Online Supplements

Title: Coarse Particulate Air Pollution and Daily Mortality: A Global Study in 205 Cities

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1. Supplemental Methods

1.1 Health and exposure data

We obtained mortality data from the Multi-City Multi-Country (MCC) database, which has been described in previous publications (1, 2). The current analysis was limited to locations with available data on $PM_{2.5\text{-}10}$, which included a total of 205 cities in 20 countries and/or regions with different study periods, including Australia (3 cities, 1988–2009), Canada (11 cities, 1986–2011), Chile (4 cities, 2006–2014), China (4 cities, 2005–2008), Estonia (3 cities, 1997–2015), Finland (1 city, 1994–2014), Germany (11 cities, 1993–2015), Greece (1 city, 2001–2010), Japan (46 cities, 2011–2015), Mexico (3 cities, 1998–2014), Norway (1 city, 1969–2016), Portugal (3 cities, 1980–2018), Romania (2 cities, 1994–2016), South Africa (5 cities, 1997–2013), Spain (15 cities, 1990–2014), Sweden (1 city, 1990–2010), Switzerland (4 cities, 1995–2013), Taiwan (3 cities, 1994–2014), United Kingdom (24 cities, 1990–2016), and United States (60 cities, 1973–2006). Concentrations of $PM_{2.5\text{-}10}$ were computed as the difference between PM_{10} and $PM_{2.5}$. Mortality data were obtained from local authorities within each country/ region. Causes of death were classified according to the 9th or 10th version of International Classification of Diseases (ICD) codes, wherever available. In each location, mortality is represented by daily counts of either non-external causes or, where not available, all-cause only (ICD-9: 0-799; ICD-10: A0-R99). We also collected mortality data for two main causes: cardiovascular disease (ICD-10, codes I00-I99) and respiratory disease (ICD-10, codes J00-J99) (3). Mortality from non-external causes were not available in Canada, Chile, Estonia, Germany, Greece, Japan, Portugal, Mexico, Romania, South Africa, Sweden, and United States. Deaths from cardiovascular and respiratory diseases were recorded in 180 cities from 15 countries, and were not available in Australia, Brazil, Chile, Estonia, Germany, and Romania (Table 1).

Daily data of other gaseous pollutants, including inhalable nitrogen dioxide (NO_2), ozone (O_3), sulfur dioxide (SO_2) and carbon monoxide (CO), were also obtained where available, to adjust for potential confounding by co-pollutants. There were 172 cities with NO_2 data, 164 cities with O_3 data, 158 cities with SO_2 data, and 107 cities with CO data. In brief, measurements for air pollutants were obtained from fixed-site monitoring networks operated in the same standard by local authorities. The majority of monitors were located in urban areas, and daily time-series of $PM_{2.5}$ and PM_{10} was derived from one or more monitoring stations in each city; when more than one monitor, an average daily measurement was derived. Only those cities with daily measurements reporting above 75% of hourly data, in more than 300 days of a year, and with a coverage over a 3-year period were included. The overall missing rate for total mortality, $PM_{2.5-10}$ and temperature time-series was 0.20%, 10.02% and 2.10%, respectively. A detailed summary of missing rates for health and exposure data was provided in Table E7.

1.2 Lag structure

We selected and compared a list of lag structures for $PM_{2.5-10}$ and temperature that were reported in previous studies (2, 4-6). The lags of $PM_{2.5-10}$ include: 1) lag 0, the present day; 2) lag 1, the previous day; 3) lag 2, the day before lag 1; 4) lag 3, the day before lag 2; and 5) lag 0–1, the two-day moving average of the present day and the previous day; 6) lag 0–2, the three-day moving average of the present day and the previous two days; 7) lag 0–3, the four-day moving average of the present day and the previous three days

For temperature, we tested the traditional single lag days and moving averages, including 1) lag 0, the present day; 2) lag 0 and lag 1, separate terms of the present and previous day; 3) lag 0–3, the 4–day moving average of the present and previous 3 days; 4) lag 0 and lag 1–3, separate terms of the present day and the average of the previous 3 days; 5) lag 0–7, the moving average of the present and previous 7 days; 6) lag 0–14, the moving average of the present and previous 14 days, and 7) lag 0–21, the moving average of the present and previous 21 days (Table E4).

1.3 Heterogeneity and effect modification analyses

We explored potential effect modifiers on the associations between $PM_{2.5-10}$ and total mortality based on the main models. First, we conducted separate analyses by regions classified by the World Health Organization (WHO) (Table E1), which include Western-Pacific Region

(WPRO), Regional Office for the Americas (AMRO), and Regional Office for Europe (EURO), and Regional Office for Africa (ROA). Then, the statistical significance for differences among groups were determined by likelihood ratio tests. Second, using the aforementioned approach, we conducted additional analyses by regions in terms of Gross Domestic Product (GDP) per capita at country/region level (Table E1). Third, we assessed potential effect modification in the $PM_{2.5-10}$-mortality associations by including annual-mean levels of all air pollutants and temperature, relative humidity, latitude of locations, region (WHO and GDP), and GDP per capita in meta-regression models all together.

2. Supplemental Results

2.1 Descriptive Statistics

Figure E1 illustrates the locations of cities included in present analysis and the average values of annual mean concentrations of $PM_{2.5-10}$ during the periods with available $PM_{2.5-10}$ ground measurements at city level. Table E1 summarizes the descriptive statistics of environmental data. The summary of missing rates for health and exposure data is provided in Table E7.

2.2 Heterogeneity, regional analyses, and effect modifications

Among all cities, heterogeneity was found in the $PM_{2.5-10}$-mortality association across city-specific estimates, with I^2 statistics of 43.16%, and Cochran Q p-value < 0.001.

In regional analyses (Table E3), the $PM_{2.5-10}$-mortality association was highest in the EURO with an average increment of 0.54% in total mortality per 10 μg/m^3 increase of $PM_{2.5-10}$ concentrations, and was lowest in the AMRO (corresponding estimate: 0.18%). The associations did not vary by GDP (p-value=0.192), with estimates of 0.32% (0.02%, 0.61%), 0.60% (0.25%, 0.95%), and 0.60% (0.28%, 0.92%) corresponding to low, medium, and high GDP areas, respectively. There was no significant effect modification by annual levels of air pollutants, temperature, relative humidity, GDP, WHO region and latitude of locations. Table

E6 lists the results for different time-periods, and no significant difference was observed.

2.3 The impact of missing values

There were two types of missing data in the current study: one was caused by complete unavailability of measurements for certain variables in a city/country; and the other was caused by a small number of missing values scattered during the study time period of each city.

For the first type of missing data, the NAs in Table E2 denote lack of co-pollutant or relative humidity data in corresponding countries/regions, which are determined by the data availability in different countries/regions. Regarding to this kind of missingness, countries or regions with unavailable co-pollutants data were excluded accordingly; therefore, the number of countries/regions in Table 2 varied by co-pollutants. We did not control relative humidity in cities without such data, and a sensitivity analysis was conducted to test influence of this missing information on results (Table E5).

For the second type of missing data, there were also some missing values for air pollutant measurements in certain periods of consecutive days, which were mainly caused by data logging errors or abnormal operations of the monitoring equipment. This kind of missing is likely to be independent from any other predictors and especially the outcome. Multiple imputation or other imputation methods has been used to handle the issue of missing values in previous studies with small sample size, but it is unfeasible and not cost-effective in this large multi-location studies across dozens of countries. We thereby provided a summary of missing rates of mortality and exposure data at the country level (Table E7). The overall missing rates for total mortality, $PM_{2.5-10}$ and temperature were 0.20%, 10.02% and 2.10%, respectively. Thus, this amount of missingness is unlikely to produce appreciable influences on our estimates in main models.

3. Supplemental Tables

Table E1. Summary of the locations, GDP, and region specification of the 20 countries/regions included in this analysis.

Country/Region	Cities	GDP per capita	WHO region	GDP region
Australia	3	54066	WPRO	2
Canada	11	45148	AMRO	2
China	4	8879	WPRO	1
Chile	4	14999	AMRO	1
Estonia	3	20388	EURO	1
Finland	1	46316	EURO	2
Germany	11	44349	EURO	2
Greece	1	18930	EURO	1
Japan	46	38386	WPRO	1
Mexico	3	9278	AMRO	1
Norway	1	75496	AMRO	3
Portugal	3	21490	EURO	1
Romania	2	10807	EURO	1
South Africa	5	6132	ROA	1
Spain	15	28170	EURO	1
Switzerland	4	80449	EURO	3
Sweden	1	53791	EURO	2
Taiwan	3	24283	WPRO	1
United Kingdom	24	40361	EURO	2
United States	60	59957	AMRO	3

Abbreviations: GDP, Gross Domestic Product; WHO, World Health Organization.

Notes: Regions by GDP: Regions classified by GDP per capita in 2017 according to World Bank (data.worldbank.org). Regions by WHO: classified by the World Health Organization, including the Western Pacific Region (Western-Pacific Regional Office, WPRO), the American Region (Regional Office for America, AMRO), the European Region (Regional Office for Europe, EURO), and the African Region (Regional Office for Africa, ROA)

Table E2. Descriptive statistics of annual-mean concentration (median, 25%-75% percentiles) of coarse particulate matter ($PM_{2.5-10}$), weather conditions and other air pollutants in each country/region throughout the study period.

Country /Region	$PM_{2.5-10}$ (μg/m^3)	$PM_{2.5}$ (μg/m^3)	NO_2 (μg/m^3)	O_3 (μg/m^3)	SO_2 (μg/m^3)	CO (mg/m^3)	Temperature (°C)	Humidity (%)
Australia	11.7 [8.6-15.4]	6 [4.3-8.4]	21.4 [14.1-27.9]	3.3 [1.4-5.7]	29.9 [22.1-37.9]	0.4 [0.2-0.7]	18.1 [14.7-21.2]	70.1 [62.5-77.2]
Canada	8.9 [5.1-14.1]	6.7 [4.3-10.2]	27.5 [19.6-37.4]	3.5 [1.7-6.5]	36.9 [24.8-50.1]	0.4 [0.3-0.5]	7.5 [-0.3-15.2]	73.5 [64.8-82.1]
Chile	24.8 [17-35]	20.8 [12.7-40.2]	21.6 [13.9-32.4]	NA	25.2 [13.8-33.7]	0.6 [0.3-1.1]	13.4 [10.3-17.3]	NA
China	32.5 [16.9-57]	92.8 [61.9-134.7]	44.8 [33.8-58]	34.6 [23.1-60.3]	NA	NA	16.2 [6.3-23.6]	65.5 [53-77.2]
Estonia	5.6 [3.2-9.4]	6.6 [3.8-10.6]	8.2 [5.6-12.4]	1.5 [0.7-3.9]	51 [38.7-64.2]	NA	5.9 [-0.3-13.6]	83.7 [74-90.7]
Finland	2 [1.1-3.9]	12.6 [7.4-21.7]	6.8 [4.3-11.7]	6.2 [3.5-11.6]	51.3 [40-63]	0.3 [0.2-0.3]	5.9 [0-13.8]	79.2 [67.8-87.7]
Germany	5.9 [3.8-8.5]	12 [8-18.8]	29.5 [21.8-38.2]	4.5 [2.9-8.3]	38.5 [21.2-54.9]	0.4 [0.3-0.6]	10.5 [4.8-15.9]	NA
Greece	12.5 [8-19.2]	20.3 [15-26.4]	50.2 [39.6-61.6]	NA	75.1 [52.8-97.5]	1.8 [1.3-2.6]	17.9 [12.9-24.9]	66 [54-75.4]
Japan	4.9 [2.9-7.6]	12.6 [8.3-18.2]	17 [12.3-23.7]	5 [3.6-7.3]	56.3 [41.3-72.3]	NA	16.1 [7.6-22.7]	69.7 [60.7-77.9]
Mexico	32 [22.4-42.7]	25.1 [18.8-32.9]	NA	NA	124.8 [96-156.8]	NA	20.3 [17.5-22.5]	58.3 [45.2-70.6]
Norway	8.5 [5.4-13.9]	9.4 [6.9-12.8]	NA	NA	42.6 [30.5-54.5]	NA	4.5 [-1.3-11.7]	NA
Portugal	8.3 [5.4-13.2]	8.2 [5.4-12.8]	12.2 [8.1-17.9]	1.3 [0.9-2.4]	55.8 [43-68]	0.3 [0.2-0.4]	15.6 [11.5-21]	NA
Romania	12.8 [7.4-19.7]	15.5 [10.1-23.3]	23.9 [17.8-33.1]	10.7 [7.6-15.2]	38.1 [25.5-52]	0.2 [0.1-0.3]	12 [4.1-19.4]	75.7 [65.3-86.3]
South Africa	26.6 [14.9-44.3]	27.3 [18.6-39.8]	NA	NA	76.6 [59-99]	NA	17.5 [12.8-20.5]	NA
Spain	12.9 [9.6-17.2]	10.2 [7.2-14.5]	29.2 [22.2-37.6]	5.9 [4.4-7.9]	48.4 [35.1-60.1]	0.3 [0.3-0.4]	14.9 [10.5-20.2]	NA
Sweden	5.3 [3.3-8.5]	6.6 [4.7-9.5]	26.8 [20-34.8]	NA	61.9 [48.9-76]	0.9 [0.6-1.5]	6.8 [1.2-13.9]	79.6 [68.4-87.6]
Switzerland	6.9 [4.5-10.2]	16.2 [10.6-24.7]	35.2 [25.7-46.1]	3.8 [1.8-7.5]	73.2 [44.5-100.6]	0.6 [0.4-0.9]	10.9 [4.6-16.7]	75.6 [66.3-83.3]
Taiwan	22.3 [15.9-30.6]	32.3 [20.6-44.6]	42.2 [31.6-54.7]	13.4 [9.6-18.7]	65 [44.5-91.6]	0.7 [0.6-0.9]	24.9 [20.4-28]	75.3 [70.3-80.2]
United Kingdom	5.3 [3.4-7.7]	9.6 [6.8-14.9]	28.5 [20.2-38.9]	5.7 [2.8-10.3]	39.9 [27.3-52.4]	0.4 [0.2-0.5]	10.4 [6.5-14.6]	NA
United States	11.5 [6.9-17.4]	10.9 [7.5-16]	32.2 [23.6-42.9]	11.3 [6.5-18.9]	50.1 [34.6-66]	1 [0.7-1.4]	14.4 [7.2-21.4]	64.2 [53.9-74.5]
Pooled	26.6 [19.4-35.7]	24.8 [17.5-35]	13.6 [9.2-20.2]	50.6 [35.6-66.1]	7.6 [4.7-12.4]	0.7 [0.5-1.0]	13.9 [7.4-19.9]	68.1 [58.4-77.3]

Abbreviations: $PM_{2.5-10}$, coarse particulate matter; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; NO_2, nitrogen dioxide;

O_3, ozone; SO_2, sulfur dioxide; CO, carbon monoxide.
Notes: NA denotes lack of specific variables in corresponding countries/regions.

Table E3. Percentage change (mean and 95% confidence intervals) in total mortality associated with a 10 μg/m^3 increase in $PM_{2.5\text{-}10}$ stratified by WHO/GDP regions and *p*-values for testing difference among regions.

Classifications	Regions	Estimates	*P*-values*
WHO	AMRO	0.18 (-0.27, 0.64)	0.031
	WPRO	0.37 (-0.09, 0.84)	
	EURO#	0.54 (0.09, 0.99)	
GDP	1	0.32 (0.02, 0.61)	0.192
	2	0.60 (0.25, 0.95)	
	3	0.60 (0.28, 0.92)	

Abbreviations as in Table E1.

Notes:

* *P*-values were obtained by likelihood ratio tests comparing the fit of a meta-regression model with the region variable to the simple meta-analysis model. *P*-values < 0.05 were considered statistically significant for regional differences.

As South Africa is the only country in ROA, it was classified in EURO for the region-specific analysis.

Table E4. Percentage changes in total mortality associated with a 10 μg/m^3 increase in $PM_{2.5\text{-}10}$ (lag 0-1), with different modelling approaches to control for temperature.

Lags of temperature	Estimates (95%CI)	qAIC
Lag 0	0.15 (0.00, 0.29)	1951796
Lag 0+1	0.14 (0.02, 0.26)	1951055
Lag 0+1–3	0.14 (0.04, 0.23)	1948415
Lag 0–3	0.51 (0.18, 0.84)	1943723
Lag 0–7,	0.85 (0.46, 1.25)	1947343
Lag 0–14	0.93 (0.50, 1.37)	1944701
Lag 0–21	0.87 (0.42, 1.31)	1956128

Notes: Lag 0, the present day; Lag 0+1, the present and the previous day; Lag 0+1–3, the present day and the mean of the previous 3 days; Lag 0–3, moving average of the present day and the previous 3 days; Lag 0–7, moving average of the present day and the previous 7 days; Lag 0–14, moving average of the present day and the previous 14 days; Lag 0–21, moving average of the present day and the previous 21 days.

Table E5. Percentage change (pooled estimate and 95% confidence intervals) in total mortality per 10 μg/m^3 increase in $PM_{2.5-10}$ (lag 0-1), with and without adjustment of relative humidity.

Endpoints	Adjustments	N	Estimates	P*
Total	RH adjusted	169	0.51 (0.44 to 0.59)	0.440
	RH unadjusted		0.54 (0.47 to 0.61)	
Cardiovascular	RH adjusted	159	0.44 (0.32 to 0.56)	0.757
	RH unadjusted		0.46 (0.34 to 0.58)	
Respiratory	RH adjusted	159	0.63 (0.53 to 0.73)	0.668
	RH unadjusted		0.67 (0.57 to 0.76)	

Abbreviations: RH, relative humidity.

* *P*-values for difference were calculated by evaluating a binary variable (with and without adjusting for humidity) in likelihood ratio tests with both model estimates. *P*-values < 0.05 were considered statistically significant for differences.

Table E6. Percentage change (pooled estimate and 95% confidence intervals) in mortality per 10 μg/m^3 increase in $PM_{2.5-10}$ (lag 0-1) for different time periods.

Mortality endpoints	Time periods	N	Estimates	P*
Total	Before 2000 (included)	69	0.67 (0.17, 1.18)	0.588
	After 2000		0.53 (0.11, 0.95)	
Cardiovascular	Before 2000 (included)	65	0.49 (-0.24, 1.23)	0.846
	After 2000		0.60 (-0.14, 1.33)	
Respiratory	Before 2000 (included)	61	0.82 (-0.48, 2.15)	0.587
	After 2000		0.31 (-0.99, 1.63)	

Notes: * *P*-values for difference were calculated by evaluating a binary variable (before or after the year 2000) in likelihood ratio tests with both model estimates. *P*-values < 0.05 were considered statistically significant for differences.

Table E7. Summary statistics on missing rates of health and exposure data at the country/region level.

Country /Region	Total	Cardiovascular	Respiratory	$PM_{2.5-10}$ (μg/m^3)	$PM_{2.5}$ (μg/m^3)	NO_2 (μg/m^3)	SO_2 (μg/m^3)	O_3 (μg/m^3)	CO (mg/m^3)	Temp (°C)	Humidity (%)
Australia	NA	NA	NA	5.13%	2.92%	4.00%	3.82%	3.11%	1.64%	0.00%	0.00%
Canada	0.61%	0.45%	1.44%	11.33%	1.71%	4.11%	2.57%	2.68%	3.18%	0.65%	0.06%
Chile	NA	NA	NA	10.79%	8.62%	10.89%	NA	14.11%	11.18%	9.98%	NA
China	0.36%	0.00%	0.00%	20.78%	2.27%	0.89%	0.89%	NA	NA	0.00%	0.00%
Estonia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Finland	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	4.97%	5.03%
Germany	NA	NA	NA	5.99%	1.78%	5.06%	6.90%	3.88%	4.23%	0.01%	NA
Greece	0.00%	0.00%	0.00%	NA	NA	NA	NA	NA	NA	NA	NA
Japan	0.00%	0.00%	0.00%	6.79%	0.60%	0.81%	3.14%	1.15%	NA	0.05%	0.13%
Mexico	0.00%	0.00%	0.00%	NA	NA	NA	NA	NA	NA	NA	NA
Norway	0.90%	1.36%	0.82%	0.90%	0.76%	NA	NA	3.45%	NA	0.00%	NA
Portugal	0.13%	0.92%	1.83%	8.62%	6.07%	13.85%	17.14%	2.98%	1.16%	7.61%	NA
Romania	NA	NA	NA	28.70%	18.14%	46.95%	34.84%	13.60%	31.91%	0.00%	0.00%
South Africa	0.00%	0.00%	0.00%	18.10%	11.95%	NA	NA	NA	NA	6.97%	NA
Spain	0.00%	0.00%	0.00%	3.58%	2.19%	4.03%	3.64%	2.52%	6.99%	0.07%	NA
Sweden	0.00%	0.00%	0.00%	NA	NA	NA	NA	NA	NA	NA	NA
Switzerland	0.00%	0.00%	0.00%	NA	NA	NA	NA	NA	NA	NA	NA
Taiwan	0.02%	0.00%	0.00%	0.02%	0.02%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%
United Kingdom	0.00%	0.00%	0.00%	10.00%	5.46%	11.84%	10.54%	12.88%	5.56%	0.00%	NA
United States	1.03%	1.03%	1.03%	19.51%	9.34%	9.77%	4.16%	21.26%	4.43%	1.25%	5.38%
Pooled	0.20%	0.25%	0.34%	10.02%	4.79%	8.63%	7.30%	6.28%	6.39%	2.10%	1.33%

Abbreviations as in Table E2.

Notes: NA denotes lack of specific variables in corresponding countries/regions.

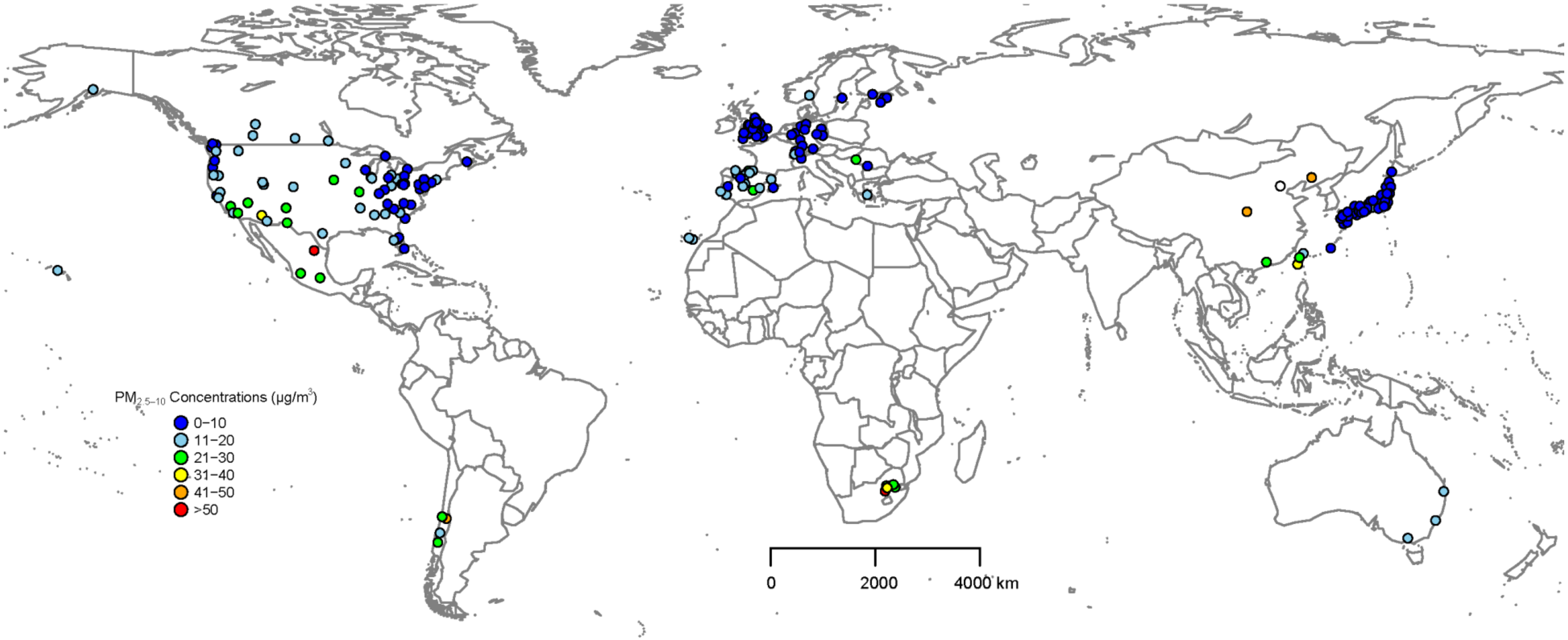

Figure E1. Geographic distributions of the 205 cities within the 20 countries included in the analysis, and the corresponding annual mean $PM_{2.5-10}$ concentrations (μg/m³).

4. References

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