Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality

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OBJECTIVES

(i) An update of the national analysis

a) to assess the confounding and modifying effect of community and neighbourhood level ecological covariates on the air pollution–mortality association at various scales;

b) to assess how spatial autocorrelation and multiple levels can be taken into account within the random effects Cox Model;

(iii) to assess the impact of refinement of air pollution exposure to the within-city or intraurban scale using land-use regression on the size and significance of health effects in Los Angeles and New York; and

(iv) to evaluate critical exposure time windows most relevant for the air pollution-mortality association.

BACKGROUND

FOLLOW-UP:

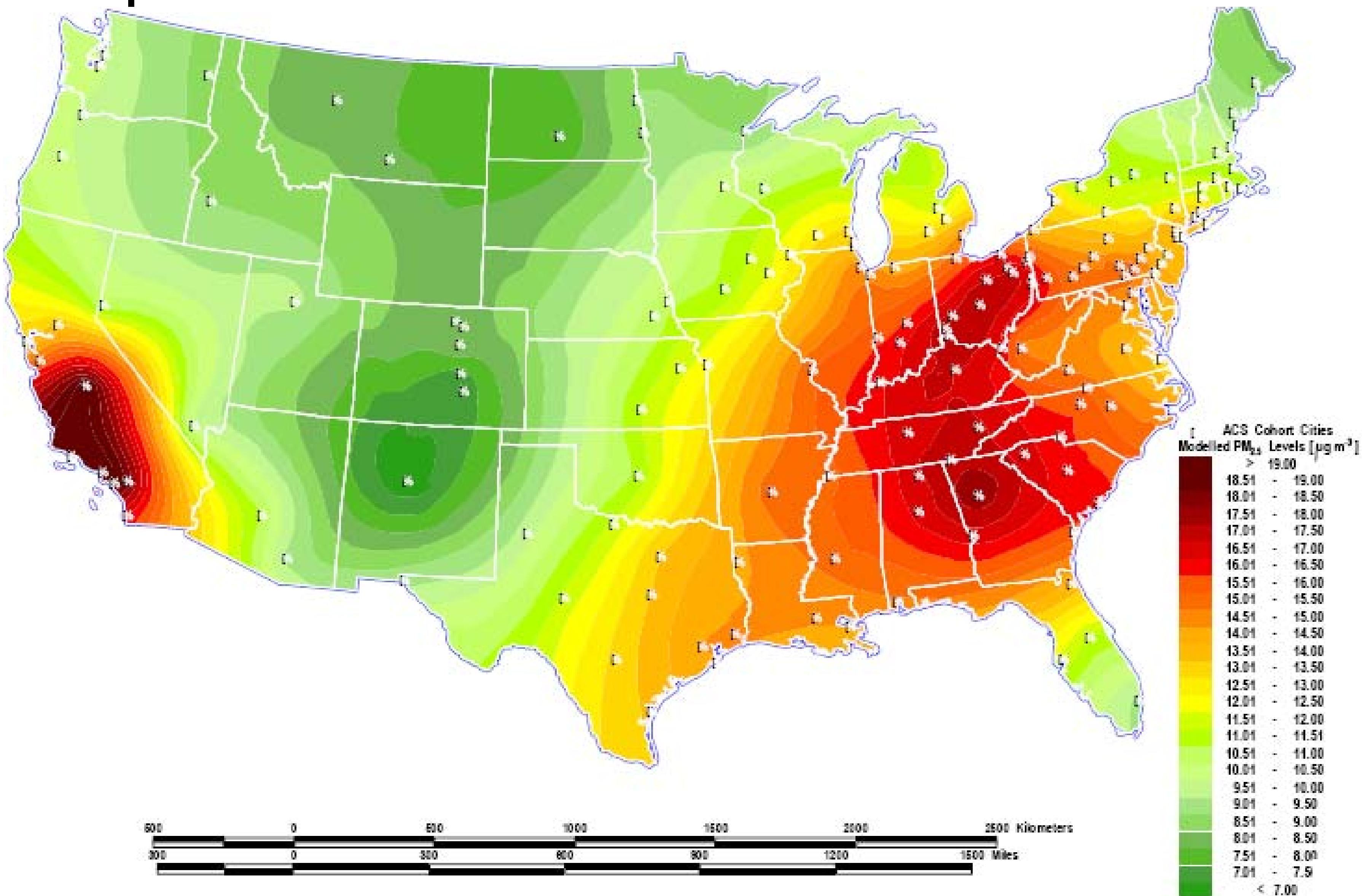
- The extended 18-year follow up included vital status data for the CPS-II cohort with multiple cause-of–death codes (through December 31, 2000) and more recent exposure data from air pollution monitoring sites for the metropolitan areas.

BACKGROUND

STUDY POPULATION:

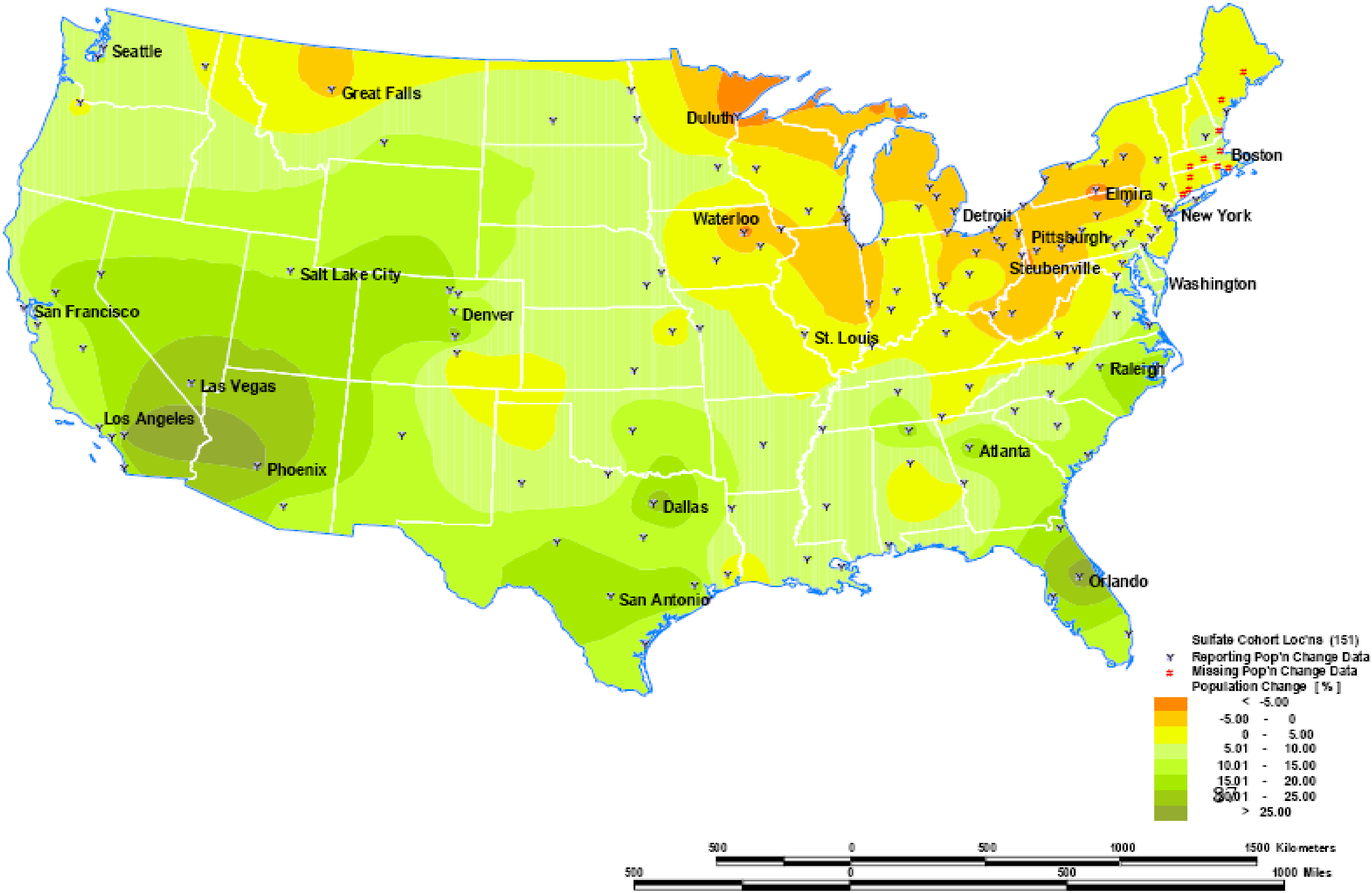
- Nearly 1.2 million adults aged $\geq$ 30 years and who were members of households with at least one individual aged > 45 years were enrolled into the study.
- The current study included only residents in U.S. metropolitan areas for which air pollution data were collected within the 48 contiguous states (including the District of Columbia), and who were enrolled by ACS volunteers in the fall of 1982.
- The analysis incorporated information from up to 172 different U.S. metropolitan areas.

Spatial distribution (kriged) of fine particles in the year 1999-2000 (mean)



Modelled (Kriged) Surface of 1980-86 Population Change

(Negative and Positive Values Indicate Percent Net Decreases and Increases Respectively)



HRs of pollution risk factors for selected causes of death with follow-up from 1982 to 2000, adjusting for 44 individual level covariates and stratifying the baseline hazard function by age, gender, and race using the standard Cox survival model (95% CIs).

Covariate	Number of MSA & Subjects	Level of Relative Risk	Cause of Death				
			All Causes	Cardiopulmonary	Ischemic Heart Disease	Lung Cancer	All Other Causes
$PM_{2.5}$ (1979-1983)	58 351338	10 $\mu g/m^3$	1.03 (1.01, 1.04)	1.06 (1.04, 1.08)	1.12 (1.09, 1.16)	1.08 (1.03, 1.14)	0.98 (0.96, 1.00)
$PM_{2.5}$ (1999-2000)	116 499968	10 $\mu g/m^3$	1.03 (1.01, 1.05)	1.09 (1.06, 1.12)	1.15 (1.11, 1. 20)	1.11 (1.04, 1.18)	0.97 (0.94, 1.00)
SO_4 (1980)	147 572312	5 $\mu g/m^3$	1.04 (1.03, 1.05)	1.04 (1.02, 1.05)	1.06 (1.04, 1.08)	1.05 (1.02, 1.09)	1.03 (1.02, 1.05)
SO_4 (1990)	52 268336	5 $\mu g/m^3$	1.07 (1.05, 1.09)	1.06 (1.03, 1.09)	1.14 (1.10, 1.19)	1.04 (0.97, 1.11)	1.08 (1.05, 1.11)
SO_2 (1980)	115 513450	5 ppb	1.02 (1.02, 1.03)	1.02 (1.01, 1.03)	1.04 (1.02, 1.05)	1.00 (0.98, 1.02)	1.02 (1.02, 1.03)
PM_{15} (1979-1983)	57 345824	15 $\mu g/m^3$	1.01 (1.00, 1.02)	1.03 (1.02, 1.05)	1.06 (1.04, 1.08)	1.00 (0.97, 1.04)	0.99 (0.97, 1.00)

HRs of pollution risk factors for selected causes of death with follow-up from 1982 to 2000, adjusting for 44 individual level covariates and stratifying the baseline hazard function by age, gender, and race using the standard Cox survival model (95% CIs).

Covariate	Number of MSA & Subjects	Level of Relative Risk	Cause of Death				
			All Causes	Cardiopulmonary	Ischemic Heart Disease	Lung Cancer	All Other Causes
O_3 (1980)	118 531826	10 ppb	1.00 (0.99, 1.01)	1.01 (1.00, 1.03)	1.01 (0.98, 1.03)	1.00 (0.96, 1.04)	0.99 (0.97, 1.00)
O_3 (1980–April-Sept)	118 531185	10 ppb	1.02 (1.01, 1.02)	1.03 (1.02, 1.04)	1.01 (0.99, 1.02)	0.99 (0.96, 1.02)	1.01 (1.00, 1.02)
NO_2 (1980)	76 406917	10 ppb	0.99 (0.99, 1.00)	1.01 (1.00, 1.02)	1.02 (1.00, 1.03)	0.99 (0.97, 1.01)	0.98 (0.97, 0.99)
CO (1980)	108 508538	1 ppm	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	1.01 (0.99, 1.03)	0.99 (0.97, 1.03)	0.99 (0.98, 1.01)

ECOLOGICAL COVARIATES

- **Air Conditioning (%)**
- **Grade 12 (%)**
- **Non White (%)**
- **Unemployment (%)**
- **Household Income ($000s)**
- **Income Disparity (GINI)**
- **Poverty (%)**

- Covariates were examined at the zip code level (ZCA), the metropolitan statistical area level (MSA) and by the value of the difference obtained between the mean ZCA value and the MSA value (DIFF):

ECOLOGICAL COVARIATES

- Risk estimates increased with the inclusion of ecologic covariates at all scales.

- The inclusion of ecologic covariates at both the MSA and DIFF scale simultaneously increased the HR for mortality from ischemic heart disease (IHD) associated with $PM_{2.5}$ (2000 levels) and SO_4 (1990 levels) by 7.5 and 12.8%, respectively.

Pollutant	Cause of Death	*Ecological Covariate Adjustment*			
		None	*ZCA*	*MSA*	*MSA & DIFF*
$PM_{2.5}$ (1999-2000)	All Causes	1.034 (1.016, 1.053)	1.054 (1.035, 1.075)	1.053 (1.031, 1.074)	*1.056 (1.035, 1.078)*
	Cardiopulmonary	1.094 (1.065, 1.124)	1.126 (1.095, 1.158)	1.126 (1.093, 1.161)	*1.129 (1.095, 1.164)*
	Ischemic Heart Disease	1.153 (1.111, 1.197)	1.210 (1.163, 1.258)	1.231 (1.181, 1.284)	*1.240 (1.189, 1.293)*
	Lung Cancer	1.108 (1.037, 1.183)	1.135 (1.059, 1.216)	1.130 (1.050, 1.216)	*1.137 (1.056, 1.225)*
	Other Causes	0.969 (0.944, 0.995)	0.978 (0.952, 1.006)	0.975 (0.946, 1.004)	*0.979 (0.950, 1.008)*

Pollutant	Cause of Death	*Ecological Covariate Adjustment* *None*	*ZCA*	*MSA*	*MSA & DIFF*
SO_4 **(1990)**	All Causes	1.069 (1.049, 1.090)	1.089 (1.066, 1.112)	1.082 (1.056, 1.109)	*1.086 (1.060, 1.113)*
	Cardiopulmonary	1.057 (1.027, 1.088)	1.095 (1.061, 1.130)	1.110 (1.070, 1.152)	*1.114 (1.074, 1.156)*
	Ischemic Heart Disease	1.142 (1.097, 1.189)	1.196 (1.145, 1.248)	1.282 (1.219, 1.349)	*1.288 (1.225, 1.355)*
	Other Causes	1.086 (1.056, 1.117)	1.090 (1.057, 1.124)	1.065 (1.027, 1.104)	*1.068 (1.030, 1.107)*
SO_2 **(1980)**	All Causes	1.021 (1.016, 1.027)	1.022 (1.016, 1.028)	1.019 (1.013, 1.025)	*1.020 (1.014, 1.026)*
	Cardiopulmonary	1.020 (1.012, 1.028)	1.021 (1.012, 1.029)	1.021 (1.012, 1.031)	*1.022 (1.013, 1.032)*
	Ischemic Heart Disease	1.037 (1.026, 1.049)	1.043 (1.031, 1.055)	1.057 (1.044, 1.071)	*1.059 (1.046, 1.072)*
	Other Causes	1.025 (1.017, 1.033)	1.025 (1.017, 1.034)	1.019 (1.009, 1.028)	*1.019 (1.010, 1.029)*

SPATIAL AUTOCORRELATION

- Cox regression models are based on the assumption that individual observations are independent.
- However, complex spatial patterns may exist leading to spatial autocorrelation:
  - survival experience may cluster by community or neighborhood.

SPATIAL AUTOCORRELATION

- A random effects Cox regression model was developed to take into account spatial patterns in the data that could be described at either one (e.g., city) or two (e.g., zip code and city) levels of clustering.

SPATIAL AUTOCORRELATION

- Cox model with two levels of spatially correlated random effects.
  - *m* spatially correlated clusters indexed by *i.*
  - *Ji* spatially correlated subclusters indexed by *(i, j).*
  - cluster-level random effects *U1, …, Um*

$$E(U_i) = 1 \text{ and } cov(U_s, U_i) = \sigma^2 \rho_1^{d(s,i)}$$

  - where $0 < \rho_1 < 1$
  - *d(s, i)* indicates the distance between clusters indexed by *s* and *i.*

SPATIAL AUTOCORRELATION

- We further assume that, given the cluster-level random effects $U^* = u^* = (u_1, \ldots, u_m)$, the subcluster-level random effects $U_{11}, \ldots, U_{mJm}$ are positive and spatially dependent with

$$E(U_{ij}|U^*) = U_i \text{ and } cov(U_{st}, U_{ij}|U^*) = \delta(s, i)v^2\rho_2^{r\{(s,t),(i,j)\}}$$

  - where $0 < \rho_2 < 1$ and $r\{(i, t), (i, j)\}$ indicates the distance between subclusters indexed by (s, t) and (i, j).

SPATIAL AUTOCORRELATION

- The inclusion of spatial autocorrelation at both the MSA and ZCA levels increased the variance of the random effects, and widened the CIs for the $PM_{2.5}$ HR, providing some evidence of spatial clustering of residual mortality coinciding with the spatial pattern of $PM_{2.5}$

Model	No Spatial Autocorrelation		Spatial Autocorrelation		
	$PM_{2.5}$ (2000) Hazard Ratio (10 µg/m^3)	ZCA Variance (x10^{-3})	$PM_{2.5}$ (2000) Hazard Ratio (10 µg/m^3)	ZCA Variance (x10^{-3})	ZCA Autocorrelation
All-cause mortality					
44 individual covariates	NA	7.008	NA	10.02	0.3307*
$PM_{2.5}$ + 44 individual covariates	1.158 (1.035, 1.295)	4.386	1.160 (1.021, 1.317)	7.591	0.3307*
$PM_{2.5}$ + 44 individual covariates + parsimonious contextual covariates	1.152 (1.034, 1.283)	0.229	1.152 (1.032, 1.286)	0.623	0.3307*
$PM_{2.5}$ + 44 individual covariates + parsimonious contextual covariates + FreeWay Int.	1.156 (1.036, 1.289)	0.233	1.156 (1.034, 1.293)	0.847	0.3307*

* rho reaches maximum value

** rho<0

EXPOSURE-TIME WINDOWS

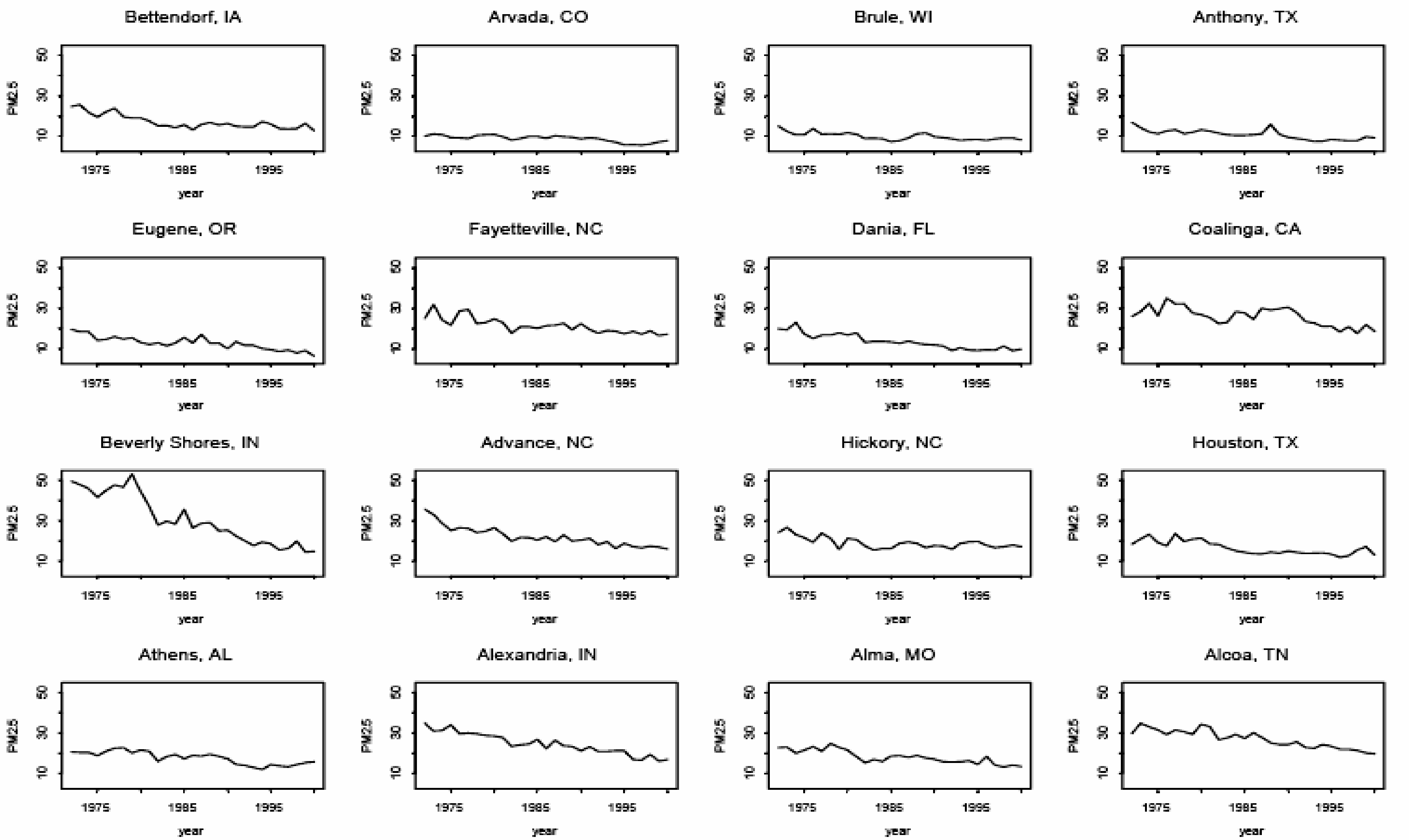
Case Study: Dublin, Ireland

- The effect of air pollution controls- ie, the ban on coal sales in 1990- on particulate air pollution and death rates in Dublin were assessed (Lancet, 2002).
  - Average black smoke concentrations in Dublin declined by 35.6 μg/m^3 (70%) after the ban on coal sales.
  - Adjusted non-trauma death rates decreased by 5.7% (95% CI 4–7, $p<0{\cdot}0001$), respiratory deaths by 15.5% (12–19, $p<0{\cdot}0001$), and cardiovascular deaths by 10.3% (8–13, $p<0{\cdot}0001$).

EXPOSURE-TIME WINDOWS

- *Is there a critical exposure-time window that is primarily responsible for the increased mortality associated with ambient air pollution?*

Time trends in $PM_{2.5}$ concentration in selected MSAs



EXPOSURE-TIME WINDOWS

- In comparison to more distal exposures, models using $PM_{2.5}$ and SO_2 exposures from the most recent five years provided a better fit to available data on all-cause, lung cancer, and cardiopulmonary mortality.

Exposure Time Window	$PM_{2.5}$ (A) (n=65,772)	$PM_{2.5}$ (B) (n=81,466)	$PM_{2.5}$ (A+B) (n=147,238)	SO_2 (n=82,230)
All cause mortality				
Years 1-5 RR (95% CI)	1.02 (0.95, 1.09)	1.01 (0.99, 1.03)	1.00 (0.99, 1.02)	1.03 (0.97-1.09)
Years 6-10 RR (95% CI)	0.97 (0.91, 1.04)	1.01 (0.99, 1.02)	1.04 (1.02, 1.05)	0.99 (0.95-1.03)
Years 11-15 RR (95% CI)	0.98 (0.92, 1.04)	1.00 (0.99, 1.02)	1.08 (1.06, 1.09)	0.99 (0.95-1.02)

[a] Age, sex, and race stratified and adjusted for smoking, education, marital status, body mass index, alcohol, occupational exposures, and diet.

Exposure Time Window	$PM_{2.5}$ (A) (n=65,772)	$PM_{2.5}$ (B) (n=81,466)	$PM_{2.5}$ (A+B) (n=147,238)	SO_2 (n=82,230)
		Cardiopulmonary mortality		
Years 1-5 RR (95% CI)	1.01 (0.90, 1.13)	1.06 (1.03, 1.09)	1.05 (1.02, 1.07)	1.06 (0.97-1.17)
Years 6-10 RR (95% CI)	0.98 (0.88, 1.08)	1.05 (1.03, 1.07)	1.07 (1.05, 1.10)	0.99 (0.93-1.05)
Years 11-15 RR (95% CI)	0.99 (0.90, 1.09)	1.04 (1.02, 1.06)	1.10 (1.08, 1.12)	1.00 (0.94-1.05)

[a] Age, sex, and race stratified and adjusted for smoking, education, marital status, body mass index, alcohol, occupational exposures, and diet.

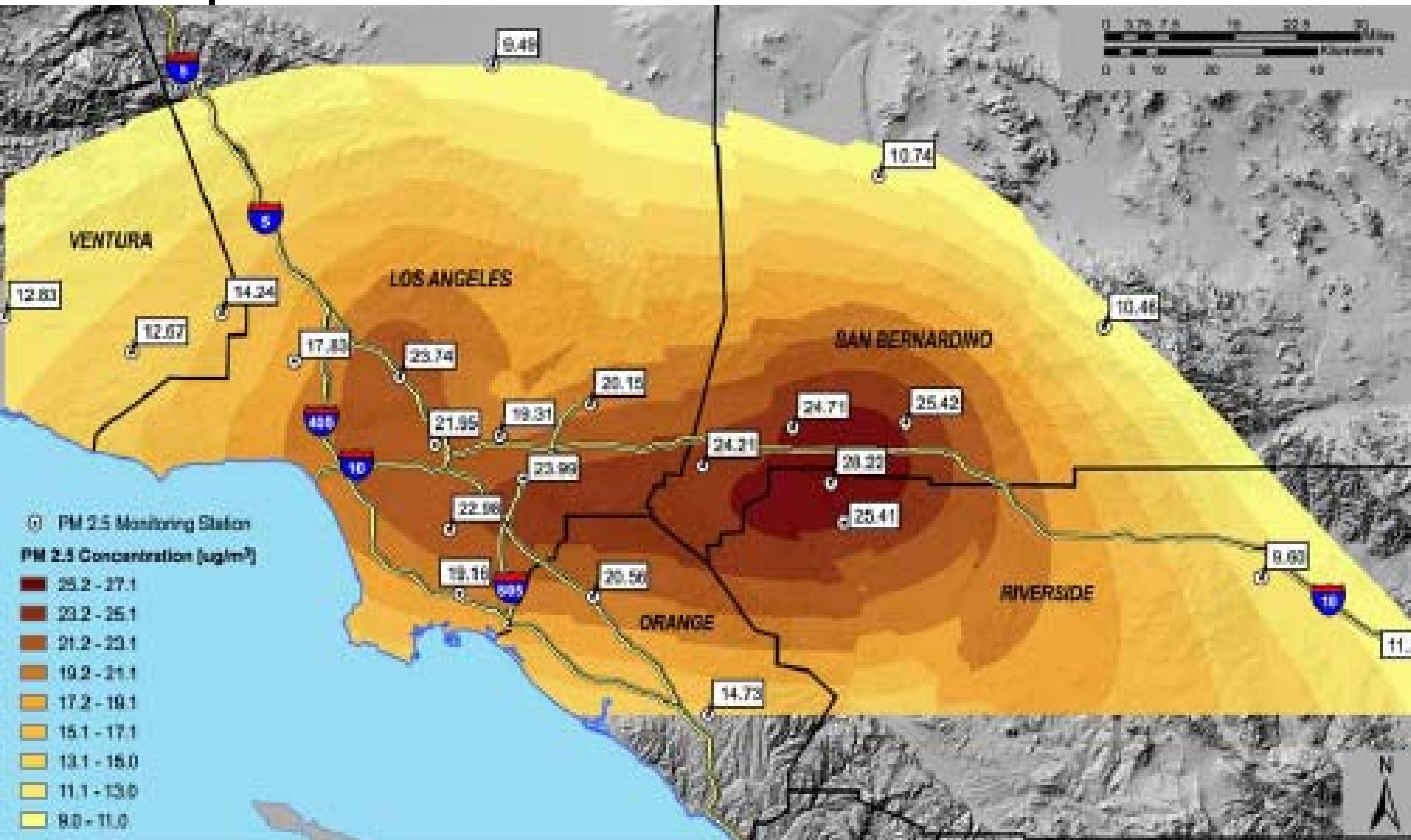
Exposure Time Window	$PM_{2.5}$ (A) (n=65,772)	$PM_{2.5}$ (B) (n=81,466)	$PM_{2.5}$ (A+B) (n=147,238)	SO_2 (n=82,230)
Lung cancer mortality				
Years 1-5 RR (95% CI)	1.15 (0.91, 1.45)	1.10 (1.04, 1.17)	1.09 (1.03, 1.16)	1.12 (0.94-1.35)
Years 6-10 RR (95% CI)	1.02 (0.83, 1.25)	1.06 (1.01, 1.12)	1.10 (1.06, 1.17)	1.03 (0.91-1.16)
Years 11-15 RR (95% CI)	1.09 (0.90, 1.32)	1.05 (1.01, 1.10)	1.15 (1.10, 1.20)	0.98 (0.87-1.09)

[a] Age, sex, and race stratified and adjusted for smoking, education, marital status, body mass index, alcohol, occupational exposures, and diet.

INTRAURBAN ANALYSES

- **LOS ANGELES**
  - Results of the LA spatial analysis found health effects nearly three times greater than earlier analyses using between-community exposure contrasts
  - This suggests chronic health effects associated with intraurban gradients in exposure to $PM_{2.5}$ may be even larger than previously reported associations across MSAs.

LOS ANGELES

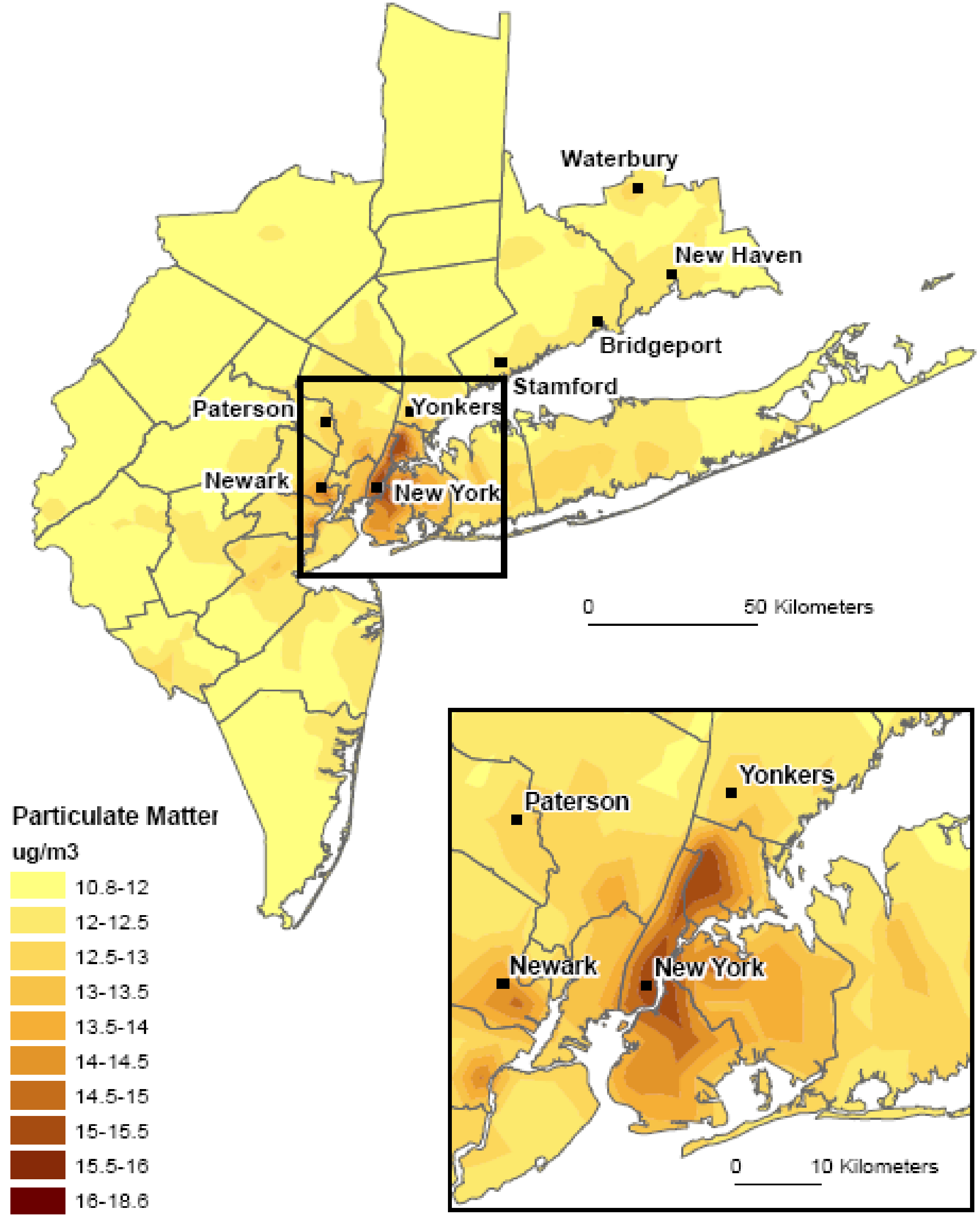


VENTURA
LOS ANGELES
SAN BERNARDINO
RIVERSIDE
ORANGE
10.74
14.24
12.67
21.95
19.31
24.71
25.42
24.31
25.41
10.46
14.73
PM 2.5 Monitoring Station
PM 2.5 Concentration (ug/m³)

LOS ANGELES

Follow up 1982-2000 Cox Model Covariates	Cause of Death			
	All Cause	IHD ICD9: 410-414	Cardiopulmonary ICD9: 400-440, 460-519	Lung Cancer ICD9: 162
Total subjects: N=22,905	5,856	1,462	3,136	434
PM2.5 (LUR28pred) only	1.197 (1.082,1.325)	1.415 (1.154,1.735)	1.179 (1.025,1.356)	1.460(1.013,2.105)
44 Individual Covariates	1.143 (1.033,1.266)	1.331 (1.084,1.634)	1.114 (0.968,1.282)	1.392(0.964,2.010)
+ Air Conditioning	1.142 (1.031,1.265)	1.333 (1.085,1.638)	1.121 (0.974,1.290)	1.376(0.952,1.989)
+ Percent of Black	1.145 (1.033,1.269)	1.347 (1.096,1.656)	1.120 (0.972,1.289)	1.411(0.976,2.041)
+ Percent of White	1.151 (1.036,1.278)	1.362 (1.103,1.682)	1.127 (0.976,1.302)	1.471(1.008,2.147)
+ Percent of Hispanic	1.132 (1.016,1.261)	1.322 (1.065,1.641)	1.113 (0.960,1.290)	1.415(0.956,2.096)
+ Percent of Unemployed	1.127 (1.015,1.252)	1.328 (1.075,1.641)	1.129 (0.977,1.305)	1.279(0.879,1.862)
+ Mean Income	1.146 (1.035,1.268)	1.332 (1.086,1.635)	1.115 (0.970,1.283)	1.388(0.963,2.001)
+ Total population	1.141 (1.030,1.264)	1.322 (1.076,1.624)	1.108 (0.963,1.275)	1.396(0.967,2.016)
+ Income inequality	1.110 (0.999,1.234)	1.254 (1.014,1.552)	1.056 (0.913,1.222)	1.306(0.893,1.910)
+ Percent of GRD12	1.144 (1.033,1.266)	1.334 (1.087,1.637)	1.118 (0.972,1.286)	1.386(0.961,2.000)
+ All social factors	1.142 (1.026,1.272)	1.322 (1.064,1.642)	1.107 (0.954,1.285)	1.399(0.949,2.061)
+ AC, Income, GRD12,SF	1.115 (1.003,1.239)	1.263 (1.020,1.563)	1.072 (0.926,1.241)	1.290(0.881,1.890)
+ Parsimonious con. Covs.	1.126 (1.014,1.251)	1.264 (1.022,1.563)	1.086 (0.939,1.256)	1.311(0.897,1.915)
Copollutant control				
44 Covs .+ O3 (EPDC)	1.191 (1.069,1.327)	1.455 (1.171,1.810)	1.187 (1.023,1.378)	1.446(0.982,2.128)
44 Covs. + O3 (Average)	1.176 (1.057,1.307)	1.431 (1.155,1.772)	1.152 (0.996,1.334)	1.489(1.018,2.178)
44 Cvos. + FreeWays	1.170 (1.054,1.299)	1.393 (1.127,1.721)	1.134 (0.982,1.310)	1.439(0.989,2.095)
Copollutant risk estimates				
Ozone (EPDC)	0.985(0.964,1.006)	0.973(0.932,1.015)	0.966 (0.938,0.994)	0.989(0.917,1.068)
Ozone (Average)	0.993(0.977,1.010)	0.984(0.952,1.017)	0.985(0.963,1.008)	0.970(0.912,1.032)
FreeWay within 500 m	0.987(0.875,1.113)	0.898(0.706,1.143)	0.915(0.775,1.081)	1.440(0.939,2.208)
FreeWay within 1000m	0.974(0.894,1.062)	1.048(0.885,1.241)	0.982(0.874,1.104)	0.942(0.685,1.295)

NEW YORK


Waterbury
New Haven
Bridgeport
Stamford
Yonkers
Paterson
Newark
New York
0 50 Kilometers
Particulate Matter
ug/m3
10.8-12
12-12.5
12.5-13
13-13.5
13.5-14
14-14.5
14.5-15
15-15.5
15.5-16
16-18.6
Yonkers
Paterson
Newark
New York
0 10 Kilometers

INTRAURBAN ANALYSES

- **NEW YORK**
  - Unlike the LA results, mortality for all-cause, cardiopulmonary, and lung cancer deaths was not elevated in the NYC spatial analysis.
  - Large and significant effects were seen for IHD, providing evidence of a specific association with a cause of death that has high biologic plausibility.

NEW YORK

Follow up 1982-2000 Cox Model Covariates	Cause of Death			
	All Cause	IHD ICD9: 410-414	Cardiopulmonary ICD9: 400-440, 460-519	Lung Cancer ICD9: 162
Total subjects: N= 44,056	10,559	2,735	4,625	853
$PM_{2.5}$ (LUR28pred) only	1.011(0.935,1.047)	1.109(1.039,1.182)	0.977(0.926,1.031)	1.036(0.911,1.179)
44 Individual Covariates	0.984(0.948,1.020)	1.072(1.003,1.147)	0.953(0.902,1.007)	0.955(0.836,1.091)
+ Air Conditioning	0.987(0.951,1.024)	1.071(1.001,1.147)	0.956(0.904,1.011)	0.962(0.841,1.102)
+ Percent of White	0.987(0.950,1.026)	1.088(1.013,1.169)	0.950(0.895,1.008)	1.002(0.872,1.151)
+ Percent of Unemployed	0.970(0.933,1.009)	1.066(0.992,1.146)	0.927(0.874,0.984)	0.962(0.835,1.108)
+ Mean HouseIncome	0.968(0.930,1.007)	1.050(0.976,1.130)	0.922(0.868,0.979)	0.950(0.824,1.095)
+ Percent of GRD12	1.006(0.968,1.045)	1.139(1.059,1.224)	0.983(0.927,1.042)	0.986(0.858,1.135)
+ GINI	0.998(0.959,1.039)	1.102(1.023,1.188)	0.969(0.912,1.029)	0.961(0.832,1.110)
+ POV124	0.979(0.940,1.021)	1.080(1.000,1.165)	0.929(0.873,0.990)	1.004(0.866,1.163)
+ All 7 ECovs	0.977(0.932,1.025)	1.072(0.980,1.172)	0.940(0.875,1.011)	0.985(0.832,1.166)
+ Ozone (q3_99_01)	0.997(0.955,1.042)	1.058(0.975,1.148)	0.963(0.902,1.029)	0.967(0.828,1.129)
+ Ozone+All 7 ECovs.	0.982(0.934,1.034)	1.054(0.957,1.161)	0.938(0.868,1.014)	1.000(0.836,1.196)

INTRAURBAN ANALYSES

A comparison of mortality hazard ratios associated with each 10 ug/m^3 increase of $PM_{2.5}$ concentrations (LA) with exposure estimated by LUR and kriging.

Cause of Death Cox Model Covariates	LA LUR	 Kriging
All Causes		
PM2.5 only	1.20 (1.08,1.32)	1.24 (1.11,1.37)
44 Individual Covariates	1.14 (1.03,1.27)	1.17 (1.05, 1.30)
IHD		
PM2.5 only	1.42 (1.15,1.74)	1.49 (1.20, 1.85)
44 Individual Covariates	1.33 (1.08,1.63)	1.39 (1.12, 1.73)
Cardiopulmonary		
PM2.5 only	1.18 (1.02,1.36)	1.20 (1.04, 1.39)
44 Individual Covariates	1.11 (0.97,1.28)	1.12 (0.97, 1.30)
Lung Cancer		
PM2.5 only	1.46(1.01,2.10)	1.60 (1.09, 2.33)
44 Individual Covariates	1.39(0.96,2.01)	1.44 (0.98, 2.11)

INTRAURBAN ANALYSES

- Upon comparing subject characteristics in LA and NYC, it appeared unlikely that the differences observed among the national study and the two intraurban analyses were attributable differences in the underlying characteristics in each cohort group.

- The differences between NYC and LA may be attributable to fundamental differences in the topographical, geographical, and urban attributes of these two megalopolisis.

PHASES I, II, III (1998-2008): Extended follow-up

Cause of Death	Krewski et al. (2000) Follow-up to 1989	Krewski et al. (2008) Follow-up to 2000	
PM2.5 Exposure	1980	1980	2000
Number of MSAs	50	58	116
Number of participants	298,825	342,521	488,370
Number of deaths			
All Cause	23,180	90,783	128,954
Cardiopulmonary	11,262	44,866	63,917
Lung Cancer	2,001	6,827	9,788
Person-Years	2,109,750	5,542,998	7,908,283

CONCLUSIONS: Mortality risk estimates

- High degree of consistency in risk estimates across the 18 year follow-up period
- IHD was consistently associated with the largest mortality risk estimates at the national and city specific (LA and NYC) level.
- Lung cancer mortality not associated with PM2.5 in Phase II, but was so in Phase III because of the larger number of lung cancer deaths

CONCLUSIONS: Ecologic covariates

- Adjustment for ecologic covariates was performed in order to attempt to more fully account for socio-demographic risks and thus yield more accurate risk estimates of air pollution.

- In nearly all models adjusting for the seven ecologic covariates simultaneously, the HR tended to increase in comparison to models with no adjustment, although many of the differences were small.

CONCLUSIONS: Spatial autocorrelation

- Clear spatial patterns in both exposure and mortality data, with positive spatial correlation coefficients
- Uncertainty in risk estimates increased with adjustment for spatial autocorrelation, but only slightly
- Random effects Cox regression model a useful tool for analysis correlated survival data

CONCLUSIONS: Exposure time windows

- Some evidence that proximal (within the last 5 years) exposures are more important than distal (more than 5 years ago) exposures to $PM_{2.5}$

- However, limited inter-individual temporal variation in exposures makes it difficult to identify the most critical period of exposure

CONCLUSIONS: Intra-urban analyses

- Comparison of the mortality risk estimates obtained in the national and intra-urban analyses of the ACS cohort indicates that the national risk estimates cannot be directly applied to all urban areas within the U.S.

- The observed differences between NYC and LA further indicate that mortality risk estimates can vary appreciably among large urban areas with different characteristics.

- Despite these quantitative differences, both the national and intra-urban analyses confirm an association between $PM_{2.5}$ and mortality in urban areas throughout the U.S.

CONCLUSIONS: Air quality management

- The epidemiological results reported here are consistent with those from other population-based studies, which collectively strongly support the hypothesis that long-term exposure to $PM_{2.5}$ increases mortality in the general population.
- Phase III of the Particle Epidemiology Reanalysis Project has provided additional support for the development of cost-effective air quality management policies and strategies.

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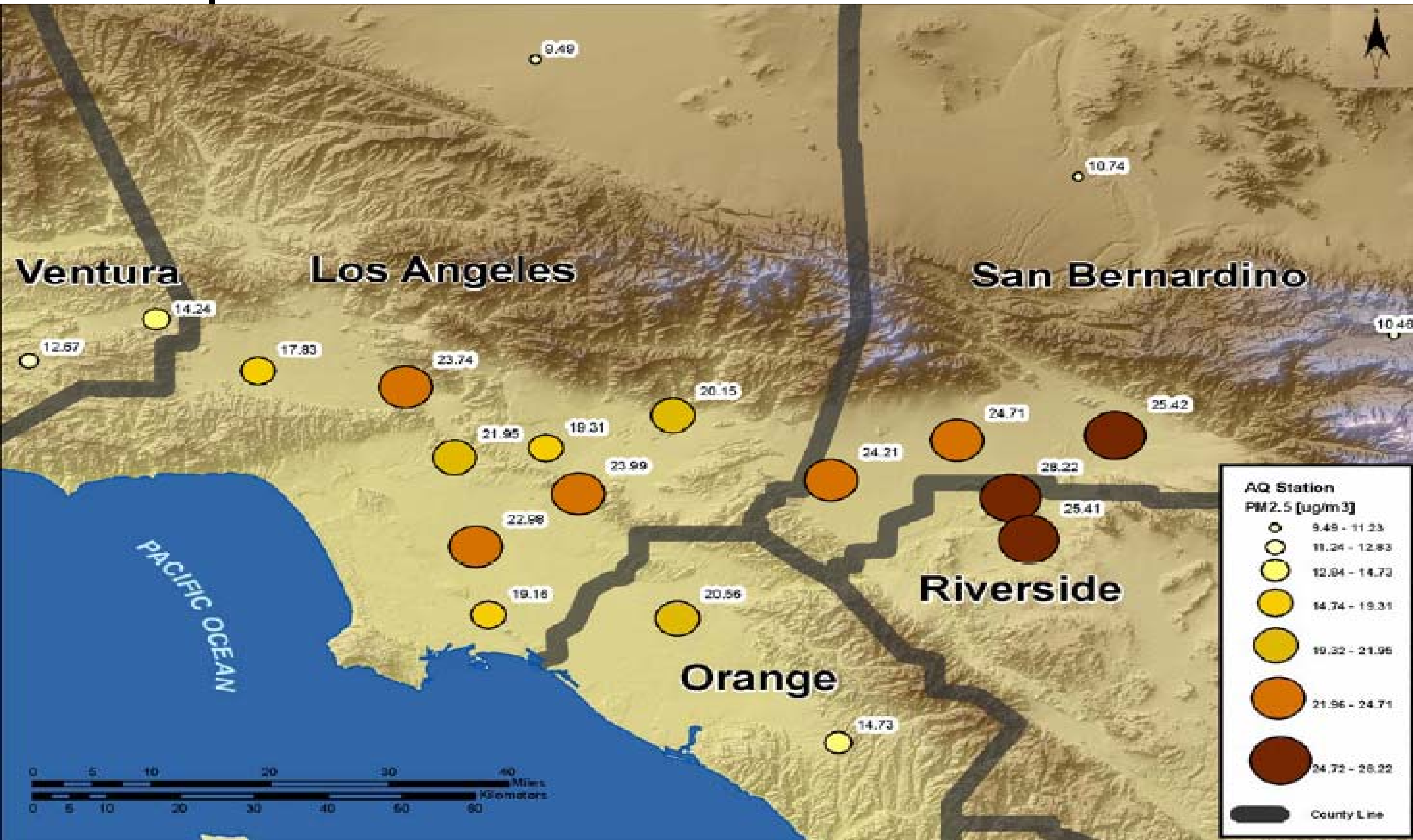
Pollutant	Cause of Death	*Ecological Covariate Adjustment* *None*	*ZCA*	*MSA*	*MSA & DIFF*
O_3 **(1980 – April to Sept.)**	All Causes	1.016 (1.008, 1.024)	1.014 (1.006, 1.023)	1.006 (0.998, 1.015)	*1.008* *(0.999, 1.017)*
	Cardiopulmonary	1.028 (1.016, 1.041)	1.027 (1.014, 1.040)	1.015 (1.002, 1.028)	*1.016* *(1.002, 1.029)*
NO_2 **(1980)**	Ischemic Heart Disease	1.018 (1.004, 1.031)	1.030 (1.015, 1.045)	1.033 (1.016, 1.051)	*1.035* *(1.017, 1.053)*
	Other Causes	*0.982* *(0.972, 0.991)*	*0.986* *(0.976, 0.997)*	*0.990* *(0.978, 1.002)*	*0.991* *(0.979, 1.003)*

*: ZCA Level – ecological covariates defined at the zip code area; MSA level – ecological covariates defined as the average of the ZCA values within each MSA.

LOS ANGELES



Ventura
Los Angeles
San Bernardino
Riverside
Orange
PACIFIC OCEAN
9.49
10.74
14.24
12.57
17.83
23.74
20.15
21.95
18.31
23.99
22.98
19.16
20.56
14.73
24.21
24.71
25.42
28.22
25.41
AQ Station
PM2.5 [ug/m3]
9.49 - 11.23
11.24 - 12.83
12.84 - 14.73
14.74 - 19.31
19.32 - 21.95
21.96 - 24.71
24.72 - 28.22
County Line
Miles
Kilometers

INTRAURBAN ANALYSES

A comparison of mortality hazard ratios associated with each 10 ug/m^3 increase of $PM_{2.5}$ concentrations (LA) or an interdecile (P_{10}-P_{90}, 1.5 µg/m^3) of $PM_{2.5}$ (NYC) with exposure estimated by LUR.

Cause of Death Cox Model Covariates	LA LUR	NYC LUR
All Causes		
PM2.5 only	1.20 (1.08,1.32)	1.01 (0.94,1.05)
44 Individual Covariates	1.14 (1.03,1.27)	0.98 (0.95,1.02)
IHD		
PM2.5 only	1.42 (1.15,1.74)	1.11 (1.04,1.18)
44 Individual Covariates	1.33 (1.08,1.63)	1.07 (1.00,1.15)
Cardiopulmonary		
PM2.5 only	1.18 (1.02,1.36)	0.98 (0.93,1.03)
44 Individual Covariates	1.11 (0.97,1.28)	0.95 (0.90,1.01)
Lung Cancer		
PM2.5 only	1.46(1.01,2.10)	1.04 (0.91,1.18)
44 Individual Covariates	1.39(0.96,2.01)	0.96 (0.84,1.09)

PHASES I, II, III (1998-2008): Extended follow-up

Cause of Death	Krewski et al. (2000) Follow-up to 1989	Pope et al. (2002) Follow-up to 1998		Krewski et al. (2008) Follow-up to 2000	
$PM_{2.5}$ Exposure	1980	1980	2000	1980	2000
Number of MSAs	50	61	116	58	116
Number of participants	298,825	360,682	499,779	342,521	488,370
Number of deaths	23,180	80,819	111,677	90,783	128,954
All Cause	11,262	35,782	49,539	44,866	63,917
Cardiopulmonary	2,001	6,335	8,754	6,827	9,788
Lung Cancer					
Person-Years	2,109,750	5,302,336.5	7,350,011	5,542,998	7,908,283

Effect of Varying Follow-up Duration

Cause of Death	Krewski et al. (2000) Follow-up to 1989	Pope et al. (2002) Follow-up to 1998		Krewski et al. (2008) Follow-up to 2000	
$PM_{2.5}$	1980	1980	2000	1980	2000
All Cause					
Standard Cox					
Same # of MSAs	1.048(1.022,1.076)	1.031(1.015,1.047)	1.032(1.012,1.053)	1.028 (1.014,1.043)	1.036 (1.017,1.054)
Different # of MSAs	1.067(1.037,1.099)	1.027(1.012,1.043)	1.028(1.009,1.048)		
RE Model					
Same # of MSAs	1.074(1.028,1.122)	1.046(1.014,1.080)	1.055(1.000,1.113)	1.048(1.017,1.080)	1.063(1.026,1.102)
Different # of MSAs	1.101(1.046,1.157)	1.044(1.011,1.078)	1.058(1.020,1.098)		
Cardiopulmonary					
Standard Cox					
Same # of MSAs	1.101(1.061,1.143)	1.071(1.048,1.095)	1.092(1.063,1.123)	1.070(1.049,1.092)	1.100(1.073,1.129)
Different # of MSAs	1.109(1.063,1.157)	1.060(1.036,1.084)	1.079(1.049,1.111)		
RE Model					
Same # of MSAs	1.116(1.055,1.180)	1.075(1.032,1.120)	1.107(1.033,1.187)	1.082(1.040,1.126)	1.105(1.050,1.162)
Different # of MSAs	1.130(1.063,1.201)	1.061(1.018,1.105)	1.081(1.025,1.141)		

Effect of Varying Follow-up Duration

Cause of Death	Krewski et al. (2000) Follow-up to 1989	Pope et al. (2002) Follow-up to 1998		Krewski et al. (2008) Follow-up to 2000	
$PM_{2.5}$	**1980**	**1980**	**2000**	**1980**	**2000**
IHD					
Standard Cox					
Same # of MSAs	1.122(1.066,1.181)	1.130(1.094,1.166)	1.143(1.099,1.190)	1.133(1.100,1.167)	1.155(1.113,1.199)
Different # of MSAs	1.122(1.059,1.189)	1.119(1.081,1.159)	1.141(1.091,1.193)		
RE Model					
Same # of MSAs	1.167(1.062,1.282)	1.160(1.074,1.252)	1.295(1.139,1.472)	1.179 (1.095,1.268)	1.200(1.106,1.301)
Different # of MSAs	1.174(1.064,1.295)	1.140(1.053,1.235)	1.192(1.085,1.310)		
Lung Cancer					
Standard Cox					
Same # of MSAs	1.053(0.963,1.150)	1.089(1.031,1.151)	1.116(1.041,1.197)	1.075 (1.021,1.132)	1.109(1.039,1.185)
Different # of MSAs	1.001(0.907,1.104)	1.072(1.017,1.130)	1.117(1.042,1.197)		
RE Model					
Same # of MSAs	1.117(0.979,1.274)	1.102(1.032,1.177)	1.160(1.045,1.288)	1.086 (1.021,1.156)	1.124(1.041,1.213)
Different # of MSAs	1.062(0.913,1.235)	1.083(1.014,1.157)	1.126(1.044,1.214)		

Effect of Varying Follow-up Duration

Cause of Death	Krewski et al. (2000) Follow-up to 1989	Pope et al. (2002) Follow-up to 1998		Krewski et al. (2008) Follow-up to 2000	
$PM_{2.5}$	1980	1980	2000	1980	2000
All Cause					
44 indi. cov.	1.048(1.022,1.076)	1.031 (1.015, 1.047)	1.032 (1.012, 1.053)	1.028 (1.014, 1.043)	1.036 (1.017, 1.054)
44 indi. Cov + Ecov	1.061(1.031,1.091)	1.047 (1.029, 1.064)	1.057 (1.033, 1.080)	1.044 (1.028, 1.060)	1.057 (1.036, 1.079)
Cardiopulmonary					
44 indi. cov.	1.101(1.061,1.143)	1.071 (1.048, 1.095)	1.092 (1.063, 1.123)	1.070 (1.049, 1.092)	1.100 (1.073, 1.129)
44 indi. Cov + Ecov	1.129(1.084,1.175)	1.098 (1.073, 1.125)	1.134 (1.099, 1.170)	1.094 (1.070, 1.118)	1.138 (1.106, 1.172)
IHD					
44 indi. cov.	1.122(1.066,1.181)	1.130 (1.094, 1.166)	1.143 (1.099, 1.190)	1.133 (1.100, 1.167)	1.155 (1.113, 1.199)
44 indi. Cov + Ecov	1.183(1.119,1.250)	1.183 (1.143, 1.225)	1.234 (1.179, 1.291)	1.184 (1.146, 1.222)	1.242 (1.191, 1.295)
Lung Cancer					
44 indi. cov.	1.053(0.963,1.150)	1.089 (1.031, 1.151)	1.116 (1.041, 1.197)	1.075 (1.021, 1.132)	1.109 (1.039, 1.185)
44 indi. Cov + Ecov	1.070(0.973,1.177)	1.104 (1.040, 1.171)	1.152 (1.065, 1.247)	1.092 (1.033, 1.154)	1.138 (1.057, 1.225)

CONCLUSIONS: Further follow-up

- Phase III used updated data on vital status in the ACS cohort through to the year 2000, thereby by providing an additional 11 years of follow-up beyond that considered in Phase II.

- Additional data on exposure to ambient air pollution was also available for use in Phase III