Supplementary Materials

A. Multi-country multi-city (MCC) data collection

A.1. Mortality

We obtained mortality data from the Multi-City Multi-Country (MCC) database. The current analysis was limited to cities that have air pollution, temperature, urban characteristics indicator and PMCI data. It includes a total of 264 urban areas in 15 countries/regions (Table 1): Canada (21 cities, 1999-2015), China (3 cities, 2013–2015), Estonia (1 city, 2008–2020), France (16 cities, 2003–2017), Germany (11 cities, 2004-2020), Greece (1 city, 2007–2010), Mexico (2 cities, 2014–2019), Norway (1 city, 2000-2018), Portugal (1 city, 2004–2018), Romania (6 cities, 2009–2016), Spain (2 cities, 2011–2012), Sweden (1 county, 2001–2010), Switzerland (4 cities, 1999–2010), United Kingdom (101 cities, 2008–2018), and United States (93 cities, 1999–2006).

In the present study, mortality is represented by daily counts of either non-external causes (International Classification of Diseases, ICD-9: 0-799; ICD-10: A00-R99) or, where not available, all-cause only. Countries/regions with mortality from non-external causes include: Australia, China and Spain.

A.2. Exposure

We obtained daily 24-h average concentrations of $PM_{2.5}$ in 264 cities as well as daily 24-h average of NO_2 concentration and maximum 8-h average of O_3 in 133 of those cities (deatil in Supplementary Table). We also collected daily mean temperature for the 264 cities in the analysis. In brief, measurements for air pollutants were obtained from fixed site monitoring networks operated by local authorities or, when available, gridded products (UK). The majority of monitors were located in urban areas, and only those daily measurements reporting above 75% of hourly data were included. On average, there were 4.7 monitors per city (ranging from 1 to 28), and measurements were averaged among all available monitors within one city to represent the exposure levels of the general population.

Table S1. Summary of the dataset restricted to locations with daily NO_2 and O_3 series available.

Country	Number of cities	Average NO_2 in ppbv (IQR)	Average O_3 in ppbv (IQR)
Canada	20	3.08 (0.75 - 4.19)	26.98 (25.14 - 30.58)
China	3	35.99 (32.08 - 40.32)	45.88 (45.40 - 46.41)
France	14	5.95 (2.05 - 7.58)	38.99 (36.98 - 40.35)
Germany	10	9.79 (6.94 - 11.24)	37.36 (36.60 - 38.14)
Mexico	2	2.55 (1.76 - 3.34)	33.66 (30.89 - 36.43)
Portugal	1	2.88 (2.88 - 2.88)	41.19 (41.19 - 41.19)
Romania	4	1.47 (1.35 - 1.61)	41.18 (40.79 - 41.31)
Spain	3	1.98 (1.35 - 2.66)	41.01 (39.58 - 41.99)
USA-Central	10	4.98 (3.11 - 6.16)	29.33 (28.52 - 29.99)
USA-NECentral	5	3.25 (1.36 - 3.36)	31.09 (30.64 - 31.37)
USA-NorthEast	14	5.33 (2.50 - 5.07)	30.66 (29.10 - 32.21)
USA-NorthWest	2	5.93 (5.09 - 6.78)	19.79 (18.14 - 21.45)
USA-South	11	1.87 (1.18 - 2.27)	31.43 (30.08 - 31.68)
USA-SouthEast	17	1.99 (0.85 - 2.31)	26.69 (22.59 - 30.47)
USA-SouthWest	7	3.17 (1.23 - 3.91)	37.40 (36.84 - 40.04)
USA-West	10	4.91 (1.73 - 7.03)	33.59 (29.85 - 38.57)
Total	**133**	**4.88 (1.41 - 5.67)**	**32.39 (28.51 - 37.50)**

B. The Pollutant Mixture Complexity Index

The Pollutant Mixture Complexity Index is derived from six gaseous pollutants (NO_2, SO_2, HCHO, NH_3, CO, O_3) and fine particulate matter ($PM_{2.5}$).[1] It is constructed by first taking the first principal component (PC) of these 7 (standardised) pollutants and scaling it to a 0-100 scale, yielding a Chronic Air Pollution Index (CAPI). The first PC included 50.5% of the seven pollutants variability. The CAPI indicates the overall amount of pollution with more emphasis on combustion gases as indicated in Table S**2**. The PMCI is obtained by comparing CAPI to $PM_{2.5}$ also scaled between 0 and 100 ($PM_{2.5}^*$) as

$$\frac{CAPI - PM_{2.5}^*}{PM_{2.5}^*} \quad (1)$$

When the PMCI is around 0, this means $PM_{2.5}$ summarises the overall air pollution appropriately. When PMCI > 0, the location is more polluted than what $PM_{2.5}$ alone suggests and conversely when PMCI < 0. Note that since both CAPI and $PM_{2.5\text{-}sc}$ are scaled between 0 and 100, this means that CAPI is bounded to -1 on the left.

Figure **S1** shows the PMCI and pollutants in each city. It shows for example that the PMCI is low in Chinese and Romanian cities since $PM_{2.5}$ and all other pollutant are equally high. On the other hand, PMCI values are substantially above 1 in Eastern USA since $PM_{2.5}$ tend to be relatively low (just above 10µg/m^3) while other pollutants such as CO and SO_2 present relatively high values compared to the other locations.

Table S2. Pollutants included in the Pollutant Mixture Complexity Index (PMCI) with the associated principal component (PC) components.

Pollutant	Unit	PC coefficient
Fine particulate matter (**$PM_{2.5}$**)	µg/m^3	0.42
Nitrogen dioxide (**NO_2**)	ppbv	0.38
Ozone (**O_3**)	Ppbv	0.37
Sulfur dioxide (**SO_2**)	DU	0.33
Formaldehyde (**HCHO**)	molecules/cm^2	0.39
Carbon monoxide (**CO**)	ppbv	0.40
Ammonia (**NH_3**)	ppbv	0.33

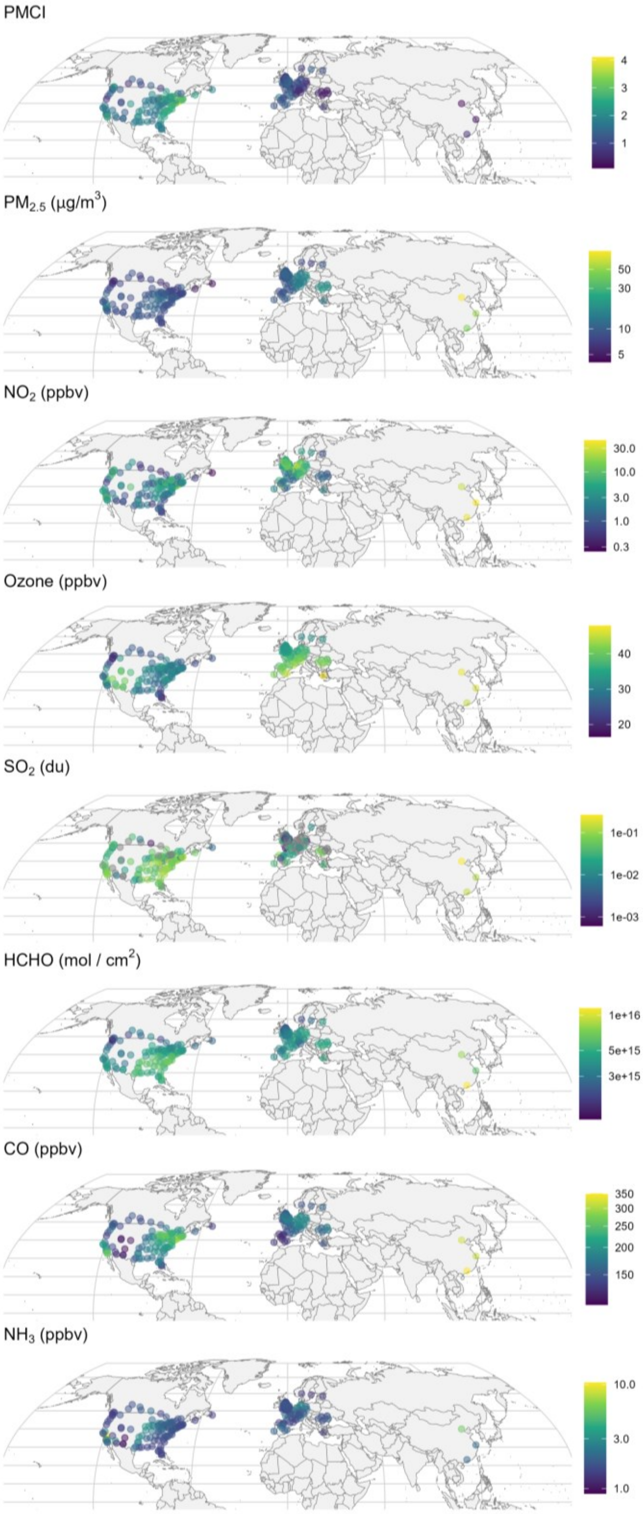

Figure S1. The Pollutant Mixture Complexity Index (PMCI) and the seven considered pollutants in all cities considered in the analysis. Note that all scale, except for PMCI and Ozone are $\log_{10}$ transformed.

C. Model Selection

The PMCI is included as a meta-predictor in the second-stage meta-regression model. We considered four different models for the PMCI: i) a linear model, ii) a log-linear model that account for the fact the PMCI is always above -1 (defined as $\log(PMCI + 1)$), iii) a natural spline with two degrees of freedom, and iv) a natural spline with three degrees of freedom. The fitted association for each model is shown in Figure S2.

The results of model selection are shown in Table S3 and suggests that the log-linear model is the most appropriate. The BIC clearly points towards this model (with a posterior probability of 79%[2]). The AIC is lower than the linear by more than two indicating substantial improvement of the fit.[3] Note that considering a nonlinear model increases estimated between country heterogeneity while decreasing within country heterogeneity.

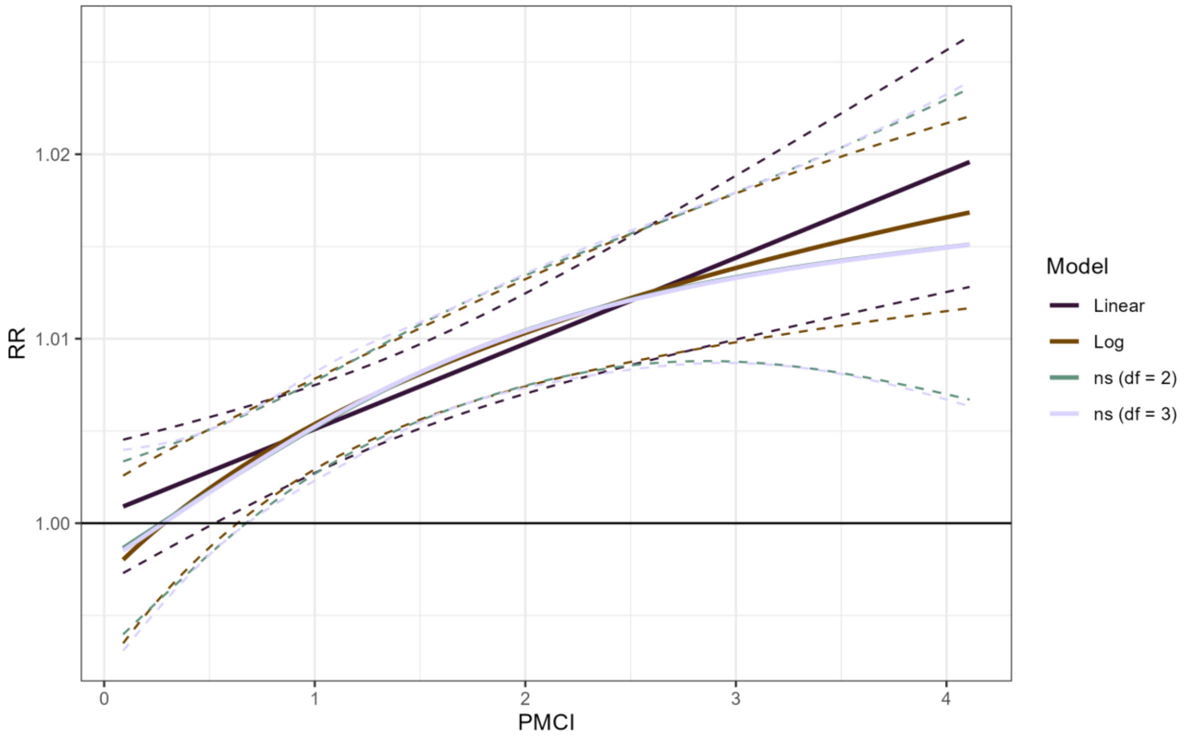

Figure S2. Estimated association between PMCI and $PM_{2.5}$-mortality relative risk (RR) according to each compared model.

Table S3. Model selection for the PMCI including the (corrected) Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and estimated random effect standard deviations.

Model	AIC	BIC	Country Std. Dev.	City Std. Dev.
Linear	-1563.44	-1542.32	0.0037	0.0023
Log	**-1566.22**	**-1545.09**	0.0041	0.0018

Model	AIC	BIC	Country Std. Dev.	City Std. Dev.
ns (df = 2)	-1563.49	-1538.90	0.0041	0.0019
ns (df = 3)	-1561.42	-1533.38	0.0041	0.0019

D. Additional results from the main analysis

Table S4. Additional results from the second-stage models. Country and city standard deviations refer to the estimated parameters for the corresponding random effect levels.

Model	Cochran's Q	I^2	Country Std. Dev.	City Std. Dev.
Main	372.21	30.15	0.0041	0.0018
Null	407.29	35.92	0.0046	0.0027
Gas Mixture	298.05	14.44	0.0035	0.0001
O_x	407.22	36.15	0.0045	0.0027
$PM_{2.5}$ Composition	305.47	16.52	0.0021	0.0024

E. Residual Analysis

Figure S3 shows marginal residuals (difference between response and fixed effects) versus several relevant city characteristics. Overall, there is little evidence of additional nonlinearity and an important part of the remaining variation can be captured by the country level random effects. Typically, the PMCI alone seems to slightly underestimate the $PM_{2.5}$-related mortality RR in northeast USA and Canada.

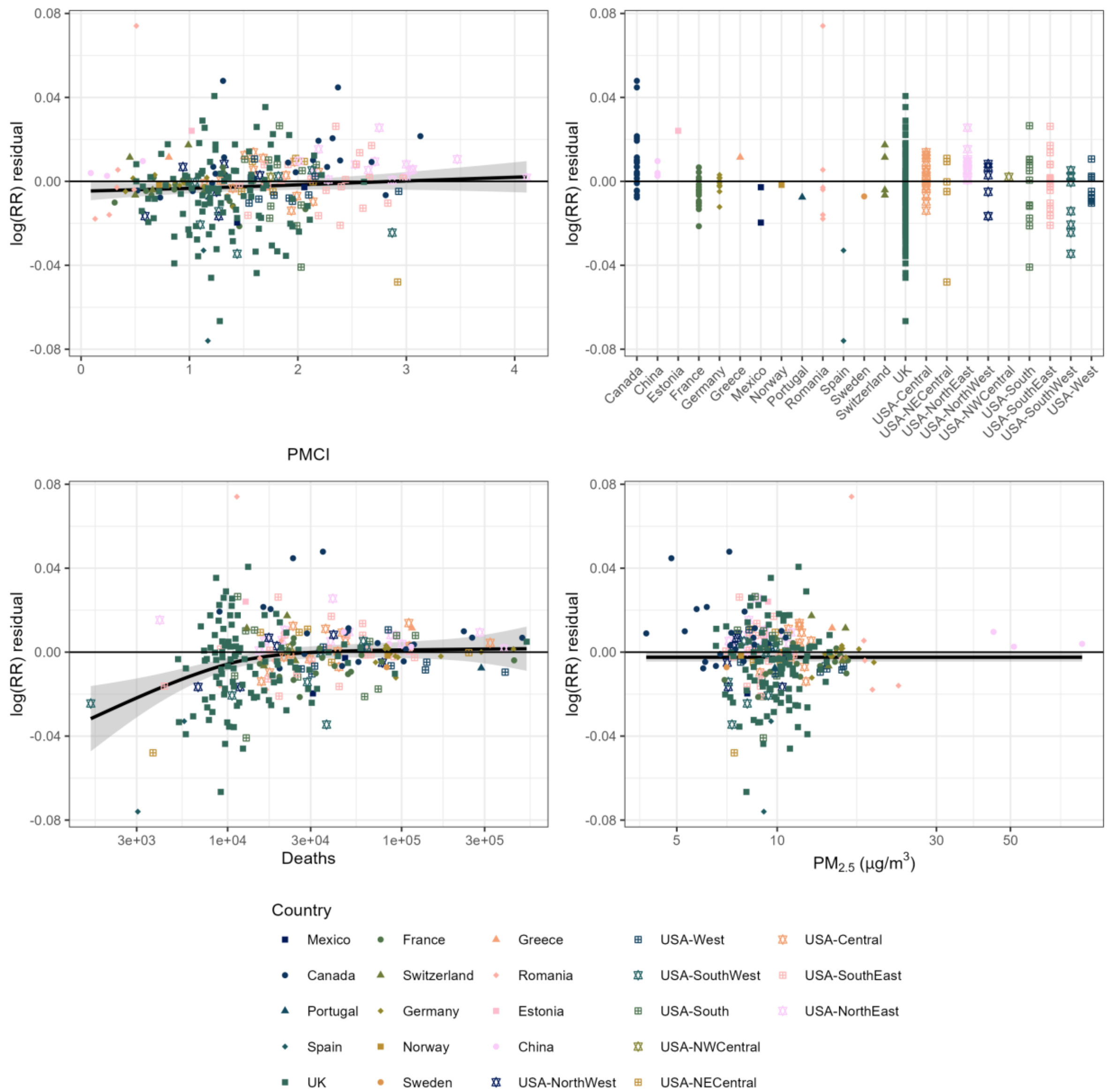

Figure S3. Marginal residuals from the fitted second-stage meta-regression models versus PMCI (topleft), $PM_{2.5}$ (topright), total deaths from the location (bottom left) and country (bottomright).

F. Sensitivity Analysis

There is evidence of short-term effects of Ozone (O_3) and nitrogen dioxides (NO_2) on mortality independently from $PM_{2.5}$,[4–6] while they also tend to be correlated since reacting in the atmosphere. As a sensitivity analysis, we performed an analysis in which both O_3 and NO_2 are controlled for by adding their lag 0-1 moving average as a linear term in the first-stage analysis.

Figure S4 compares the resulting first-stage RR from this sensitivity analysis, to the first-stage RR from the main analysis. Overall, there is a slight attenuation with 60% of cities having lower RRs when adjusted for O_3 and NO_2 and an average difference of RRs of 0.0034. There are two main outliers that are Galati (Romania) and Seattle (US). Since daily O_3 and

NO$_2$ data are not available everywhere, this reduces the number of cities in the analysis to 133, resulting in a slight loss of power as shown in Table S5.

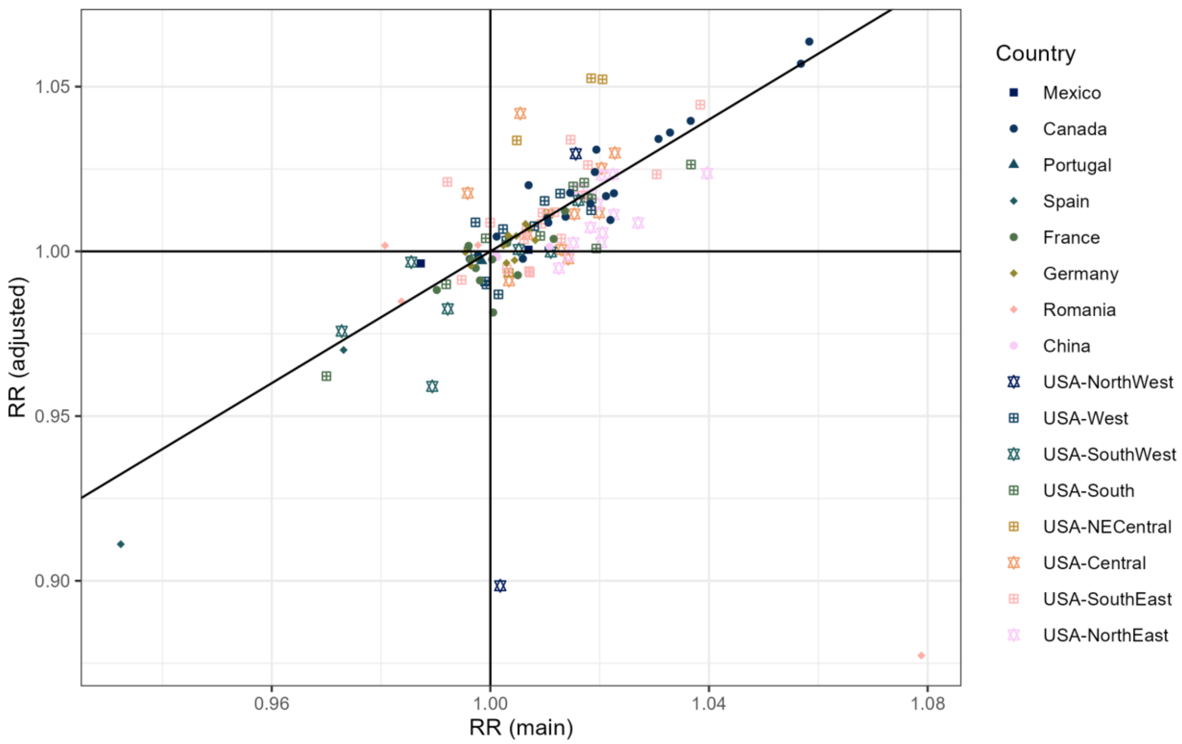

Figure S4. First-stage relative risks (RR) adjusted for O3 and NO2 versus RRs used in the main analysis.

Table S5. Results of the analysis with RR adjusted for both O_3 and NO_2. Table includes the same information as Table 2 in the main manuscript.

Model		RER (95% CI)	LRT P-value	AIC	BIC
Main	PMCI	1.0037 (1.0010 - 1.0065)	0.0087	-760.68	**-744.00**
Null			1.0000	-755.98	-742.00
Gas Mixture	NO_2	0.9994 (0.9986 - 1.0002)	0.0017	-763.44	-733.83
	SO_2	0.9992 (0.9974 - 1.0010)			
	O_3	0.9947 (0.9913 - 0.9980)			
	HCHO	1.0011 (0.9989 - 1.0033)			
	CO	1.0053 (1.0023 - 1.0083)			
	NH_3	1.0001 (0.9995 - 1.0006)			
O_x	O_x	0.9981 (0.9956 - 1.0007)	0.1559	-755.80	-739.12
$PM_{2.5}$ Composition	SO_4^{2-}	0.9982 (0.9914 - 1.0050)	**0.0004**	**-766.99**	-737.38
	NH_4^+	1.0035 (0.9996 - 1.0074)			
	NO_3^-	0.9967 (0.9944 - 0.9989)			
	BC	1.0043 (1.0018 - 1.0067)			
	OC	1.0007 (0.9983 - 1.0032)			
	SS	1.0002 (0.9934 - 1.0071)			
	DUST	0.9972 (0.9819 - 1.0128)			

References

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3. Burnham, K. P. & Anderson, D. R. Multimodel Inference: Understanding AIC and BIC in Model Selection. *Sociol. Methods Res.* **33**, 261–304 (2004).
4. Orellano, P., Reynoso, J., Quaranta, N., Bardach, A. & Ciapponi, A. Short-term exposure to particulate matter (PM10 and PM2.5), nitrogen dioxide (NO2), and ozone (O3) and all-cause and cause-specific mortality: Systematic review and *meta*-analysis. *Environ. Int.* **142**, 105876 (2020).
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6. Meng, X. *et al.* Short term associations of ambient nitrogen dioxide with daily total, cardiovascular, and respiratory mortality: multilocation analysis in 398 cities. *BMJ* **372**, n534 (2021).