk factors. Furthermore, graphical examination of the correlations of the residual mortality with distance between metropolitan areas did not reveal significant spatial autocorrelation (results not shown). Nevertheless, the incorporation of spatial smoothing was included to further investigate the robustness of the estimated particulate pollution effect. Effect estimates were not highly sensitive to the incorporation of spatial smoothing to account for regional clustering or other spatial patterns in the data.

FIGURE 4 presents fine particle air pollution–related mortality RR ratios after stratifying by age, sex, education, and smoking status, and adjusting for all other risk factors. The differences across age and sex strata were not generally consistent or statistically significant. However, a consistent pattern emerged from this stratified analysis: the association with particulate pollution was stronger for both cardiopulmo-

Table 2. Adjusted Mortality Relative Risk (RR) Associated With a 10-µg/m³ Change in Fine Particles Measuring Less Than 2.5 µm in Diameter

	Adjusted RR (95% CI)*		
Cause of Mortality	1979-1983	1999-2000	Average
All-cause	1.04 (1.01-1.08)	1.06 (1.02-1.10)	1.06 (1.02-1.11)
Cardiopulmonary	1.06 (1.02-1.10)	1.08 (1.02-1.14)	1.09 (1.03-1.16)
Lung cancer	1.08 (1.01-1.16)	1.13 (1.04-1.22)	1.14 (1.04-1.23)
All other cause	1.01 (0.97-1.05)	1.01 (0.97-1.06)	1.01 (0.95-1.06)

*Estimated and adjusted based on the baseline random-effects Cox proportional hazards model, controlling for age, sex, race, smoking, education, marital status, body mass, alcohol consumption, occupational exposure, and diet. CI indicates confidence interval.

nary and lung cancer mortality for participants with less education. Also, for both cardiopulmonary and lung cancer mortality, the RR estimates were higher for nonsmokers.

FIGURE 5 summarizes the associations between mortality risk and air pollutant concentrations listed in Table 1. Statistically significant and relatively consistent mortality associations existed for all measures of fine particulate exposure, including $PM_{2.5}$ and sulfate particles. Weaker less consistent mortality associations were observed with PM_{10} and PM_{15}. Measures of the coarse particle fraction ($PM_{15\text{-}2.5}$) and total suspended particles were not consistently associated with mortality. Of the gaseous pollutants, only sulfur dioxide was associated with elevated mortality risk. Interestingly, measures of $PM_{2.5}$ were associated with all-cause cardiopulmonary, and lung cancer mortality, but not with all other mortality. However, sulfur oxide pollution (as measured by sulfate particles and/or sulfur dioxide) was significantly associated with mortality from all other causes in addition to all-cause, cardiopulmonary, and lung cancer mortality.

COMMENT

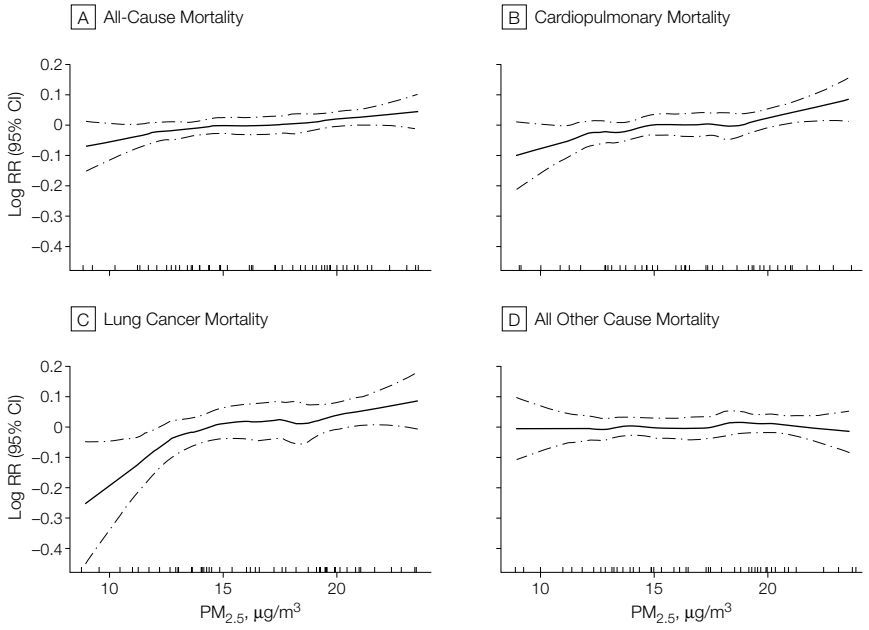
This study demonstrated associations between ambient fine particulate air pollution and elevated risks of both cardiopulmonary and lung cancer mortality. Each 10-μg/m^3 elevation in long-term average $PM_{2.5}$ ambient concentrations was associated with approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively, although the magnitude of the effect somewhat depended on the time frame of pollution monitoring. In addition, this analysis addresses many of the important questions concerning the earlier, more limited analysis of the large CPS-II cohort, including the following issues.

First, does the apparent association between pollution and mortality persist with longer follow-up and as the cohort ages and dies? The present analysis more than doubled the follow-up time to more than 16 years, resulting in approximately triple the number of deaths, yet the associations between pollution and mortality persisted.

Second, can the association between fine particulate air pollution and increased cardiopulmonary and lung cancer mortality be due to inadequate control of important individual risk factors? After aggressively controlling for smoking, the estimated fine particulate pollution effect on mortality was remarkably robust. When the analysis was stratified by smoking status, the estimated pollution effect on both cardiopulmonary and lung cancer mortality was strongest for never smokers vs former or current smokers. This analysis also controlled for education, marital status, BMI, and alcohol consumption. This analysis used improved variables to control for occupational exposures and incorporated diet variables that accounted for total fat consumption, as well as for consumption of vegetables, citrus, and high-fiber grains. The mortality associations with fine particulate air pollution were largely unaffected by the inclusion of these individual risk factors in the models. The data on smoking and other individual risk factors, however, were obtained directly by questionnaire at time of enrollment and do not reflect changes that may have occurred following enrollment. The lack of risk factor follow-up data results in some misclassification of exposure, reduces the precision of control for risk factors, and constrains our ability to differentiate time dependency.

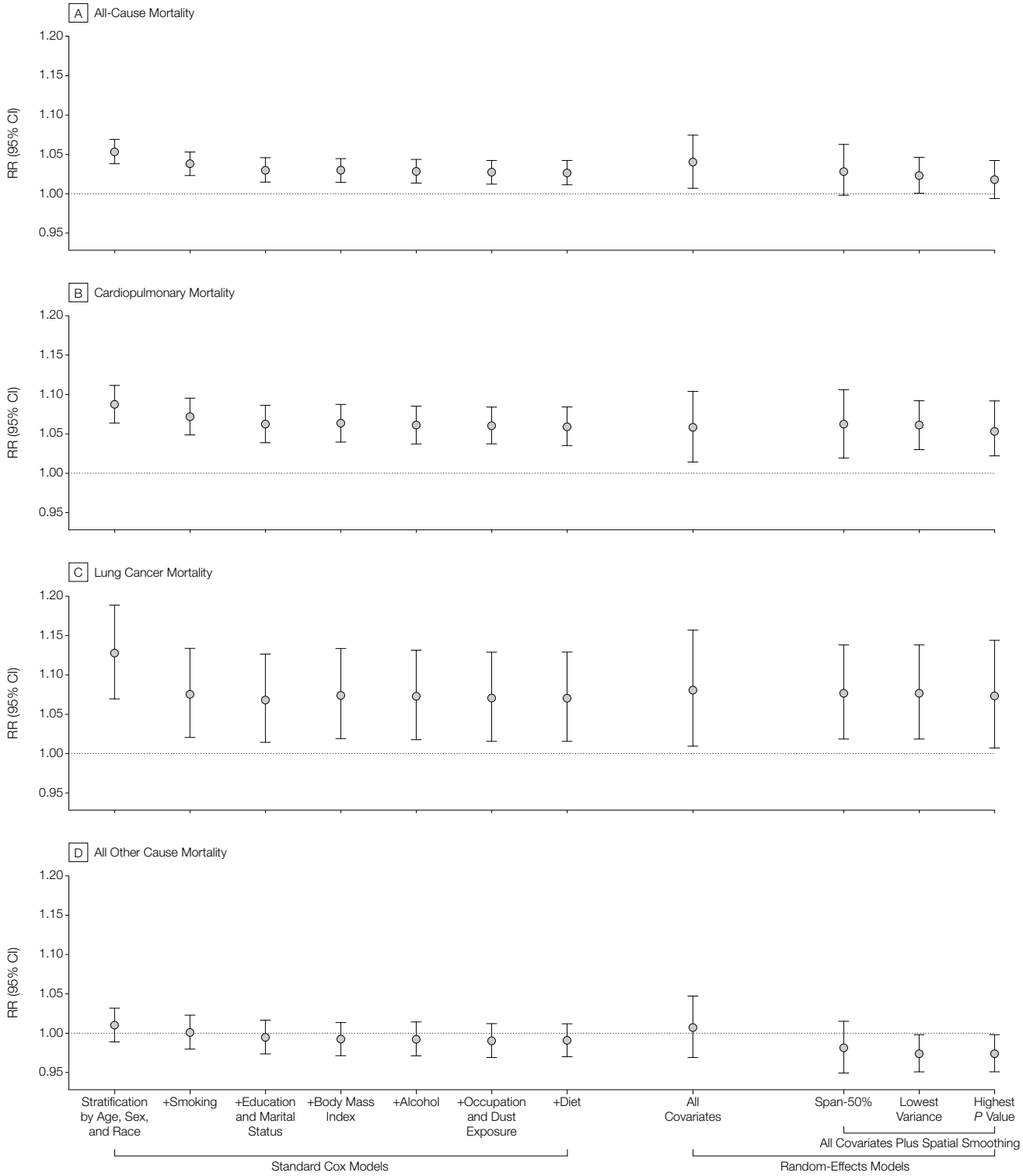
Third, are the associations between fine particulate air pollution and mortality due to regional or other spatial differences that are not adequately controlled for in the analysis? If there are unmeasured or inadequately modeled risk factors that are different across locations, then spatial clustering will occur. If this clustering is independent or random across metropolitan areas, then the spatial clustering can be modeled by adding a random-effects component to the Cox proportional hazards model as was done in our analysis. The clustering may not be independent or random across metropolitan areas due to inadequately measured or modeled

Figure 2. Nonparametric Smoothed Exposure Response Relationship



Vertical lines along x-axes indicate rug or frequency plot of mean fine particulate pollution; $PM_{2.5}$, mean fine particles measuring less than 2.5 μm in diameter; RR, relative risk; and CI, confidence interval.

Figure 3. Mortality Relative Risk (RR) Ratio Associated With 10-μg/m³ Differences of $PM_{2.5}$ Concentrations



Data presented are for 1979-1983 for the different causes of death, with various levels of controlling for individual risk factors, and using alternative modeling approaches. The 3 models with spatial smoothing allow for increasingly aggressive fitting of the spatial structure. Plus sign indicates model included previous variables (ie, smoking included stratification by age, sex, and race); $PM_{2.5}$, mean fine particles measuring less than 2.5 μm in diameter; and CI, confidence interval.

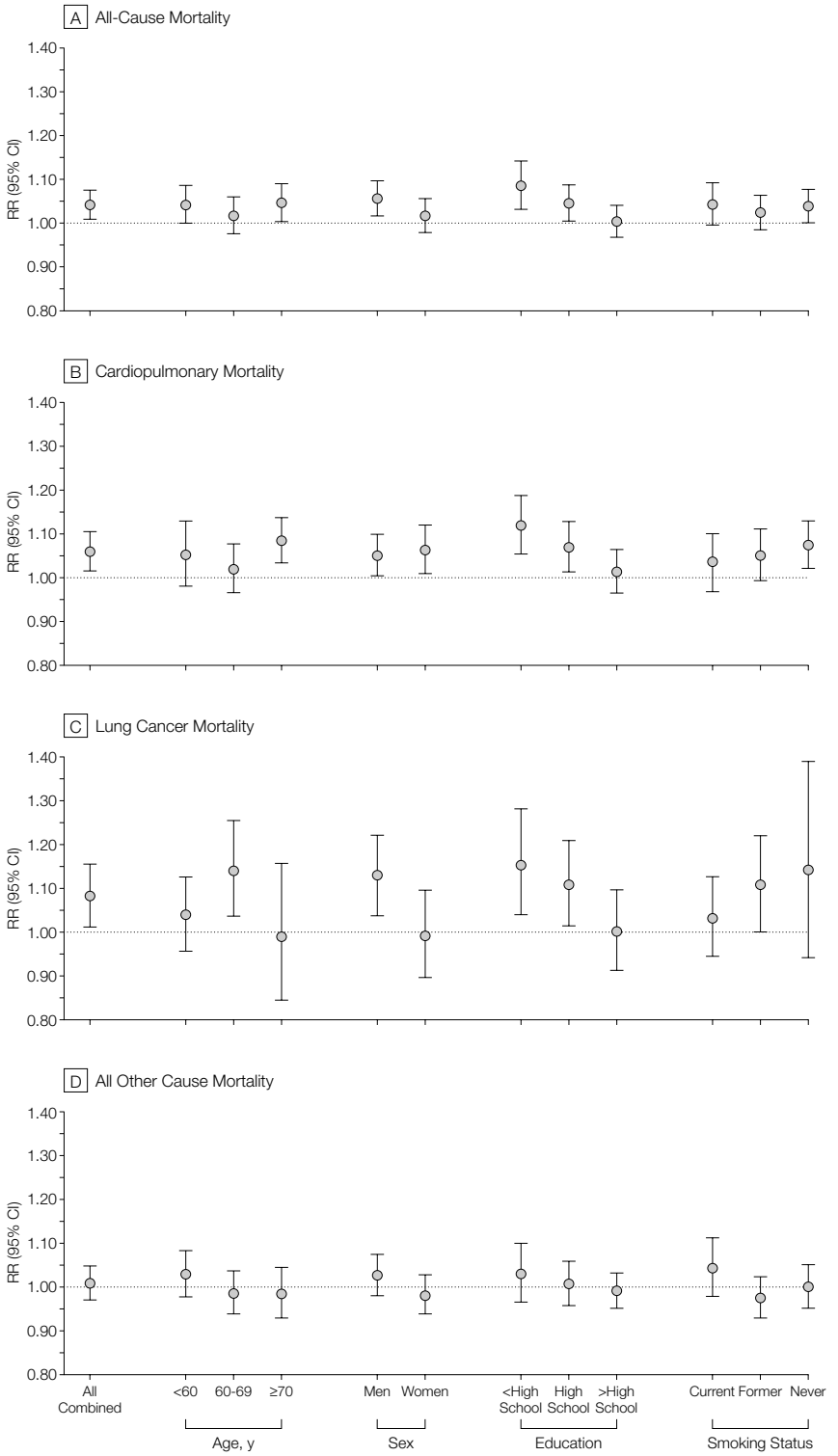
risk factors (either individual or ecological). If these inadequately measured or modeled risk factors are also spatially correlated with air pollution, then biased pollution effects estimates may occur due to confounding. However, in this analysis, significant spatial autocorrelation was not observed after controlling for fine particulate air pollution and the various individual risk factors. Furthermore, to minimize any potential confounding bias, sensitivity analyses, which directly modeled spatial trends using nonparametric smoothing techniques, were conducted. A contribution of this analysis is that it included the incorporation of both random effects and nonparametric spatial smoothing components to the Cox proportional hazards model. Even after accounting for random effects across metropolitan areas and aggressively modeling a spatial structure that accounts for regional differences, the association between fine particulate air pollution and cardiopulmonary and lung cancer mortality persists.

Fourth, is mortality associated primarily with fine particulate air pollution or is mortality also associated with other measures of particulate air pollution, such as PM_{10}, total suspended particles, or with various gaseous pollutants? Elevated mortality risks were associated primarily with measures of fine particulate and sulfur oxide pollution. Coarse particles and gaseous pollutants, except for sulfur dioxide, were generally not significantly associated with elevated mortality risk.

Fifth, what is the shape of the concentration-response function? Within the range of pollution observed in this analysis, the concentration-response function appears to be monotonic and nearly linear. However, this does not preclude a leveling off (or even steepening) at much higher levels of air pollution.

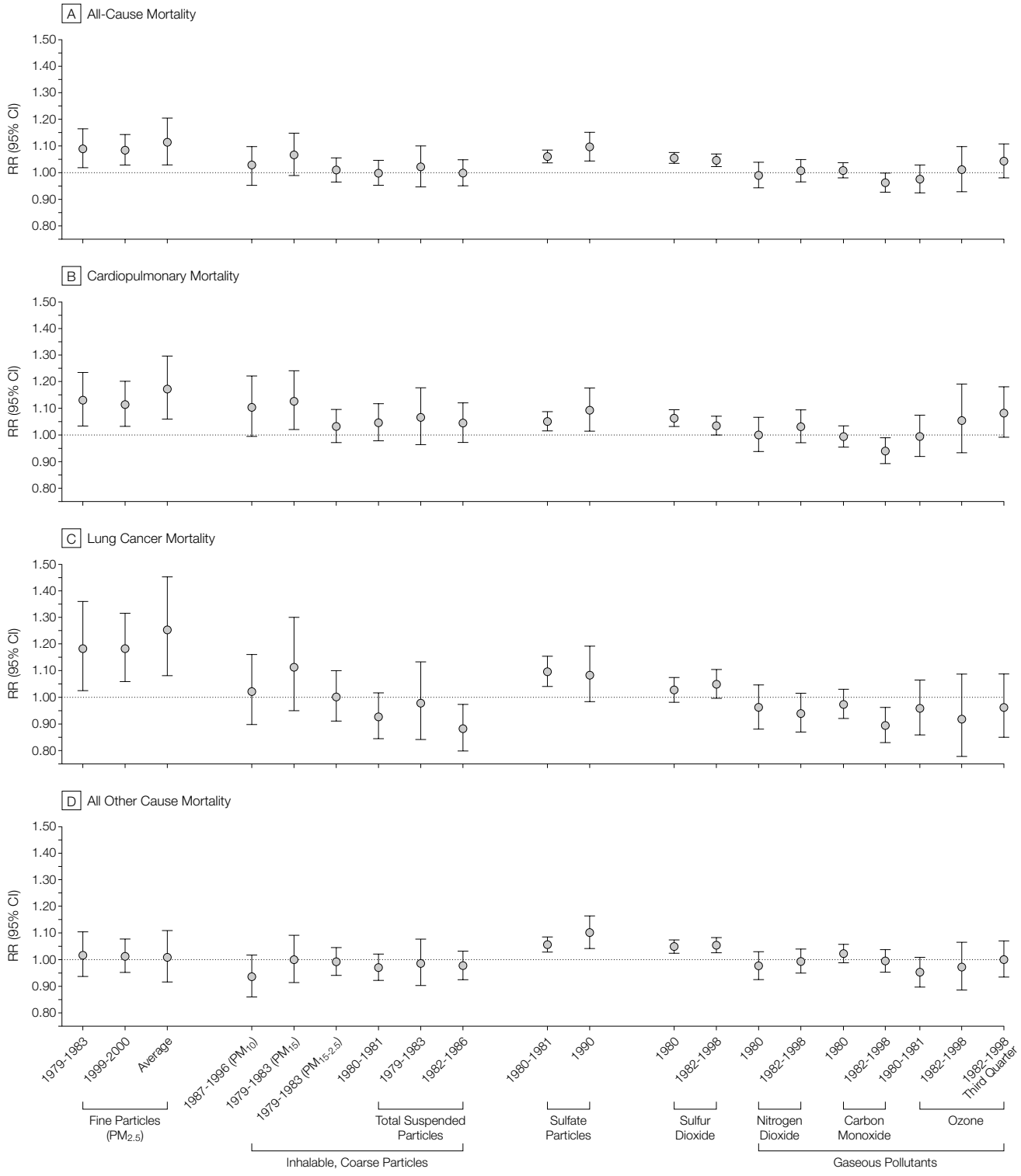
Sixth, how large is the estimated mortality effect of exposure to fine particulate air pollution relative to other risk factors? A detailed description and interpretation of the many individual risk factors that are controlled for in the analysis goes well beyond the scope of

Figure 4. Adjusted Mortality Relative Risk (RR) Ratio Associated With 10-μg/m³ Differences of $PM_{2.5}$ Concentrations



Data presented are for 1979-1983 for the different causes of death stratified by age, sex, education, and smoking status. $PM_{2.5}$ indicates mean fine particles measuring less than 2.5 μm in diameter; CI, confidence interval.

Figure 5. Adjusted Mortality Relative Risk (RR) Ratio Evaluated at Subject-Weighted Mean Concentrations



$PM_{2.5}$ indicates particles measuring less than 2.5 μm in diameter; PM_{10}, particles measuring less than 10 μm in diameter; PM_{15}, particles measuring less than 15 μm in diameter; $PM_{15\text{-}2.5}$, particles measuring between 2.5 and 15 μm in diameter; and CI, confidence interval.

this report. However, the mortality risk associated with cigarette smoking has been well documented using the CPS-II cohort.[16] The risk imposed by exposure to fine particulate air pollution is obviously much smaller than the risk of cigarette smoking. Another risk factor that has been well documented using the CPS-II cohort data is body mass as measured by BMI.[30] The Word Health Organization has categorized BMI values between 18.5-24.9 kg/m^2 as normal; 25-29.9 kg/m^2, grade 1 overweight; 30-39.9 kg/m^2, grade 2 overweight; and 40 kg/m^2 or higher, grade 3 overweight.[31] In the present analysis, BMI values and BMI values squared were included in the proportional hazards models. Consistent with previous ACS analysis,[30] BMI was significantly associated with mortality, optimal BMI was between approximately 23.5 and 24.9 kg/m^2, and the RR of mortality for different BMI values relative to the optimal were dependent on sex and smoking status. For example, the RRs associated with BMI values between 30.0 and 31.9 kg/m^2 (vs optimal) would be up to approximately 1.33 for never smokers. Based on these calculations, mortality risks associated with fine particulate air pollution at levels found in more polluted US metropolitan areas are less than those associated with substantial obesity (grade 3 overweight), but comparable with the estimated effect of being moderately overweight (grade 1 to 2).

In conclusion, the findings of this study provide the strongest evidence to date that long-term exposure to fine particulate air pollution common to many metropolitan areas is an important risk factor for cardiopulmonary mortality. In addition, the large cohort and extended follow-up have provided an unprecedented opportunity to evaluate associations between air pollution and lung cancer mortality. Elevated fine particulate air pollution exposures were associated with significant increases in lung cancer mortality. Although potential effects of other unaccounted for factors cannot be excluded with certainty, the associations between fine particulate air pollution and lung cancer mortality, as well as cardiopulmonary mortality, are observed even after controlling for cigarette smoking, BMI, diet, occupational exposure, other individual risk factors, and after controlling for regional and other spatial differences.

Author Contributions: *Study concept and design:* Pope, Burnett, Krewski, Thurston.
Acquisition of data: Thun, Calle, Krewski, Ito, Thurston.
Analysis and interpretation of data: Pope, Burnett, Krewski, Thurston.
Drafting of the manuscript: Pope, Burnett, Ito, Thurston.
Critical revision of the manuscript for important intellectual content: Pope, Thun, Calle, Krewski, Thurston.
Statistical expertise: Pope, Burnett, Krewski.
Obtained funding: Pope, Thun, Thurston.
Administrative, technical, or material support: Pope, Calle, Krewski, Ito, Thurston.
Study supervision: Pope, Krewski.
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Cardiorespiratory and all-cause mortality after restrictions on sulphur content of fuel in Hong Kong: an intervention study

Anthony Johnson Hedley, Chit-Ming Wong, Thuan Quoc Thach, Stefan Ma, Tai-Hing Lam, Hugh Ross Anderson

Summary

Background In July, 1990, a restriction was introduced over one weekend that required all power plants and road vehicles in Hong Kong to use fuel oil with a sulphur content of not more than 0·5% by weight. This intervention led to an immediate fall in ambient sulphur dioxide (SO_2). We assessed the effect of this intervention on mortality over the next 5 years.

Methods Changes in trends in deaths were estimated by a Poisson regression model of deaths each month between 1985 and 1995. Changes in seasonal deaths immediately after the intervention were measured by the increase in deaths from warm to cool season. We also estimated the annual proportional change in number of deaths before and after the intervention. We used age-specific death rates to estimate person-years of life gained.

Findings In the first 12 months after introduction of the restriction, a substantial reduction in seasonal deaths was noted, followed by a peak in the cool-season death rate between 13 and 24 months, returning to the expected pattern during years 3–5. Compared with predictions, the intervention led to a significant decline in the average annual trend in deaths from all causes (2·1%; p=0·001), respiratory (3·9%; p=0·0014) and cardiovascular (2·0%; p=0·0214) diseases, but not from other causes. The average gain in life expectancy per year of exposure to the lower pollutant concentration was 20 days (females) to 41 days (males).

Interpretation Pollution resulting from sulphur-rich fuels has an effect on death rates, especially respiratory and cardiovascular deaths. The outcome of the Hong Kong intervention provides direct evidence that control of this pollution has immediate and long-term health benefits.

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Department of Community Medicine, University of Hong Kong, Pokfulam, Hong Kong (Prof A J Hedley MD, C-M Wong PhD, T Q Thach PhD, S Ma MStat, Prof T-H Lam MD); **and Department of Public Health Sciences, St George's Hospital Medical School, University of London, London, UK** (Prof H R Anderson MD)

Correspondence to: Prof A J Hedley, Department of Community Medicine, University of Hong Kong, 5/F Academic and Administration Block, Faculty of Medicine Building, 21 Sassoon Road, Pokfulam, Hong Kong
(e-mail: commed@hkucc.hku.hk)

Introduction

The association between air pollution and health effects including death has been established from reports on high-pollution incidents,[1] time-series analyses,[2] and cohort studies.[3,4] The strongest evidence is for respirable particulates (PM_{10}),[5] but many researchers have reported associations with gaseous pollutants, especially sulphur dioxide (SO_2).[6] Questions remain about the public-health effect of air pollution, particularly about death rates and life expectancy.[7,8] Very few opportunities have arisen to do epidemiological studies of the effects of interventions or of individual components of pollution.

Absence of data from intervention studies means that inconsistencies between studies on the importance of particulates or gases in pollutant mixtures, as causes of health problems and premature deaths, have not been resolved. One difficulty relevant to assessment of the public-health and economic analyses is the issue of mortality displacement or so-called harvesting.[9,10] Do deaths associated with fluctuations in pollutant concentrations arise mainly in sick or highly vulnerable groups of people, who would have died anyway in the short term, or are there longer-term effects from exposures? Time-series and cohort studies have both investigated the relation between pollution and years of life lost, but each has inherent limitations.

SO_2 has been described as a pollutant of public-health concern. The US Clean Air Act Amendments of 1990 proposed a reduction of 10 million tonnes of SO_2 emissions by 2010, with the aim to reduce SO_2, sulphate particulates, and acid precipitation.[11] In the first half of 1990, ambient monthly SO_2 concentrations monitored in Hong Kong ranged from 3 μg/m³ to 145 μg/m³ between the least and most polluted districts, with a regional mean of 37 μg/m³. On July 1, 1990, all power plants and road vehicles in Hong Kong were restricted to use of fuel oil with a sulphur content of not more than 0·5% by weight.[12] This intervention led to an immediate improvement in air quality, which was associated with a fall in SO_2 and sulphate in respirable particulates by up to 80% and 41%, respectively, in the most polluted areas. No great change in any of the other main pollutants was recorded.

In the 2 years after the intervention we showed a reduction of chronic bronchitic symptoms[13] and bronchial hyper-responsiveness[14] in young children. We aimed to assess the immediate and longer-term effect of the air-quality intervention on deaths in the Hong Kong population.

Methods

Procedures

From July, 1985, to June, 1995, we obtained data for deaths per month from all causes, respiratory disease (international classification of diseases 9th revision [ICD9] 460–519), cardiovascular disease (ICD9 390–459), and neoplasms (ICD9 140–239), and other causes (ICD9

001–009; 140–161; 163–246; 280–294; 320–326; 520–629; 710–719) from the Census and Statistics Department databases.[15] We stratified these data into three groups by age: 15–64 years; 65 and older; and all ages.

Air-pollutant concentrations were obtained from the Environmental Protection Department[16] for the period 1988–95. From five stations with almost complete data (97%), we plotted monthly mean concentrations of SO_2, sulphate in respirable particulates, nitrogen dioxide (NO_2), ozone (O_3; two stations only), and PM_{10} to investigate changes in concentrations of pollutants at each station 2 years before and 5 years after introduction of the fuel regulations. Daily pollutant concentrations measured by the five stations showed an average correlation of r=0·5 (range 0·3–0·7). A further three stations had useable data for 1 year before and up to 3 years after the intervention. The average correlation for all eight stations was r=0·4 (0·1–0·7) over the period 1990–92.

We used District Board resident populations to estimate the population covered by the different monitoring stations. We estimated that five stations covered 54% of the population, and all eight, 73%.

We assessed the overall change from baseline in average monthly concentration of each pollutant, by corresponding month and station for 5 years after the intervention. We applied a two-tailed t test to establish whether the means of the 5-year differences (maximum n=300) for each pollutant were different from zero.

Statistical analysis

We obtained a measure (λ) of change in death rates, relative to the mean, in the warm (April–September) or cool (October–March) seasons, by three methods. We first obtained monthly expected values from a linear regression model of monthly deaths. Second, we fitted a Poisson regression with observed/expected deaths as the dependent variable and a pair of $\alpha\times$sine and $\beta\times$cosine terms as the independent variables to model one cycle per year, where α and β are coefficients to be estimated from the regression. This model is sufficient to show the major warm to cool season changes. Third, we calculated the value of λ, using the equation shown in the panel, with 95% CIs. We did this calculation for every year after the intervention and for every cause of death by all ages and specific age-groups, and compared the values with those derived from the period before the intervention.[17]

We used the Poisson regression to model monthly deaths as a dependent variable,[18] taking into account trends, seasonality (by pairs of sine and cosine terms, allowing for one to three cycles per year to capture the main seasonal variations per year), temperature, and relative humidity, with stratification into two 5-year periods, before and after the intervention. We used the coefficient from the regression model to derive the average annual change in number of deaths in each of the two 5-year periods. We calculated the relative change in these estimates between the two periods, by causes of death and age-groups, with an interaction term representing the relative change in trend between the two periods. This term directly indicates the effect of the intervention in terms of average annual reduction in mortality.

Equation used to calculate λ

$$\lambda=\sqrt{\alpha^2+\beta^2}$$

We investigated differences in deaths over 5 years between districts with and without sustained reductions in SO_2 versus baseline. These districts were grouped in accordance with their reduction in SO_2 up to 2·5 years after the intervention, as indicated by eight monitoring stations. Over this period, the average change at the four stations with a consistently sustained reduction in SO_2 over 2·5 years was a 52·8% decrease versus an 8·7% increase at the four stations with reductions for shorter periods. These two groups of districts were defined as high and low SO_2 reduction areas. We assessed excess risk of death with Poisson regression on monthly death rates. Covariates included time trend, seasonality (sine and cosine terms), temperature and humidity, and a dummy variable for 5 years before and after the intervention.

We used age at death before intervention (1985–90) to calculate potential years of life lost due to death from all causes and cardiorespiratory disease, on the basis of life expectancy in those years. We calculated years of life that were saved by the intervention by applying the relative change in trend for deaths after the intervention to the years of life lost before the intervention.

We used differences in age-specific death rates, based on the population at the midpoint of two 2-year periods immediately before and after the intervention, to calculate change in life expectancy per year of exposure to the reduced pollutant levels, expressed per 10 $\mu g/m^3$ of SO_2. Furthermore, we estimated gain in life expectancy with the annual relative risk per 10 $\mu g/m^3$ SO_2, for a hypothetical cohort of people age 25–100 years.[8] We obtained numbers of survivors for each 5-year age-group (25–29, 30–34, 35–39, etc) from the 1991 Hong Kong life-table.

All tests of significance are two tailed unless otherwise stated.

Role of the funding source

The sponsors had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

	Baseline*	After intervention									
		1 year†			2·5 years‡			5 years§			
	Mean (SD) ($\mu g/m^3$)	Mean (SD) ($\mu g/m^3$)	Absolute change	Relative change (%)	Mean (SD) ($\mu g/m^3$)	Absolute change	Relative change (%)	Mean (SD) ($\mu g/m^3$)	Absolute change	Relative change (%)	p¶
Pollutant											
SO_2	44·2 (40·1)	20·8 (9·9)	–23·4	–53·0	22·3 (10·8)	–21·9	–49·6	24·5 (12·2)	–19·7	–44·7	<0·0001
SO_4 RSP	8·9 (3·2)	6·9 (2·0)	–2·0	–22·9	7·9 (2·8)	–1·0	–11·7	8·9 (3·1)	0·0	–0·3	0·896
NO_2	54·7 (22·8)	48·1 (12·0)	–6·7	–12·2	52·8 (15·1)	–1·9	–3·5	54·7 (14·7)	0·0	–0·1	0·205
O_3	18·5 (7·5)	21·3 (9·1)	2·8	15·2	22·1 (10·2)	3·6	19·6	23·8 (11·4)	5·2	28·3	<0·0001
PM_{10}	59·8 (17·0)	59·8 (16·9)	0·0	0·0	61·7 (17·4)	1·9	3·2	60·2 (17·6)	0·4	0·6	0·926

SO_4 RSP=sulphate in respirable particulates. *July, 1989, to June, 1990. †July, 1990, to June, 1991. ‡July, 1990, to December, 1992. §July, 1990, to June, 1995. ¶For difference from baseline concentration to corresponding month and stations over the 5 years after the intervention.

Table 1: **Mean (SD) concentration of pollutants based on five stations at baseline and after intervention with mean absolute and relative changes**

Results

In the first year after introduction of the intervention, mean fall in SO_2 concentration at five stations was 53% (table 1). Reduction in SO_2 concentration was sustained between 35% and 53% (mean 45%) of the mean value before the intervention, over 5 years. At eight stations for which complete data were available for up to 2·5 years, the average reduction in SO_2 concentration over this period was 50%.

Mean concentration of sulphate in respirable particulates at five stations for 2 years before the intervention was 8·9 μg/m³. This concentration fell by 15–23% for 2 years but rose again to between 110% and 114% of the concentration before 1990 in years 3–5 after the intervention (data not shown). No significant change in mean concentration of PM_{10} ($p=0·926$) and NO_2 ($p=0·205$)—but a significant increase of O_3 ($p<0·0001$)—was noted over the 5 years after the restriction on fuel sulphur content (figure 1).

Over the 5 years before the intervention, number of deaths per month showed a stable seasonal pattern for all causes and cardiorespiratory diseases. In the year after the restriction on fuel sulphur content was introduced, the expected cool season peak was absent (figure 2).

The noted seasonal mortality cycle closely fitted the model for the 5 years before introduction of the intervention. In the first 12 months after the intervention, amplitude of the cycle was low compared with that predicted because of a striking reduction in deaths in the cool season (figure 3). This fall was associated with a reduction in the warm to cool season mortality gradient, for every age-group, for all causes, respiratory, and cardiovascular deaths. For example, the seasonal percentage increase for all causes and all ages declined from the average 5-year baseline of 10·3% to 4·2% and respiratory deaths from 20·3% to 5·3% (table 2). In people aged 65 or older, seasonal deaths for all causes declined from 14·7% to 6·1% and respiratory deaths from 22·7% to 5·4%. No consistent change in seasonal pattern of deaths in any age-group for neoplasms or other causes was noted. In the second 12 months a striking rebound in deaths in the cool season deaths arose, followed by a gradual return during years 3–5 to the seasonal pattern before intervention.

The reduction in cool-season deaths in the first year after the intervention showed a consistent pattern across the eight stations, except in one district, which only contributed 1·3% of total deaths covered by air-pollutant monitoring.

The average annual proportional change in number of deaths, for all causes and all ages, was an increase of 3·5% per year in 1985–90, in accordance with the increase in size and ageing of the population. After the intervention

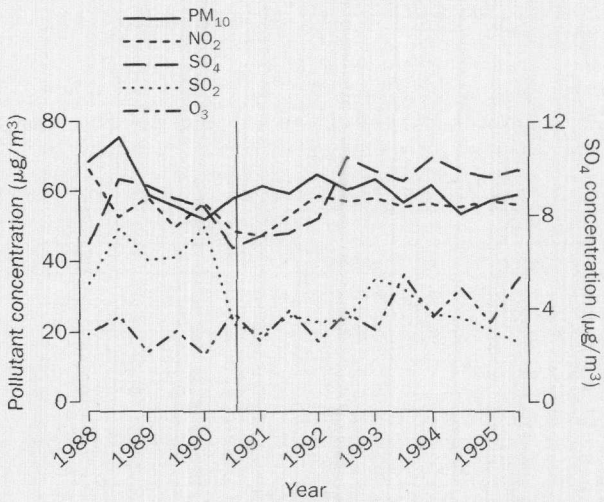

Figure 1: **Average of pollutant concentrations at five monitoring stations**
Vertical line represents date of introduction of fuel regulation.

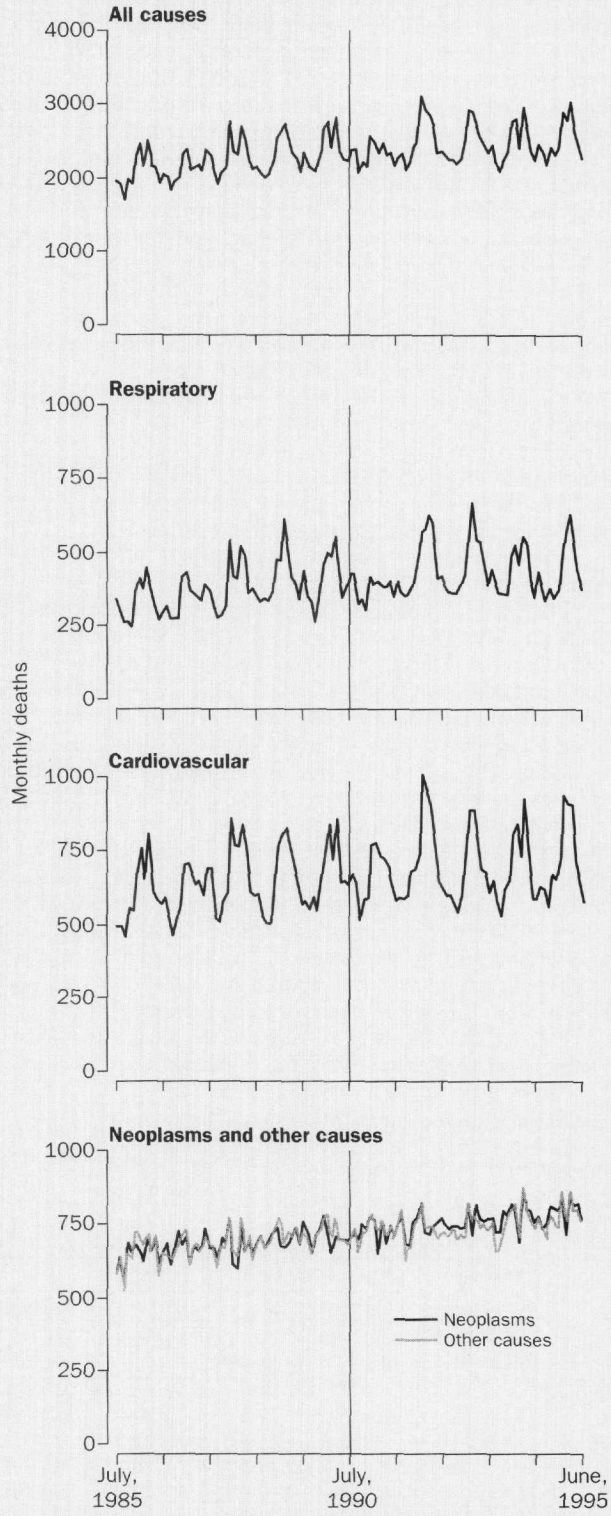

Figure 2: **Number of deaths per month for all ages from July, 1985, to June, 1995, for all causes, respiratory, cardiovascular, and neoplasms and other causes**
Vertical line represents date of introduction of fuel regulation.

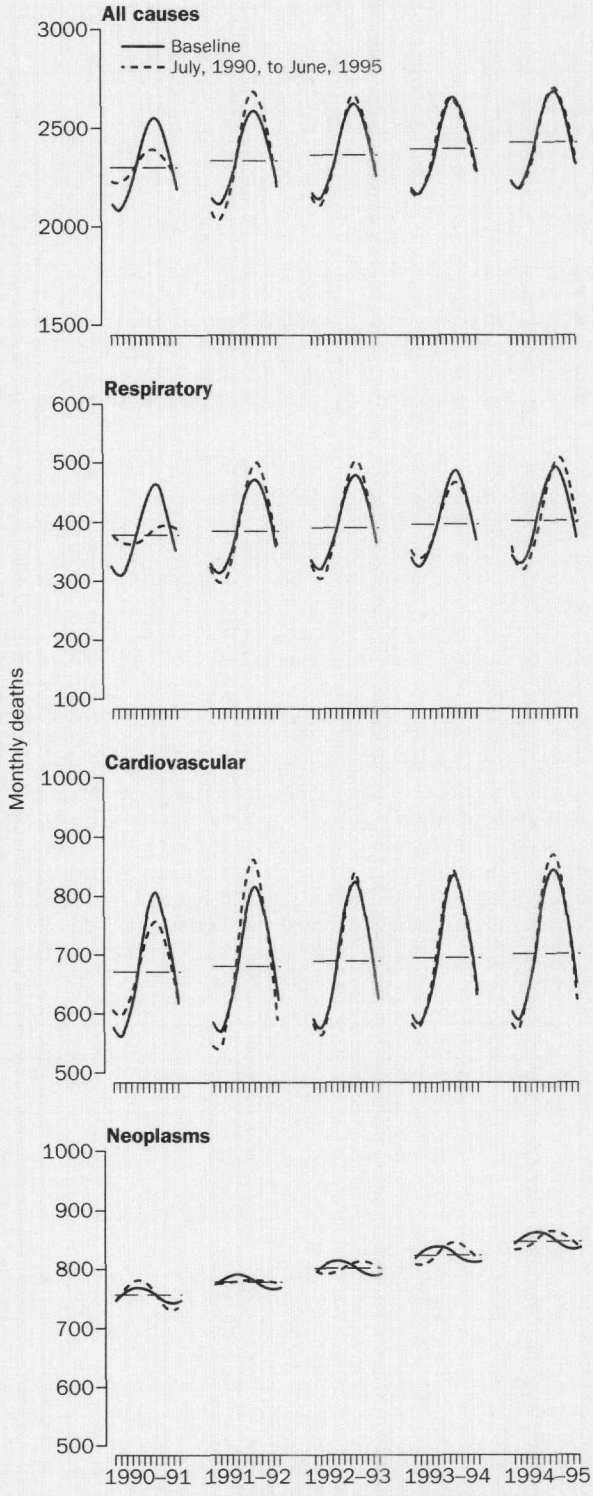

Figure 3: **Annual cycle of monthly deaths for all ages, for baseline and for each year after the intervention (July, 1990), for all causes, respiratory, cardiovascular, and neoplasms**
Mid-point of each period at January. Horizontal lines indicate mean monthly deaths.

was introduced, the average annual percentage change (increase) in deaths for 1990–95 declined for all causes, respiratory, and cardiovascular deaths compared with the 5 years before the intervention (table 3). For all causes and all ages, the average annual percentage change in death rates over 5 years showed a decline of 2·1% (95% CI 0·9–3·3), and for those aged 65 years or older the reduction was 2·8% (1·4–4·2). The biggest relative change was seen for respiratory deaths for the 15–64 age-group (4·8%; 1·2–8·3), with a smaller but significant change for cardiovascular deaths of 2·0% for all ages and 2·4% for those aged 65 years or older. No significant ($p>0·05$) post-intervention difference in annual rate of change was found at any age for deaths from neoplasms including lung cancer, or from other causes at age older than 65 or all ages (table 3).

A greater decline in mortality was noted in areas with a higher reduction in SO_2 during the first 2·5 years (–3·27%; 95% CI –7·10 to 0·83) than in areas with less reduction (1·35%; –3·63 to 6·61; $p=0·08$ one tailed test of significance, for reduction in average deaths between the two districts).

Estimated deaths and mean potential life years lost, for all causes and all ages, in 1985–90, based on the post-intervention decline in annual proportional change in deaths of 2·1%, was 600 deaths per year associated with 10 268 person-years of life per year.

Age-standardised death rates for all causes declined during the 10-year period of the study. The decline was greatest after the intervention, with a corresponding increase in life expectancy. In the 1991 population of Hong Kong, of about 5·8 million, person-years of life gained were 667 095 for males and 308 614 for females over the 2 years after the intervention, which represents an average lifetime gain, adjusted for the baseline trend, of 31 days (0·085 years) for each individual in the population, or 15 days per 10 $\mu g/m^3$ reduction in SO_2 per year of exposure.

On the basis of age-specific death rates, the estimate of gain in life expectancy (after 15 years of exposure to the lower pollutant concentrations) for men age 25 years and older is 0·73 years per 10 $\mu g/m^3$ reduction in SO_2. In an alternative approach described by Brunekreef,[8] using the 15-year relative risk of 1·18 obtained from our model of change in death rates, the estimate for a 25-year-old man is 2·58 years per 10 $\mu g/m^3$ reduction in SO_2.

An appendix with further webtables and figures is available on our website.[19]

Discussion

After introduction of the air-quality intervention in Hong Kong, in addition to the 45% average reduction in SO_2 over 5 years, we noted that sulphate in respirable particulates had sustained reduction up to 2 years, but concentrations rose again and stabilised as part of a regional pattern of sulphate pollution in southern China. No comparable reductions or downward trends in the other main pollutants, PM_{10}, NO_2 and O_3, were recorded. These immediate changes in concentration of sulphur-derived pollutants were associated with the seasonal mortality cycle in the first year, and the estimated change in the proportional mortality trend based on 5-year analysis also suggested that reduction of SO_2 concentration had an important longer-term effect on death rates.

We reported an immediate reduction in cool-season deaths, which suggested that in the first year, many people survived who would have otherwise died. The rebound in cool-season deaths in the second year, followed by a return to the pre-intervention seasonal cyclical pattern, suggested that these later deaths arose in susceptible people whose death had been delayed by the air-quality improvement. This finding, which is the reverse of the postulated occurrence of harvesting and which was closely related to the reduction in sulphur oxides, lends support to the hypothesis that a proportion of the deaths

	Cool season increase in mortality (%) (95% CI)				
	All causes	Respiratory	Cardiovascular	Neoplasms	Other causes
Period					
Baseline (July, 1985, to June, 1990)	10·2 (9·5 to 11·0)	20·3 (18·4 to 22·2)	18·0 (16·6 to 19·4)	1·1 (–0·3 to 2·4)	4·2 (2·9 to 5·6)
Year 1 (July, 1990, to June, 1991)	4·2 (2·5 to 5·8)	5·3 (1·2 to 9·4)	12·3 (9·2 to 15·4)	2·8 (–0·2 to 5·8)	3·7 (0·7 to 6·6)
Year 2 (July, 1991, to June, 1992)	14·6 (13·0 to 16·2)	27·7 (23·9 to 31·5)	24·1 (21·2 to 27·1)	1·1 (–1·9 to 4·0)	3·6 (0·7 to 6·6)
Year 3 (July, 1992, to June, 1993)	12·5 (10·8 to 14·1)	26·6 (22·8 to 30·4)	20·1 (17·0 to 23·2)	2·0 (–0·9 to 4·9)	4·9 (2·0 to 7·8)
Year 4 (July, 1993, to June, 1994)	11·3 (9·6 to 12·9)	17·2 (13·3 to 21·0)	19·8 (16·7 to 22·9)	2·7 (–0·2 to 5·5)	6·8 (3·9 to 9·7)
Year 5 (July, 1994, to June, 1995)	11·3 (9·7 to 12·9)	24·2 (20·4 to 28·1)	21·4 (18·4 to 24·4)	2·1 (–0·7 to 5·0)	5·1 (2·2 to 7·9)

Table 2: **Cool season increase in mortality and 95% CI for all ages after intervention compared with mean (baseline) for all causes, respiratory, and cardiovascular, neoplasms, and other causes**

associated with air-pollution episodes are in individuals who are frail and already have a short life-expectancy.

In addition to short-term seasonal fluctuations in death rates, we recorded a decline in the average annual proportional increase in deaths in the period after the intervention, which also provides evidence of a longer-term benefit from removal of sulphur. As with the early effect on seasonal deaths, the largest decline over 5 years was for respiratory deaths. Reduction in risk for overall mortality was greater in districts that had large reductions in SO_2 than in those that did not.

Differences in age-specific death rates before and after the intervention suggest that it led to an average gain in life expectancy for men aged 25–100 years of 0·73 years for 15 years' exposure per 10 μg/m³ reduction in SO_2. For a man aged 25–29 years, the lifetime gain would be 1·14 years. Brunekreef[8] applied a relative risk of 1·10—derived from US cohort studies, with relative risk per 10 μg/m³ for PM_{10} ranging from 1·07[4] to 1·17[3]—to the 1992 life-table for people aged 25–100 years to obtain an estimated gain of 1·51 years for a 25-year old Dutch man with 15 years of exposure. This finding indicates the expected difference in life expectancy between populations living in polluted or clean air. On the basis of the relative risk of 1·18 from our Poisson regression, the comparable gain in life expectancy per 10 μg/m³ SO_2 for a 25-year old Hong Kong man is 2·58 years. The short-term analysis of changes in risk of death could have underestimated the benefits, in terms of life expectancy, of the restriction on sulphur in fuel.

Further benefits arising from reductions in the other pollutants, including respirable particulates and the other gaseous pollutants, could be expected in addition to those derived from sulphur sources. The strong association between reduced risk of death and the acute fall in sulphur oxides contrasts strikingly with the conclusions of other analyses—based on time series and cohort studies—of SO_2 and deaths in the USA and the Netherlands. Schwartz[20]

	Average annual proportional change (%) (95% CI)*		Relative change (%) (95% CI) per year	
	Pre-intervention	Post-intervention	From pre-intervention to post-intervention period†	Intrapolated to 10 μg/m³ change in SO_2‡
All causes				
Age 15–64 years	0·65 (–0·01 to 1·31)	–1·16 (–1·83 to –0·48)	–1·75 (–2·98 to –0·50)	–0·89
Age 65 years and older	5·40 (4·93 to 5·88)	2·40 (1·96 to 2·83)	–2·81 (–4·20 to –1·39)	–1·44
All ages	3·50 (3·12 to 3·88)	1·20 (0·84 to 1·56)	–2·11 (–3·32 to –0·89)	–1·08
Respiratory				
Age 15–64 years	2·28 (0·12 to 4·44)	–3·36 (–5·64 to –1·07)	–4·80 (–8·28 to –1·18)	–2·47
Age 65 years and older	7·79 (6·75 to 8·83)	2·91 (1·97 to 3·85)	–4·17 (–6·59 to –1·69)	–2·14
All ages	6·55 (5·62 to 7·48)	1·88 (1·02 to 2·74)	–3·94 (–6·23 to –1·60)	–2·02
Cardiovascular				
Age 15–64 years	–1·33 (–2·78 to 0·12)	–3·12 (–4·64 to –1·59)	–1·64 (–3·95 to 0·72)	–0·84
Age 65 years and older	4·17 (3·36 to 4·99)	1·81 (1·04 to 2·57)	–2·44 (–4·20 to –0·65)	–1·25
All ages	2·79 (2·08 to 3·49)	0·77 (0·09 to 1·45)	–2·01 (–3·66 to –0·33)	–1·03
Neoplasm, without lung cancer				
Age 15–64 years	0·73 (–0·47 to 1·94)	–0·64 (1·90 to 0·63)	–1·34 (–2·95 to 0·30)	–0·68
Age 65 years and older	3·53 (2·16 to 4·91)	4·53 (3·44 to 5·64)	1·06 (–0·64 to 2·79)	0·54
All ages	2·04 (1·03 to 3·05)	2·16 (1·34 to 2·99)	0·17 (–1·08 to 1·44)	0·09
Lung cancer				
Age 15–64 years	–0·48 (–2·54 to 1·63)	–0·52 (–2·62 to 1·63)	0·17 (–2·67 to 3·08)	0·09
Age 65 years and older	5·41 (3·60 to 7·25)	3·00 (1·32 to 4·70)	–2·16 (–4·40 to 0·12)	–1·10
All ages	3·12 (1·82 to 4·43)	1·83 (0·50 to 3·19)	–1·08 (–2·89 to 0·77)	–0·55
Other causes				
Age 15–64 years	0·73 (–0·29 to 1·76)	–1·28 (–2·42 to –0·13)	–1·95 (–3·43 to –0·45)	–0·99
Age 65 years and older	3·99 (2·88 to 5·16)	3·53 (2·46 to 4·62)	–0·50 (–2·04 to 1·06)	–0·25
All ages	2·41 (1·51 to 3·31)	1·55 (0·70 to 2·41)	–0·85 (–2·06 to 0·37)	–0·43

*Estimate obtained from fitting of the Poisson regression model in the stratified pre-intervention and post-intervention period. †Estimated by the intervention by trend interaction term in the Poisson regression model. ‡Estimates derived from column 4, which show reduction in excess risk (relative proportional change) after the intervention. Reduction in excess risk was converted to be associated with 10 μg/m³ by the log linear assumption.

Table 3: **Average annual percentage change in mortality and 95% CI before and after the intervention, with relative change in annual trend from before to after the intervention**

concluded that there was no association between SO_2 and death rates after modelling SO_2 and total suspended particles separately for season and year, and controlling for climatic and other factors. The estimated unconfounded effect of SO_2 on daily deaths was not significantly different from zero and particulates showed the strongest effect on daily deaths when their association with SO_2 was weakest. In the Netherlands[21] two approaches based on time-series analyses, and trends in death rates over periods when SO_2 concentrations varied, also led to the conclusion that SO_2 is not a causal agent in mortality associated with air pollution. Furthermore, criticisms of the hypothesis that respirable particulates are the main component of pollution mixtures that cause deaths have been extensively reviewed and refuted in view of new analyses of data from US cities, and associations between SO_2 and NO_2 and daily deaths are weak and inconsistent.[5] By contrast, strong associations with respirable particulates and cardio-respiratory deaths were reported. However, results of other time-series analyses have shown strong associations between SO_2 and daily deaths in Europe.[6,22] Associations between SO_2 and deaths[23] and hospital admissions[24] in time-series analyses in Hong Kong are closely similar to those in London, UK.[25,26]

In a time-series analysis on air pollution and deaths,[23] the strongest effects we noted were for gases including SO_2, rather than respirable particulates. Katsouyanni and colleagues[6] also recorded evidence for an independent effect of both SO_2 and particulates in 12 European cities. The effects for SO_2 were similar or stronger than for PM_{10}, and these researchers suggested that this effect might be the result of more complex pollutant mixtures and lower particulate concentrations in Europe than the USA; however in Hong Kong, respirable particulate concentrations are high and about twice those in London, UK.[24]

Public-health policy on air-quality improvement would be strengthened by better data on the effect of pollution on life expectancy.[7] Even if one pollutant greatly affects death rates, do increases in deaths from pollution episodes arise only in susceptible individuals with pre-existing disease, whose life expectancy is already short? The issue of mortality displacement is important for epidemiological studies based on time-series, because if susceptible people die early on in the pollution episode, death rates after the episode will be lower than expected. The resulting average death rate over time could fail to show an association between pollution and death rates.[27]

Time-series analyses have been used to investigate mortality displacement on different time scales after a pollution episode.[9,10] Results of these analyses suggest that although some harvesting takes place for pneumonia, the health effects from a pollution episode continue and actually increase over long periods for respiratory and cardiovascular disease. The conclusion of these analyses was that deaths were displaced by at least 2 months, but that the limitation of the time-series approach does not allow the effects beyond that period to be defined. Results of cohort studies suggest an effect of 1 year or more, and Künzli and colleagues[28] conclude that time-series studies underestimate deaths, and that the effect of air pollution should be based on prospective cohort studies.

The outcome of our study could be challenged on grounds of biological plausibility. The mechanism underlying the immediate health benefits arising from use of low sulphur fuel is unknown. SO_2 is a chemical irritant, but in support of an argument against a role for SO_2, Schwartz[20] cites the finding that 80% of ambient SO_2 is removed by the nose and exhaled. However, scrubbing efficiency could be reduced at low ambient concentrations, and penetration to the lungs is high with oral breathing, and little experimental data on the effects of usual ambient concentrations of SO_2 on healthy people is reported. At high concentrations, SO_2 alters nasal and tracheo bronchial mucociliary clearance rates in both human beings and animals.[29] Bronchoconstriction happens in people with asthma and in those with hyper-reactive airways, but after the air-quality intervention in Hong Kong, the decline in bronchial hyper-responsiveness in children without asthma or wheezing,[14] and chronic bronchitic symptoms in children[13] and adults,[30] provided evidence that important components of ambient pollutant mixtures derived from sulphur were greatly reduced.

However, the apparent benefits of the reduction in SO_2 could have been attributable to other combustion products that are not generated by low-sulphur fuels. Changes in concentration of SO_2 after the fuel regulation was introduced could simply be an indicator of other qualitative changes in fuel and products of combustion, with reduction in another unidentified agent that causes the health effects. Concentrations of PM_{10} were unchanged after the intervention, but SO_2 could be a modifier of the effect of respirable particulates. SO_2 is converted to sulphuric acid, which can be carried into small airways by respirable particulates and impair lung function in children,[31] but no monitoring data are available for free sulphuric acid across the period of intervention.

The benefits to health resulting from the 1990 industrial fuel intervention were achieved with only a moderate effect on overall production costs.[32] As a result of licensing controls, high sulphur fuels have been banned in Hong Kong since 1990, and in 2000 SO_2 concentrations were maintained at below 20 $\mu g/m^3$, more than 50% below pre-intervention concentrations. Use of ultra-low sulphur (0·005%) diesel fuel for public and private transport, conversions to alternative fuels, and tightening of legislation is continuing.

Contributors

A J Hedley and C-M Wong had the idea for and directed the study jointly. T Q Thach and S Ma analysed data. A J Hedley, C-M Wong, T-H Lam, and H R Anderson discussed and interpreted data. A J Hedley and C-M Wong wrote the report, with reviews and contributions from H R Anderson and T-H Lam.

Conflict of interest statement

None declared.

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Abstract

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Associations between short-term changes in nitrogen dioxide and mortality in Canadian cities.

Burnett RT[1], Stieb D, Brook JR, Cakmak S, Dales R, Raizenne M, Vincent R, Dann T.

Author information

Abstract

The association between daily variations in ambient concentrations of **nitrogen dioxide** (NO2) and **mortality** was examined in 12 of Canada's largest **cities**, using a 19-yr time-series analysis (from 1981-1999). The authors employed parametric statistical methods that are not subject to the recently discovered convergence and error estimation problems of generalized additive models. An increase in the 3-d moving average of NO2 concentrations equivalent to the population-weighted study mean of 22.4 ppb was associated with a 2.25% (t = 4.45) increase in the daily nonaccidental **mortality** rate and was insensitive to adjustment for ozone, sulfur **dioxide**, carbon monoxide, coefficient of haze, size-fractionated particulate mass, and the sulfate ion measured on an every-6th-day sampling schedule. The 3-d moving average of NO2 was sensitive to adjustment for fine particulate matter measured daily during the 1998-2000 time period.

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Effect of Air Pollution on Daily Mortality in Hong Kong

Chit-Ming Wong, Stefan Ma, Anthony Johnson Hedley, and Tai-Hing Lam

Department of Community Medicine, The University of Hong Kong, Hong Kong, China

In different weather conditions, constituents and concentrations of pollutants, personal exposure, and biologic responses to air pollution may vary. In this study we assessed the effects of four air pollutants on mortality in both cool and warm seasons in Hong Kong, a subtropical city. Daily counts of mortality, due to all nonaccidental causes, and cardiovascular and respiratory diseases were modeled with daily pollutant concentrations [24-hr means for nitrogen dioxide, sulfur dioxide, and particulate matter < 10 μm in aerodynamic diameter (PM_{10}); 8-hr mean for ozone]. using Poisson regression. We controlled for confounding factors by fitting the terms in models, in line with those recommended by the APHEA (Air Pollution and Health: a European Approach) protocol. Exposure–response relationships in warm and cool seasons were examined using generalized additive modeling. During the cool season, for a linear extrapolation of 10th–90th percentiles in the pollutant concentrations of all oxidant pollutants, NO_2, SO_2, and O_3, we found significant effects on all the mortality outcomes under study, with relative risks (RR) of 1.04–1.10 ($p < 0.038$, except $p = 0.079$ for SO_2 on respiratory mortality). We observed consistent positive exposure–response relationships during the cool season but not during the warm season. The effects of PM_{10} were marginally significant (RR = 1.06; $p = 0.054$) for respiratory mortality but not for the other outcomes ($p > 0.135$). In this subtropical city, local air quality objectives should take into account that air pollution has stronger health effects during the cool rather than warm season and that oxidant pollutants are more important indicators of health effects than particulates. *Key words*: air pollutant concentrations, daily mortality, exposure–response, offset, stratification by seasons. *Environ Health Perspect* 109:335–340 (2001). [Online 8 March 2001]
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Time–series methods are widely used for assessment of short-term health effects of air pollution (*1*). Although limitations arise from ecologic fallacy (*2*) and the harvesting effect (*3–5*), time–series methods are more powerful and better able to characterize the population exposure effects than those based on geographic aggregations in cross-sectional studies (*6*). Also, methods to control for time-related confounding factors are well established (*7*). Daily time–series analysis is not applicable to the estimation of longer-term chronic exposure effects of air pollution (*8*), which are public health concerns. Daily time–series analysis may be better estimated from longitudinal studies, but it can be used to assess the potential health benefits of air quality intervention in terms of the number of hospital admissions and deaths avoidable if days with high concentrations (according to a chosen reference value) were eliminated, thus providing information to support the setting of air quality objectives (*9*,*10*).

To date, there is coherent evidence that air pollution has short-term effects on mortality (*9*,*11–15*), but the questions whether there are independent effects of a single pollutant to account for a health outcome under study and whether there are thresholds and linear or non-linear relationships are still not settled.

In the United States, particulates are regarded as the pollutants that account for most excess mortality due to air pollution (*16*), but in Europe several studies indicated a stronger association with sulfur dioxide (*17*). Some showed that it might be the sulfuric acid (*18*), acid aerosol (*19*), and mass concentration (*20*) associated with particulates that are responsible for the effects. Other studies showed that independent effects of individual pollutants cannot be identified in light of the complexity and variability of the air pollution mixtures to which people are exposed (*21*,*22*).

In this study we assessed the effects of air pollution on mortality outcomes and identified which pollutants would contribute most to the effect in Hong Kong, a subtropical city in the Asian Pacific rim. Patterns of exposure–response relationships for four criteria pollutants, nitrogen dioxide, sulfur dioxide, particulate matter < 10 μm in aerodynamic diameter (PM_{10}), and ozone were assessed during warm and cool seasons with a view to ascertaining their effects on the commonly used mortality outcomes.

Materials and Methods

Data. For the period 1995–1997, we obtained daily death counts for all nonaccidental causes [*International Classification of Diseases, Revision 9* (ICD-9) < 800 (*23*)], respiratory disease (ICD-9 460–519), and cardiovascular disease (ICD-9 390–459) from the Census & Statistics Department (Hong Kong Special Administrative Region, People's Republic of China); meteorologic data (daily mean temperature and relative humidity) from the Hong Kong Observatory; and air pollutant concentrations (from two to seven monitoring stations) from the Environmental Protection Department. Daily means of 24-hr concentrations of NO_2, SO_2, and PM_{10} and 8-hr (900 hr–1700 hr) concentrations of O_3 were derived if they were non-missing. Daily concentrations were defined as non-missing if more than 17/24 hr concentrations and more than 5/8 hr concentrations were valid. According to the second phase guidelines of APHEA (Air Pollution and Health: a European Approach), non-missing daily means were first centered for each station i [i.e., individual daily concentrations (X_{ij}) were subtracted by an annual station mean (X_i) for each day j]. The centered data from all centers were then combined and added into the annual mean of all stations (X) to form $X'_{ij} = (X_{ij} - X_i + X)$. The daily (mean) concentrations of individual pollutants were computed for analysis by taking the mean of X'_{ij} over all stations (*24*).

Statistical methods. We used Poisson regression with daily mortality counts as the dependent variable. To obtain a core model for each of the mortality outcomes for all ages, nonparametric smoothing (by means of the Loess function) terms for trend on days (1–1,096), seasonality, temperature, and humidity; and dummy variables for days of the week, holidays, and influenza epidemics [weeks with number of hospital admissions for influenza (ICD-9 487) in the upper quartile, which was on average over 8/week in 1995, 1996, and 1997, respectively] were fitted as the independent variables. In addition, we also considered the lag effects of temperature and humidity in building the core models. Residuals of each core model were examined to check whether there were discernible patterns and autocorrelation by means of residual plots and partial autocorrelation function plots, respectively (*7*). If necessary, both overdispersions and autocorrelations were further adjusted for the model using statistical procedures (*7*) implemented in S-Plus (MathSoft, Inc., Seattle, WA, USA). We paid special attention to ensure that there were no differences in the residuals

Address correspondence to A.J. Hedley, Department of Community Medicine, The University of Hong Kong, Patrick Manson Building South Wing, 7 Sassoon Road, Hong Kong, China. Telephone: (852) 2819 9282 / 2819 9280. Fax: (852) 2855 9528. E-mail: hrmrajh@hkucc.hku.hk

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between warm (April–September) and cool (other months) seasons.

We estimated concentrations of current day up to the previous 5 days for O_3 and up to 3 days for other pollutants and identified the best lagged day by a modified version of Akaike's Information Criterion (ACI) (*25*). The analysis was also performed using the Loess smoothing function to adjust for nonlinear effect of a copollutant. Differences in pollutant effects between seasons were assessed by a season-by-pollutant concentration interaction term in each model, and the effect estimates for cool and warm seasons were derived from the model with the interaction terms.

To perform the stratified analyses, we first obtained expected mortality counts (ξ) from the core model for all seasons. Poisson regression for the mortality outcomes (Y) was then fitted on pollutant concentrations (X) to obtain the log relative risk (β) estimate with offset on log(ξ) (*26*) separately for warm and cool seasons. Offset is a computation procedure to treat log(ξ) as a reference value and does not proceed to estimate a parameter for it in the Poisson regression $\log[E(Y)] = \log(\xi) + \alpha + \beta x$ (where α is a parameter for the constant term). Exposure–response curves in warm and cool seasons were examined using generalized additive modeling (*25*).

Results

Summary statistics. Summary statistics of mortality counts, air pollutant concentrations, and meteorologic measurements are presented in Table 1. There were more deaths, higher concentrations of pollutants (except for SO_2, which was about the same), and drier weather conditions in the cool season than in the warm season.

Lag effects. In whole-year analysis, NO_2, SO_2, and PM_{10} showed similar patterns for their effects on all the mortality outcomes in that the relative risks (RRs) increased from lag-day 0, were maximal at either lag-day 1 or lag-day 2, and declined to the lowest at lag-day 3. The RRs at the best lagged day (i.e., the day with minimum AIC) were significant in all three categories of deaths ($p < 0.01$) for NO_2 and SO_2, and was significant ($p = 0.024$) only for respiratory mortality for PM_{10}. For O_3, the RRs were not significant ($p > 0.05$) for any of the lagged days or for any mortality outcomes. With adjustment for autocorrelation, there was little change in the RRs and *p*-values. However, with adjustment for a copollutant, only the RR for NO_2 in cardiovascular mortality ($p = 0.046$) and for SO_2 in nonaccidental ($p = 0.003$) and cardiovascular ($p = 0.023$) mortality remained significant (Table 2).

Effects by seasons. During the warm season, there were no significant effects ($p > 0.1$) for all pollutants for all mortality outcomes (Table 3). During the cool season, without adjustment for copollutants, *a*) all of the RRs at the best lagged days were significantly greater than unity in all the mortality

Table 1. Summary statistics of mortality outcome, air pollution levels, and meteorologic measures by season.

	No. (day)	Mean	SD	Min	P_{10}	Median	P_{90}	Max
Mortality counts								
Nonaccident (ICD-9: < 800)								
Warm	552	75.0	9.7	47	62	75	87	103
Cool	544	87.4	12.7	53	71	88	103	129
Cardiovascular (ICD-9: 390-456)								
Warm	552	19.5	4.7	8	14	19	26	35
Cool	544	26.2	6.4	12	18	26	35	53
Respiratory (ICD-9: 460-519)								
Warm	552	15.9	4.9	5	10	16	22	31
Cool	544	18.3	5.3	3	12	18	26	33
Air pollution concentrations (μg/m^3)								
NO_2 (24-hr)								
Warm	552	48.1	18.2	15.3	27.4	45.5	72.8	125.8
Cool	544	63.8	17.5	28.7	45.2	60.6	87.3	151.5
SO_2 (24-hr)								
Warm	550	18.3	13.0	1.9	5.9	15.0	35.3	83.6
Cool	544	17.2	11.6	1.1	6.4	14.4	30.8	90.1
PM_{10} (24-hr)								
Warm	552	42.2	21.3	14.1	23.0	35.6	70.6	163.8
Cool	544	61.7	24.7	14.1	33.3	58.7	95.1	156.6
O_3 (8-hr)								
Warm	548	32.0	24.5	0	8.1	23.9	64.7	168.9
Cool	538	35.1	21.3	0	7.9	33.2	62.8	101.6
Meteorologic measurements:								
Temperature (°C)								
Warm	552	27.3	1.9	21.0	24.5	27.4	29.6	30.9
Cool	544	19.0	3.6	6.9	14.5	18.9	23.8	27.4
Humidity (%)								
Warm	552	80.7	7.4	46	73	80	91	97
Cool	544	74.7	12.4	31	58	76.5	89	95

Abbreviations: Max, maximum; Min, minimum; P_{10}, 10th percentile; P_{90}, 90th percentile.

Table 2. Relative risk (RR) and 95% confidence interval (CI) of the best single lagged-day effects by linear extrapolation for a 10th–90th percentile change in pollutant concentration (1995–1997): whole year.

		Unadjusted		Autocorrelation adjusted			Adjusted for copollutant	
Causes of mortality	Lag day	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value	Copollutant[a]	RR (95% CI)	*p*-Value
NO_2								
Nonaccident	1	1.04 (1.01–1.05)	0.001	1.03 (1.01–1.05)	0.003	SO_2	1.00 (0.97–1.03)	0.896
Cardiovascular	2	1.06 (1.03–1.10)	0.001	1.06 (1.02–1.10)	0.003	SO_2	1.04 (1.00–1.08)	0.046
Respiratory	0	1.08 (1.02–1.13)	0.003	1.07 (1.02–1.12)	0.008	SO_2	1.05 (0.98–1.12)	0.168
SO_2								
Nonaccident	1	1.03 (1.02–1.05)	0.000	1.03 (1.01–1.05)	0.000	NO_2	1.03 (1.01–1.05)	0.003
Cardiovascular	1	1.05 (1.02–1.08)	0.001	1.05 (1.02–1.08)	0.003	NO_2	1.04 (1.00–1.07)	0.023
Respiratory	0	1.04 (1.01–1.08)	0.010	1.04 (1.01–1.07)	0.016	NO_2	1.02 (0.97–1.06)	0.450
PM_{10}								
Nonaccident	1	1.02 (1.00–1.04)	0.102	1.02 (1.00–1.04)	0.132	SO_2	0.99 (0.97–1.01)	0.397
Cardiovascular	2	1.03 (0.99–1.06)	0.165	1.02 (0.99–1.06)	0.201	NO_2	0.98 (0.92–1.03)	0.363
Respiratory	1	1.06 (1.01–1.11)	0.024	1.05 (1.01–1.10)	0.028	NO_2	1.04 (0.99–1.10)	0.093
O_3								
Nonaccident	5	1.01 (0.99–1.03)	0.224	1.01 (0.99–1.03)	0.226	NO_2	1.01 (0.99–1.03)	0.288
Cardiovascular	3	1.01 (0.98–1.05)	0.479	1.01 (0.98–1.05)	0.426	NO_2	1.00 (0.96–1.04)	0.997
Respiratory	4	1.04 (1.00–1.08)	0.078	1.03 (0.99–1.07)	0.145	NO_2	1.03 (0.99–1.07)	0.163

[a]The copollutant that produced the least significant effect in the pollutant after adjustment.

outcomes ($p < 0.015$) for NO_2; *b*) they were significant in nonaccidental and cardiovascular mortality ($p < 0.002$) for SO_2; *c*) they were marginally significant in respiratory mortality ($p = 0.054$) for PM_{10}; and *d*) they were all significant ($p < 0.038$) for O_3. During the cool season with adjustment for copollutants, only the effects of NO_2 on cardiovascular mortality, SO_2 on nonaccident and cardiovascular mortality, and O_3 on nonaccident and respiratory mortality remained significant ($p < 0.05$). However, the between-season differences were statistically significant for NO_2 in cardiovascular mortality with and without adjustment for copollutants ($p < 0.039$) and for O_3 in all mortality outcomes ($p < 0.044$) without adjustment and in nonaccident and respiratory mortality ($p < 0.032$) with adjustment for copollutant.

Seasonal exposure–response relationships. Figures 1–4 show the exposure–response relationships for each pollutant for the three mortality outcomes at the best lagged day.

NO_2. During the warm season, we observed no clear exposure–response relationships for the three outcomes for NO_2. However, during the cool season there were observable linear exposure–response relationships throughout the concentration levels in nonaccidental mortality, but the curves showed positive and nonlinear relationships at concentrations higher than 80 μg/m^3 in the other two outcomes.

SO_2. During the warm season, no exposure–response relationships were observed when SO_2 was < 30 μg/m^3, but there were some linear or nonlinear relationships above that concentration. During the cool season, we observed positive exposure–response relationships for concentrations of 0–40 μg/m^3 SO_2.

PM_{10}. For PM_{10}, no clear exposure–response relationships were observed for the three outcomes in warm seasons, but in the cool season there was a positive exposure–response relationship for respiratory mortality for concentrations up to 80 μg/m^3.

O_3. There were no clear relationships for any of the three outcomes for O_3 during the warm season. However, during the cool season all of the mortality outcomes tended to increase with increasing concentrations.

Discussion

All pollutant levels are high in Hong Kong. Although SO_2 has been reduced substantially due to government limits on the sulfur content of fuels in the early 1990s (*27*), the level of SO_2 in Hong Kong still ranks in the middle among more than 30 metropolitan cities in the world. The SO_2 level in Hong Kong is higher than those in Berlin, Germany; Boston, Massachusetts (USA); Brisbane, Australia; Kuala Lumpur, Malaysia; London, United Kingdom; and Paris, France (*28*).

The levels of NO_2 and O_3 have been increasing along with increasing vehicular traffic volume. Levels of PM_{10}, which is primarily related to the use of diesel engines, in Hong Kong are among the highest in the world: they are only lower than those in the most polluted cities such as Barcelona, Spain; Guangzhou, China; Manila, Republic of the Philippines; Mexico City, Mexico; Philadelphia, Pennsylvania (USA); Santiago, Chile; Shanghai, China; and Taipei, Taiwan.

In the present study the estimated effects of the pollutants on mortality reached a maximum at a lag of 1–2 days. These observations are consistent with those reported by Bremner et al. (*29*) in London: the effects increased from lag-day 0 to a maximum at lag-day 1 for NO_2, SO_2, and PM_{10}.

A major finding of this study is that O_3 had effects on all three mortality outcomes during the cool season, and the effects were greater than those in the warm season; this is unlike several other reports in which the effects were found in the warm season (*9,12,29*). This is consistent with our previous report on the effects of pollution on hospital admissions due to heart failure in subjects ≥ 65 years of age (*30*). The effects of the other oxidant pollutants (NO_2 and SO_2) were also significant for all of the mortality outcomes in the cool season but not in the warm season. In Athens, Greece, effects of SO_2 on all causes of nonaccidental mortality were also observed in the cool season (*31*), but in London, the effects for NO_2 and SO_2 were observed in the warm season (*12*). When the data from five western European cities and four central European cities were combined, SO_2 also showed slightly stronger effects during the warm season than during the cool season (*32*).

In Hong Kong in the cool season, air pollutant levels were higher (NO_2, 64 vs. 48; PM_{10}, 62 vs. 42; O_3, 35 vs. 32 μg/m^3) than those in the warm season, except SO_2, which was slightly lower (17 vs. 18). Because pollutants were correlated (r = 0.54–0.72 between NO_2, SO_2, and PM_{10} during the cool season), greater effects observed during cool weather may be due to other pollutants that were also at higher levels during the cool season. The cool season in Hong Kong is drier (humidity 75% vs. 81%), less cloudy (63% vs. 72%), and less variable, so people are more likely to go outdoors and open the windows, thus being exposed to higher levels of air pollution. In contrast, during the warm season (temperatures of 25°C–30°C and humidity of 73%–91% between 10th to 90th percentiles) people usually use air-conditioning, thus

Table 3. Relative risk (RR) and 95% confidence interval (CI) of best single lagged day effects by linear extrapolation for a 10th–90th percentile change in pollutant concentration (1995–1997), without[a] and with[b] adjustment for a copollutant.

Causes of mortality	Copollutant	Warm season RR (95% CI)	Warm season *p*-Value	Cool season RR (95% CI)	Cool season *p*-Value	Between season *p*-value
NO_2						
Nonaccident	–	1.02 (0.99–1.05)	0.243	1.05 (1.02–1.08)	0.003	0.193
	SO_2	1.00 (0.97–1.04)	0.927	1.01 (0.97–1.05)	0.694	0.795
Cardiovascular	–	1.00 (0.94–1.06)	0.981	1.10 (1.05–1.16)	0.000	0.013
	SO_2	0.99 (0.94–1.05)	0.793	1.08 (1.02–1.14)	0.007	0.039
Respiratory	–	1.05 (0.99–1.13)	0.126	1.09 (1.02–1.16)	0.015	0.509
	SO_2	1.03 (0.95–1.12)	0.529	1.08 (0.98–1.19)	0.120	0.408
SO_2						
Nonaccident	–	1.02 (0.99–1.04)	0.170	1.04 (1.02–1.07)	0.001	0.101
	NO_2	1.02 (0.99–1.04)	0.252	1.04 (1.00–1.07)	0.030	0.292
Cardiovascular	–	1.01 (0.97–1.05)	0.546	1.07 (1.02–1.11)	0.002	0.070
	NO_2	1.01 (0.97–1.06)	0.520	1.05 (1.00–1.09)	0.045	0.310
Respiratory	–	1.04 (0.99–1.09)	0.101	1.04 (1.00–1.09)	0.079	0.877
	NO_2	1.03 (0.97–1.08)	0.363	1.01 (0.94–1.08)	0.890	0.625
PM_{10}						
Nonaccident	–	1.01 (0.98–1.04)	0.529	1.02 (0.99–1.05)	0.168	0.659
	SO_2	1.00 (0.96–1.03)	0.802	0.99 (0.96–1.02)	0.437	0.715
Cardiovascular	–	1.00 (0.94–1.06)	0.911	1.04 (0.99–1.09)	0.135	0.306
	NO_2	1.00 (0.91–1.10)	0.983	0.97 (0.91–1.03)	0.349	0.614
Respiratory	–	1.05 (0.98–1.12)	0.194	1.06 (1.00–1.13)	0.054	0.761
	NO_2	1.04 (0.96–1.12)	0.379	1.05 (0.99–1.12)	0.139	0.810
O_3						
Nonaccident	–	0.99 (0.97–1.02)	0.609	1.04 (1.01–1.06)	0.012	0.026
	NO_2	0.99 (0.97–1.02)	0.537	1.03 (1.01–1.06)	0.021	0.032
Cardiovascular	–	0.98 (0.94–1.03)	0.485	1.05 (1.00–1.11)	0.038	0.044
	NO_2	0.98 (0.94–1.03)	0.513	1.04 (0.99–1.09)	0.150	0.132
Respiratory	–	0.99 (0.94–1.05)	0.750	1.08 (1.02–1.15)	0.011	0.027
	NO_2	0.99 (0.94–1.04)	0.710	1.08 (1.02–1.15)	0.013	0.030

Warm season, April–September; cool season, October–March.
[a]<1> Estimated from core model + pollutant + season + pollutant × season. [b]Estimated from <1> + copollutant + copollutant × season.

reducing the risks of outdoor ambient air pollution exposure.

Another major finding in this study is the positive exposure–response relationships for NO_2 and SO_2 and all the outcomes during the cool season. There were no thresholds, and the effects showed an inverted "J" shape at higher concentrations. At very high concentrations, the risks of mortality could be reduced possibly because vulnerable subjects may have died before the concentration had reached the maximum levels (*4*). During the warm season, we observed no consistent positive or negative relationships for all the pollutants. In Hong Kong, there are greater variations in weather conditions in the warm season, when heavy rain, rain storms, and typhoons are common. These factors, in addition to the frequent use of air-conditioning, would prevent the actual exposure–response relationships between air pollution and mortality from being readily observable.

In the absence of an observed linear exposure–response relationship, generalized additive modelling (GAM) could be used to examine whether there are any other forms of relationships. Instead of obtaining a single parameter for the effect, GAM is fitted to obtain a parameter at each point of the independent variable after applying some smoothing function to the data. The fitted values (presented as deviation from an overall mean), along with values of the independent variable, produce an exposure–response plot. It is useful, as demonstrated in this study, in the interpretation of results of daily time–series studies for health effects of air pollution.

Morris and Naumova (*33*) reported synergistic effects of carbon monoxide and lower temperatures on hospital admissions due to congestive heart failure in Chicago, Illinois (USA). Both CO and cold temperature can increase the load on the heart and thus increase the effect on cardiovascular morbidity (*33*). For other pollutants, including SO_2, the production of synergistic effects was biologically plausible, as both lower temperatures and high air pollutant concentrations were related to increased blood viscosity. Changes in blood rheology may be caused by an inflammatory process in the lung induced by air pollution or by thermoregulatory adjustment to mild surface cooling in cold weather (*34*,*35*). This study in Hong Kong is the first to show that all of the oxidant pollutants under study increased effects ($p < 0.07$) on cardiovascular mortality in the cool season. It is also the first study to demonstrate the relationship between pollutant concentration and mortality stratified by cool and warm seasons, on the basis of statistical models with offset on expected counts from the same core model, thus ensuring comparability in the effect estimates between the two seasons. Overall, during the cool season there was a 5–10% ($p < 0.038$) increase in nonaccidental and cardiovascular mortality; this results in an increase from the 10th to the 90th percentile (from linear extrapolation) for each of the oxidant pollutants under study. The nonsignificant relative risk estimate for SO_2 on respiratory disease may be due to the small change in concentration from the warm season to the cool season. In a sensitivity analysis using the method with offset on expected counts, the estimated increases were consistent but lower, with increases of 2–7% ($p < 0.046$)

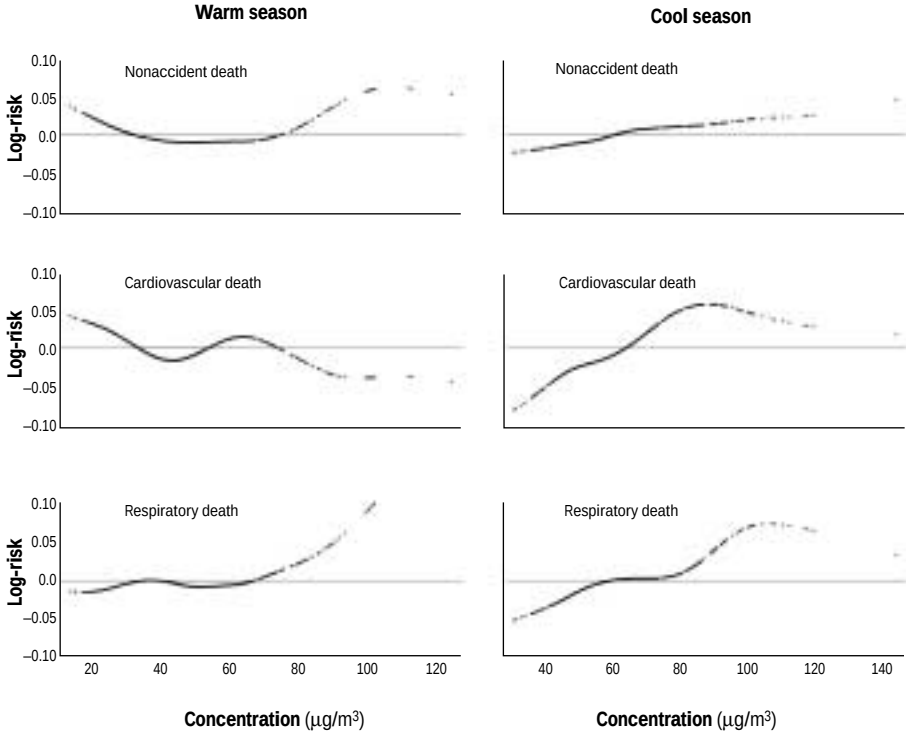

Figure 1. Smoothed plots of NO_2 against mortality risk in log scale (deviated from overall mean) at the best lagged day.

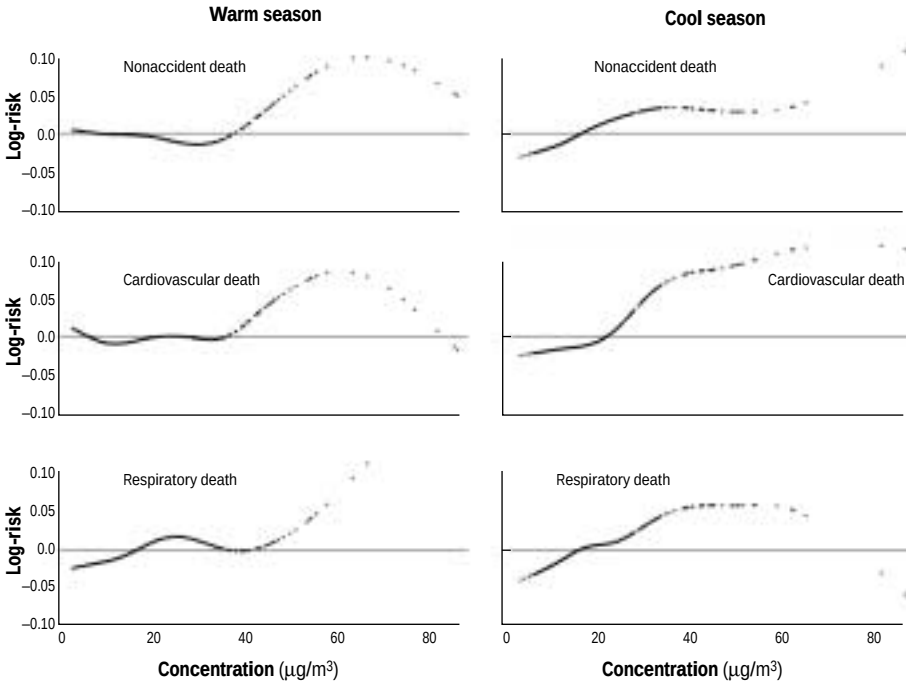

Figure 2. Smoothed plots of SO_2 against mortality risk in log scale (deviated from overall mean) at the best lagged day.

(data not shown). The larger *p*-values may be due to lower power in stratified analysis when the sample size was halved.

Except for respiratory mortality, no strong effects of particulate pollutants were observed in Hong Kong, unlike in other places, although the levels were high. This should be investigated further. The difference may arise from the use of a time–series study, in that the magnitude of the effect estimates depends on the day-to-day covariation of the daily health outcomes and pollutant concentrations instead of the absolute levels of the pollutant concentrations. However, PM_{10} was found to have a significant effect on respiratory mortality (RR = 1.05; $p = 0.028$) in both seasons combined, but the effects remain approximately the same (RR = 1.05–1.06) although nonsignificant ($p > 0.054$) in the by-season estimates. The importance of PM_{10} should not be diminished by this finding. NO_2 is important because of increasing volumes of vehicular traffic on the roads. SO_2 continues to have a strong effect, even though the concentrations have decreased and have been maintained at low levels. The formation of O_3 in the ambient air depends on a series of complicated photochemical reactions of oxygen, nitrogen oxides, and reactive hydrocarbons in the presence of sunlight. O_3 had been increasing until recently, and it is difficult and costly to control as a regional pollutant. However, for most of the pollutants, the effects were nonsignificant after adjusting for a copollutant; this may arise from a problem of multicollinearity, except for NO_2 in cardiovascular mortality and SO_2 in both nonaccidental and cardiovascular mortality. These observations, together with strong positive exposure–response relationships for NO_2 and SO_2, suggested that NO_2 and SO_2 have independent effects and may be better indicators of effects on mortality in this subtropical city. For O_3 all of the RR estimates were not significantly greater than unity; the RR estimates were insensitive to adjustment either for autocorrelation or copollutant (Tables 2 and 3) and were insensitive to the use of maximum, minimum, or mean temperature in the model (data not shown).

In setting air pollution control policy from a public health viewpoint, it is important to identify the health effects of air pollutants from local data. Because of the lack of data, there are few studies based on daily hospital admissions and mortality in the Asian Pacific region. For hospital admissions, there has been only one study in Australia (*36*) and two in Hong Kong (*30,37*). For mortality studies, there have been one in Beijing, China (*38*) based on 1-year daily data, two in Australia (*36,39*), and two in Korea (*40,41*). Our report should contribute to the understanding of the effects of air pollutants in this region and may clarify the differences in effects and mechanisms between Western and Eastern populations.

Local data on health effects of air pollution are required for setting standards and objectives for air pollution controls. When local data are not available, foreign data may be helpful, but they may not be relevant or applicable because of a difference in climate or other conditions. Our findings in this study provide information to support a review of air quality objectives with consideration of their effects on health (*10*).

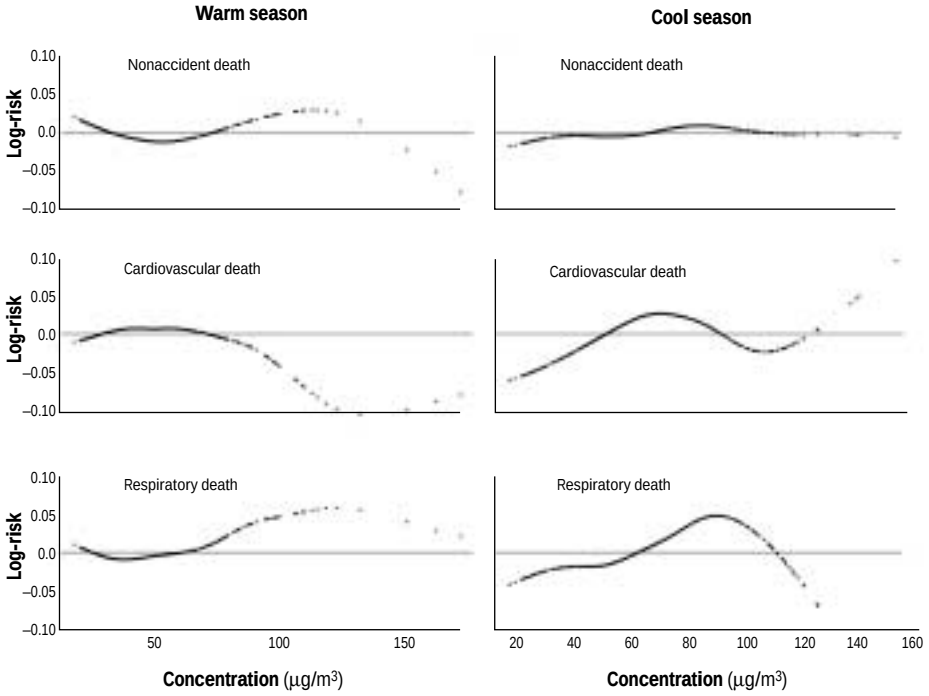

Figure 3. Smoothed plots of PM_{10} against mortality risk in log scale (deviated from overall mean) at the best lagged day.

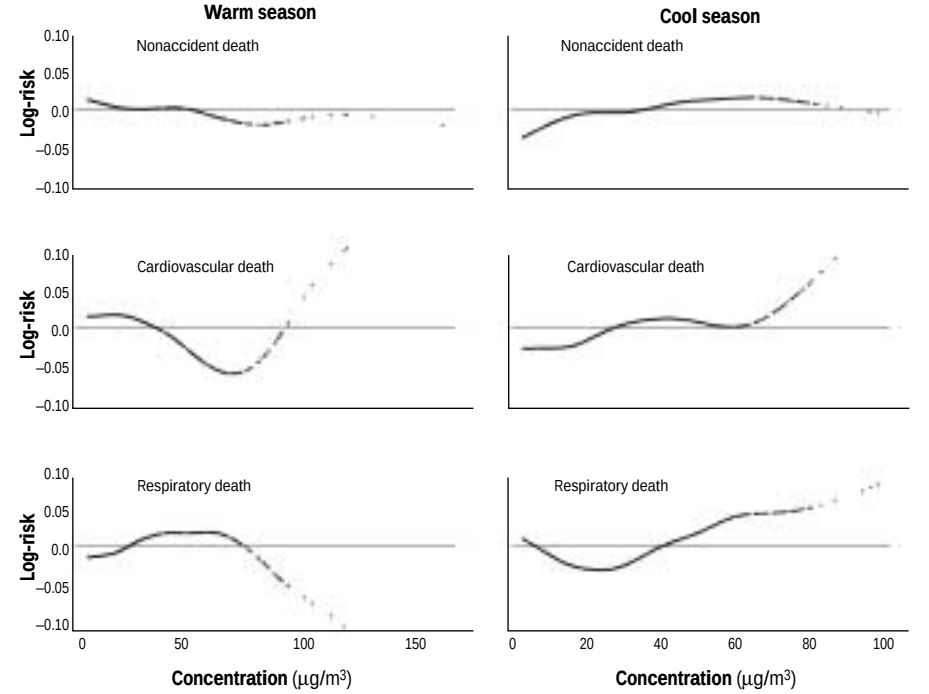

Figure 4. Smoothed plots of O_3 against mortality risk in log scale (deviated from overall mean) at the best lagged day.

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Minuta
Caso peruano: Estándares Nacionales de Calidad Ambiental para Dióxido de Azufre (SO_2).

1. Antecedentes

En Perú, a fines de la década del 90, se establecen como objetivos ambientales los Estándares Nacionales de Calidad Ambiental (ECA). En ese momento se hablaba de objetivos, porque se entendía que eran metas a ser alcanzadas por el conjunto de actividades de una zona (cuenca atmosférica).

Para elaborar estos Estándares de Calidad Ambiental, el Consejo Nacional del Ambiente (CONAM) aprobó un mecanismo llamado Grupos de Estudios Técnicos Ambientales (GESTA) para elaborar estas normas. GESTA estaba conformado por representantes del gobierno, industria, sociedad civil, academia, etc.

En el 2001, luego de dos años de trabajo en debates técnicos y normativos se aprobaron los primeros Estándares de Calidad Ambiental en el aire para dióxido de azufre (SO_2), el valor de 24 horas era 365 $\mu g/m^3$; el valor ECA para dióxido de azufre (SO_2) anual era 80 $\mu g/m^3$.

En la aprobación de la Ley General del Ambiente se señala que a partir de ese momento los ECA serán de cumplimiento obligatorio en todo el país. A partir del año 2008, cuando el Ministerio del Ambiente (MINAM) del Perú entra en funcionamiento, son aprobados los nuevos Estándares de Calidad Ambiental para Aire en agosto del 2008 (Decreto Supremo N°003-2008-MINAM). En estos se establece el valor ECA para dióxido de azufre (SO_2) de 24 horas en 80 $\mu g/m^3$ a partir del 1 de enero del 2009 y que a partir del 1 de enero del 2014 será de 20 $\mu g/m^3$ (valor guía de la Organización Mundial de la Salud). El valor ECA para dióxido de azufre (SO_2) anual se elimina.

La industria indicaba que ninguna de las zonas, en que se encuentran 4 fundiciones en el Perú, iba a cumplir con el valor de 80 $\mu g/m^3$ para 24 horas y menos con el valor de 20 $\mu g/m^3$. Atendido a lo anterior, la fundición de Ilo de la empresa Southern Copper se ha visto obligada a recortar producción cuando predicen que las condiciones meteorológicas serán desfavorables. Hay que considerar que para cumplir el valor de 80 $\mu g/m^3$ para 24 horas se dieron 4 meses para lograr el cumplimiento (agosto 2008 - 31 de diciembre 2008) y por esto la única opción que quedó fue reducir fusión.

El 1 de enero de 2014 entró en vigencia el valor de 20 $\mu g/m^3$ de dióxido de azufre (SO_2) para 24 horas. Los operadores de las 4 fundiciones y la Sociedad Nacional de Minería, Petróleo y Energía (SNMPE) llevaron su preocupación e información técnica a diferentes Ministerios y niveles del gobierno, explicando que no hay tecnología en el mundo que permita cumplir continuamente con 80 $\mu g/m^3$ y menos con 20 $\mu g/m^3$.

El Ministerio del Ambiente entrega como respuesta las normas complementarias (Decreto Supremo N°006-2013-MINAM), donde se señala que el valor de 20 $\mu g/m^3$ es obligatorio en todo el territorio nacional, exceptuando algunas ciudades (cuencas atmosféricas) como las de Ilo, La Oroya y Arequipa. La ciudad de Ilo tiene la única fundición de cobre en operación en el país; mientras la ciudad de La Oroya tiene una fundición polimetálica y en la ciudad de Arequipa el problema es el transporte.

Por lo anterior, las ciudades de Ilo, La Oroya y Arequipa deben cumplir con el valor de 80 $\mu g/m^3$ de dióxido de azufre para 24 horas, aunque no queda claro si se debe cumplir con el valor de 80 $\mu g/m^3$ en forma permanente o se deben implementar planes que permitan cumplir con el valor de 20 $\mu g/m^3$.

En conclusión, es posible aseverar que la norma de calidad de dióxido de azufre (SO_2) de Perú es un ejemplo de diseño de regulación que no considero algunos criterios regulatorios esenciales, tales como: principio de gradualidad y realismo, coherencia regulatoria, coordinación con otros instrumentos regulatorios, antecedentes y evolución de la regulación internacional.

Minuta elaborada a partir de información entregada por CODELCO:

- Cristián Ibarra, coordinador del proceso de revisión de la norma primaria de calidad SO_2, del Departamento de Normas.