Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Materials

Title: Ambient particulate air pollution and daily mortality in 652 cities

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1. Methods

1.1 Mortality data collection

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 cities that have air pollution and temperature data, and includes a total of 652 urban areas in 24 countries/regions (Table S1): Australia (3 cities, 2000–2009), Brazil (one city, 1997–2011), Canada (25 cities, 1986–2011), Chile (4 cities, 2004–2014), China (272 cities, 2013–2015), Colombia (1 city, 1998–2013), Czech Republic (1 city, 1994–2015), Estonia (4 cities, 1997–2015), Finland (1 city, 1994–2014), France (18 cities, 2000–2010), Greece (1 city, 2001–2010), Italy (18 cities, 2006–2015), Japan (47 cities, 2011–2015), Mexico (8 cities, 1998–2014), Portugal (2 cities, 1995–2012), South Africa (6 cities, 2004–2013), South Korea (7 cities, 1992–2015), Spain (45 cities, 2001–2014), Sweden (1 county, 1994–2010), Switzerland (8 cities, 1995–2013), Taiwan (3 cities, 1994–2014), Thailand (19 cities, 1999–2008), United Kingdom (15 cities, 1993–2006), and United States (142 cities, 1987–2006).

Table S1. Summary of locations, study periods, and number of deaths in 24 countries/regions included in this analysis.

Country/Region	Cities	Time periods	Total / Non-accidental deaths (in thousands)	Cardiovascular deaths (in thousands)	Respiratory deaths (in thousands)
Australia	3	2000–2009	547.9	NA	NA
Brazil	1	1997–2011	916.3	331.3	118.1
Canada	25	1986–2011	2891.1	1019.0	230.0
Chile	4	2004–2014	463.4	NA	NA
China	272	2013–2015	4788.9	2335.7	612.5
Colombia	1	1998–2013	369.1	123.8	46.3
Czech Republic	1	1994–2015	270.5	145.0	13.9
Estonia	4	1997–2015	133.8	NA	NA
Finland	1	1994–2014	139.5	57.4	9.7
France	18	2000–2010	1197.6	NA	NA

Greece	1	2001–2010	288.0	136.2	28.8
Italy	18	2006–2015	804.3	NA	NA
Japan	47	2011–2015	1885.0	496.7	296.0
Mexico	8	1998–2014	2806.3	721.6	268.9
Portugal	2	1995–2012	1066.3	NA	NA
South Africa	6	2004–2013	1601.4	267.6	210.7
South Korea	7	1992–2015	502.9	547.5	133.3
Spain	45	2001–2014	2867.2	990.8	323.8
Sweden	1	1994–2010	201.2	91.3	15.9
Switzerland	8	1995–2013	235.9	90.7	16.0
Taiwan	3	1994–2014	688.4	269.4	116.5
Thailand	19	1999–2008	854.3	NA	NA
United Kingdom	15	1993–2006	2241.5	874.2	357.9

United States	142	1987–2006	31832.4	11617.9	2783.7
Total	652	1986–2015	59593.0	20116.2	5582.0

Notes: Mortality data from cardiovascular and respiratory diseases were not available in Australia, Chile, Estonia, France, Italy, Portugal, and Thailand.

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. Mortality data for two main causes were also collected where available: cardiovascular disease (ICD-10: I00-I99) and respiratory disease (ICD-10: J00-J99)[3]. Deaths from cardiovascular and respiratory diseases were recorded in 597 cities from 17 countries, and were not available in Australia, Chile, Estonia, France, Italy, Portugal, and Thailand (Table S1). We calculated the missing rate in each city by dividing the number of missing days by the total number of days in respective study periods. Only 20 cities had missing values in daily mortality data, ranging from 0.005% in a city of Japan to 9.9% in a city of Italy. We obtained a mean of 0.52% by averaging the missing rates across all cities.

Countries/regions with morality from non-external causes include: Australia, Brazil, China, Columbia, Czech Republic, Finland, Japan, Portugal, South Africa, South Korea, Spain, Switzerland, Taiwan, the United Kingdom, and the United States. Countries/regions with morality from total causes include: Canada, Chile, Estonia, France, Italy, Mexico, Sweden, and Thailand.

1.2 Exposure measurements

We obtained daily 24-h average concentrations of PM_{10} in 598 cities and of $PM_{2.5}$ in 499 cities. Both pollutants were available in 445 cities of 16 countries or regions. The geographic distributions of cities with PM_{10} and $PM_{2.5}$ data and the corresponding annual-mean concentrations during respective study periods were listed in Figure 1 and Figure 2, respectively. Daily 24-h average concentrations of gaseous pollutants, including ozone (O_3, maximum 8-h average), nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and carbon monoxide (CO), were also obtained where available, to allow for the adjustment for their simultaneous exposures. There were 623 cities with O_3 data, 552 cities with NO_2 data, 540 cities with SO_2 data, and 500 cities with CO data. We collected daily data on weather variables including daily mean temperature and daily mean relative humidity. In brief, measurements for air pollutants were obtained from fixed-site monitoring networks operated by local authorities. 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. The overall missing rate was 5.2% for PM_{10}, 2.0% for $PM_{2.5}$, and 0.95% for weather conditions. In the main statistical analyses, we excluded the highest 5% and lowest 5% of PM_{10} and $PM_{2.5}$ measurements to avoid the potential consequences in relation to inaccuracies driven by the outlying data points [4]. We also conducted an additional analysis based on the non-trimmed data using the same models as in main analyses.

1.3 Lag structure

We compared several lag days of PM_{10}, $PM_{2.5}$ and temperature that were often used in previous studies [5-8]. The lag that generated the minimum generalized cross validation (GCV) scores, indicating the best model fitting, was then used in main analyses. The overall GCV was obtained by averaging GCV scores from all city-specific models. The lags of PM include: 1) lag 0, the present day; 2) lag 1, the previous day; 3) lag 2, the previous two day; 4) lag 0–1, the two-day moving average of the present day and the previous day; 5) lag 0–2, the three-day moving average of the present and previous two days. The lags of temperature include: a) lag 0, the present day; b) lag 0 and lag 1, separate terms of the present and previous day; c) lag 0–3, the 4-day moving average of the present and previous 3 days; d) lag 0 and lag 1–3, separate terms of the present day and the average of the previous 3 days; e) lag 0–7, the moving average of the present and previous 7 days; f) lag 0–14, the moving average of the present and previous 14 days, and g) lag 0–21, the moving average of the present and previous 21 days.

1.4 Heterogeneity and effect modification analyses

We explored potential heterogeneity factors and effect modifiers on the associations between PM_{10}, $PM_{2.5}$ and total mortality based on the main models. First, we conducted separate analyses by region according to the classification proposed by the World Health Organization (WHO) (Table S2), which includes the Western-Pacific Region (Western-Pacific Regional Office, WPRO), the Region of the Americas (Regional Office for the Americas, AMRO), and the European Region (Regional Office for Europe, EURO). As South Africa (6 cities) is the only country in the African Region (Regional Office for Africa, ROA) and may not represent the whole Region, we thus excluded the African Region in this regional analysis. Then, we obtained *p*-values for differences among regions using likelihood ratio tests in comparing the fit of a meta-regression model with the potential modifier to the simple meta-analysis model [9]. Second, we conducted additional separate analyses by region using the same two-stage approach in terms of Gross Domestic Product (GDP) per capita at the country/region level (Table S2). Third, we assessed potential effect modification in the PM_{10}- and $PM_{2.5}$- mortality associations by annual-mean levels of all air pollutants and temperature, latitude of locations, region (classifications by WHO and GDP), and GDP per capita in meta-regression models because of their correlations with daily PM levels, mortality and population exposure patterns. These effect modifiers were entered all together in meta-regression models.

Table S2. Summary statistics on cities with available PM data, GDP per capita and region classification for 24 countries/regions included in this analysis.

Country/Region	Cities with PM_{10}	Cities with $PM_{2.5}$	GDP per capita (US dollars)	Regions by WHO	Regions by GDP
Australia	3	3	56,135	WPRO	3
Brazil	1	0	10,019	AMRO	1
Canada	13	25	44,773	AMRO	3
Chile	4	4	14,314	AMRO	1
China	272	272	9,482	WPRO	1
Colombia	1	0	6,237	AMRO	1
Czech Republic	1	0	19,818	EURO	2
Estonia	4	3	19,618	EURO	2
Finland	1	1	45,692	EURO	3

France	18	0	39,673	EURO	3
Greece	1	1	18,945	EURO	2
Italy	18	0	31,618	EURO	2
Japan	47	47	38,550	WPRO	2
Mexico	8	3	9,249	AMRO	1
Portugal	2	1	20,575	EURO	2
South Africa	6	5	6,089	ROA	1
South Korea	7	0	29,730	WPRO	2
Spain	45	19	28,212	EURO	2
Sweden	1	1	53,248	EURO	3
Switzerland	8	4	80,836	EURO	3
Taiwan	3	3	24,228	WPRO	2
Thailand	19	0	6,336	WPRO	1

United Kingdom	15	0	38,846	EURO	2
United States	100	107	59,495	AMRO	3

Abbreviations: GDP, Gross Domestic Product; PM, particulate matter; PM_{10}, particulate matter with an aerodynamic diameter less than or equal to 10 µm; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 µm; 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 Region of Americas (Regional Office for the Americas, AMRO), the European Region (Regional Office for Europe, EURO) and the African Region (Regional Office for Africa, ROA).

1.5 Concentration–response curves

To get an overall shape of PM_{10}- and $PM_{2.5}$- mortality associations at a global level, we estimated concentration–response (C–R) curves using the same approach as done in APHENA-2 study [7,10]. The model specifications were the same as aforementioned main model other than the replacement of the linear term of PM with an assumed nonlinear term. Following the distribution of daily PM_{10} and $PM_{2.5}$ concentrations in each city, we firstly used a quadratic B-spline for PM_{10} with two common knots at 35 $\mu g/m^3$ and 70 $\mu g/m^3$ (almost corresponding to the average of the 25^{th} and of the 75^{th} percentiles, respectively), and another quadratic B-spline for $PM_{2.5}$ with two common knots at 20 $\mu g/m^3$ and 45 $\mu g/m^3$ (almost corresponding to the average of the 25^{th} and of the 75^{th} percentiles). The use of B-spline function in main models would produce 5 regression coefficients and a 5×5 variance–covariance matrix, which might sufficiently account for the PM-mortality association in a wide range of concentrations in each city. Specifically, the between-city variance-covariance matrix is a 5 × 5 matrix covariance (δ^c) = D. It is assumed that δ^c follows the multivariate normal distribution (MVN) with mean 0 and variance-covariance matrix D, that is, $\delta c \sim MVN(0, D)$, and $\varepsilon c \sim MVN(0, Sc)$, $\beta c \sim MVN(Zc\alpha, D + Sc)$ where Sc is the covariance matrix of the five regression coefficients of the spline function in city c that is estimated in the first stage of the analysis. When $D \approx 0$, we get the corresponding fixed-effects estimates, whereas when $D \neq 0$ we get the random effects estimates. Finally, we combined city-specific components of the spline estimates using random-effect models. Apart from the pooled C-R curves at global level, we also pooled the C-R curves at country/region level. The knots of B-spline were also selected according to the distribution of PM_{10} and $PM_{2.5}$ concentrations in each country/region (i.e. the 25th percentile and 75th percentile). In the sensitivity analysis, we placed knots at different PM values for the global C-R curves, including (35, 75) μg/m^3, (30, 75) μg/m^3, and (30, 80) μg/m^3 for PM_{10}; (20, 40) μg/m^3, (20, 50) μg/m^3, and (25, 45) μg/m^3 for $PM_{2.5}$.

1.6 Percent change calculation

The percent change in mortality for a 10 μg/m^3 increase in PM concentrations was calculated from log relative risks following this equation: Percent change= (exp (β×10) –1)×100%, Lower 95% CI= (exp ((β–1.96×SE) ×10) –1) ×100%, Upper 95% CI= (exp ((β+1.96×SE) ×10) –1) ×100%, where β is the regression coefficient as the log relative risks, and SE is the standard error.

1.7 Additional information on data collection

Australia

We collected data from Melbourne, Sydney and Brisbane between 1st of January 2000 and 31st of December 2009. Daily mortality, obtained from the Australian Bureau of Statistics, is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99). Mean daily temperature (˚**C**) and relative humidity (%) were obtained from the Australian Bureau of Meteorology. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), nitrogen dioxide (NO_2, in ppb), sulfur dioxide (SO_2, in ppb), carbon monoxide (CO, in ppm), and ozone (O_3, in ppb) were obtained from Queensland EPA, NSW EPA, and Victoria EPA. The units for gaseous pollutants in Sydney were originally recorded in pphm. The measurements were from urban monitoring stations, and were computed as the 24-hour average based on hourly measurements. In total, missing data amount for 0.00% and 4.52% of the mortality and PM air pollution, respectively. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3).

Brazil

We collected data from 1 city between 1st of January 1997 and 31st of December 2011. Daily mortality, obtained from the Ministry of Health, Brazil, is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed from the 24-h average of hourly measurements) were obtained from the National Institute of Meteorology of Brazil. A single weather station located within the urban area was selected. Measures of inhalable particles (PM_{10}, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), sulfur dioxide (SO_2, in μg/m^3), carbon monoxide (CO, in ppm), and ozone (O_3, in μg/m^3) were available in the same period. Monitoring the samples are collected in the field and brought for analysis in the CETESB (Company of Technology of Environmental Sanitation) laboratory. All monitor used are in urban area, with minimum 20 measures hourly. We used Pearson correlation to choose stations, all stations with R> 0.90 were accepted, and then we calculated average of all stations. In total, missing data amount for 6.10% and 0.00% of the mortality and PM air pollution, respectively. In the present study, the unit for CO was unified to mg/m^3.

Canada

We collected data from 25 census metropolitan areas (CMA) between 1st of January 1986 and 31st of December 2011. Daily mortality, obtained from Statistics Canada through access to the Canadian Mortality Database, is represented by counts of deaths for all causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚C) and relative humidity (in %), computed as the 24-hour average based on hourly measurements, were obtained from Environment Canada. A single weather station was selected for each city using the airport monitoring station located closest to the CMA center. Measures of inhalable particles (PM_{10}, in μg/m^3) were available in 16 cities, fine particles ($PM_{2.5}$, in μg/m^3) were available in 25 cities, measures of ozone (O_3, in ppb), nitrogen dioxide (NO_2, in ppb), sulfur dioxide (SO_2, in ppb), and carbon monoxide (CO, in ppm) were available in the same period from the National Air Pollution Surveillance (NAPS) network of Environment Canada, a government institution that operates ground monitoring stations across Canada. Monitors are located in urban areas. Daily level of pollutants were computed as the 24-hour mean based on hourly measurements in different stations, and then averaged across stations with no missing data, with an average of 4 stations per city. In total, missing data amount for 0.22% and 12.50% of the mortality and PM air pollution, respectively. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3).

Chile

We collected data from 4 cities in the period 2004–2014. Daily mortality is represented by counts of deaths for all causes (ICD-10: A00-R99). Mean daily temperature (in ˚**C**) was computed as the 24-hour average based on hourly measurements. The air pollution data were obtained from Chile's national system (SINCA=Sistema informatico nacional de calidad de aire). All of those stations are located in urban areas. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), ozone (O_3, in ppb), nitrogen dioxide (NO_2, in ppb), and carbon monoxide (CO, in ppm) were available. Measurements were computed as the 24-hour average based on hourly measurements. In total, missing data amount for 0.50% and 10.76% of the mortality and air pollution, respectively. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3).

China

We collected data in 272 Chinese cities from China's Disease Surveillance Points System (DSPS) from 2013 to 2015. Daily mortality is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), and sulfur dioxide (SO_2, in μg/m^3) and carbon monoxide (CO, mg/m^3) were available in 272 cities in the same period. Daily level of pollutants were computed as the 24-hour mean based on hourly measurements. In total, missing data amount for 0.00% and 1.08% of the mortality and PM air pollution, respectively. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3).

Columbia

We collected data from 5 cities between 1st of January 1998 and 31st of December 2013. Daily mortality is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-h average based on hourly measurements were available. Measures of inhalable particles (PM_{10}, in μg/m^3), nitrogen dioxide (NO_2, in ppb), ozone (O_3, ppb), and sulfur dioxide (SO_2, in ppb) were available in 1 city from the Environmental Secretary of Bogotá. Monitoring stations measure air pollutants hourly, for each station and pollutant 24h average was calculated; for each pollutant, city average among monitoring stations was calculated. In total, missing data amount for 0.00% and 0.14% of mortality and PM air pollution, respectively. In the present study, all concentration units were unified to μg/m^3.

Czech Republic

We collected data from 1 city of Prague between 1st of January 1994 and 31st of December 2015. Mortality data were obtained from the Czech Statistical Office and the Institute of Health Information and Statistics. Daily mortality is represented by counts of deaths for non-external causes (ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-h average based on hourly measurements were available from the Czech Hydrometeorological Institute. Air pollution daily values were also obtained from Czech Hydrometeorological Institute, and were calculated from 4 stations (2 urban + 2 suburban). Measures of inhalable particles (PM_{10}, in μg/m^3), nitrogen dioxide (NO_2, in ppb), ozone (O_3, ppb), and sulfur dioxide (SO_2, in ppb), carbon monoxide (CO, in ppm) were available. In the present study, all concentration units were unified to μg/m^3. In total, missing data amount for 0.00% and 0.12% of mortality and PM air pollution, respectively.

Estonia

We collected data from 4 cities between 1st of January 1997 and 31st of December 2015. Daily mortality, obtained from the Estonian Causes of Death Registry, is represented by counts of deaths for different causes (ICD-10: A00-R99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-h average based on hourly measurements were available from the Estonian Environment Agency. The source of air quality is national air quality network: http://airviro.klab.ee/en carried out by Estonian Environmental Research Centre. Measures of inhalable particles (PM_{10}, in μg/m^3), nitrogen dioxide (NO_2, μg/m^3), ozone (O_3, μg/m^3), and sulfur dioxide (SO_2, μg/m^3) were available. A single urban background station data was selected for each city. In total, missing data amount for 0.00% and 3.48% of mortality and PM air pollution, respectively.

Finland

We collected data from one city of Helsinki between 1st of January 1994 and 31st of December 2014. Daily number of deaths in the Capital Region of Finland was obtained from Statistics Finland, and is represented by counts of deaths for non-external causes

(ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). A dataset containing weather variables was obtained from Helsinki Region Environmental Services Authority. Measures of SO_2, NO_2, O_3, PM_{10}, PM_{25}, and CO were available in 1 city from Finnish Meteorological Institute. Data were extracted from GIS with kind assistance from Dr. Harri Antikainen, Unit of Geography, University of Oulu, Finland. In the present study, all concentration units were unified to $\mu g/m^3$. There were no missing values for mortality and air pollution series.

France

We collected data from 18 cities between 1st of January 2000 and 31st of December 2010. Daily mortality is represented by counts of deaths for all causes (ICD-10: A00-R99). Mean daily temperature (in °**C**), computed as the 24-h average based on hourly measurements was available. Measures of inhalable particles (PM_{10}, in $\mu g/m^3$) and ozone (O_3, in $\mu g/m^3$) were obtained by the French local air quality monitoring network (Associations Agréées de Surveillance de la Qualité de l’Air AASQA). Measurements were obtained from multiple stations (with different numbers for each city). For PM_{10}, we used only urban stations, and for ozone, urban and peri-urban stations. In total, missing data amount for 0.00% and 1.09% of mortality and PM air pollution, respectively.

Greece

We collected data from 1 city of Athens between 1st of January 2001 and 31st of December 2010. The mortality data were provided by the Hellenic Statistical Authority (http://www.statistics.gr/en/home/). The database includes the daily number of deaths from all natural (ICD-9: 1-799), cardiovascular (ICD-9: 390-459) and respiratory causes (ICD-9: 460-519). Meteorological data were obtained from National observatory of Athens (http://www.noa.gr/) from site "Thisio" located in the city of Athens. Mean daily temperature (in ˚**C**) and mean relative humidity (%), were computed as the 24-h average based on hourly measurements was available. Air pollution data were obtained by the Ministry of Environment and Energy fixed site monitoring network. Urban or suburban fixed monitoring background or traffic sites with at least 75% complete information per year of the study period were selected. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), ozone (O_3, μg/m^3), and carbon monoxide (CO, in mg/m^3). In total, there were no missing data for mortality, missing data amount for 0.00% and 1.73% of mortality and PM air pollution, respectively.

Italy

We collected data from 18 cities, between 1st of January 2006 to 31st of December 2015. Daily mortality, obtained from local mortality registries and from the rapid mortality surveillance system operational since 2004, is represented by counts of deaths for all causes (ICD-10: A00-R99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-h average based on 6-h measurements, were obtained from the Meteorological Service of the Italian Air Force. A single weather station was selected for each city, using the airport monitoring station located closest to the city center. Measures of inhalable particles (PM_{10}, in μg/m^3) were obtained from the same period. In total, missing data amount for 0.59% and 2.63% of the mortality and air pollution series, respectively.

Japan

We collected data from 47 prefectures between 1st of January 2011 and 31st of December 2015. Daily mortality, obtained from computerized death certificate data from the Ministry of Health, Labour and Welfare, Japan, is represented by counts of deaths for all causes and for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-hour average based on hourly measurements, were obtained from the Japan Meteorology Agency. A single weather station located within the urban area of the capital city was selected for each prefecture. Measures of, fine particles ($PM_{2.5}$, in μg/m^3), ozone (O_3, in ppb), nitrogen dioxide (NO_2, in ppb), sulfur dioxide (SO_2, in ppb), and carbon monoxide (CO, in ppm) were available during the study period. Measure of suspended particulate matter (SPM) with aerodynamic diameter < 7 microns was calculated with a correction a factor of 90% to PM_{10} (in μg/m^3). In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3). In total, missing data amount for less than 0.00% and 1.90% of mortality and PM air pollution, respectively.

Mexico

We collected data from 10 cities between 1st of January 1998 and 31st of December 2014. Daily mortality is represented by counts of deaths for all causes (ICD-9: 0-799;

ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), and ozone (O_3, in μg/m^3) were available in 2000-2012. In total, missing data amount for 0.0% and 7.04% of the mortality and PM air pollution, respectively.

Portugal

We collected data from 2 cities between 1st of January 1995 and 31st of December 2012. Daily mortality is represented by counts of deaths for non-external causes only (ICD-10: A00-R99). Mean daily temperature (in ˚**C**) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements. We obtained air pollution data from the "online database of air quality" through Portuguese Environment Agency. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), carbon monoxide (CO, in μg/m^3), ozone (O_3, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), and sulfur dioxide (SO_2, in μg/m^3) were available from 1999 to 2012. In total, missing data amount for 0.00% and 5.36% of the mortality and PM air pollution, respectively.

South Africa

We collected data from 6 cites from January 2004 and 31st of December 2013. Daily mortality is represented by counts of deaths for non-external causes (ICD-9: codes 0-799; ICD-10: codes A00-R99), cardiovascular causes (ICD-10: codes I00-I99) and respiratory disease causes (ICD-10: codes J00-J98). Mortality data was provided by

Statistics South Africa and is from the country's civil registration system. Mean daily temperature (in ˚C) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements from the National Oceanic and Atmospheric Administration (NOAA) and Agricultural Research Council of South Africa. Measures of inhalable particles (PM_{10}, in μg/m^3) were available in 3 cities, fine particles ($PM_{2.5}$, in μg/m^3) were available in Johannesburg and Sedibeng, and were calculated as 24-h averages based on hourly measurements. Air quality data for City of Johannesburg and City of Tshwane are from the corresponding municipal government monitoring stations. Data for Sedibeng is from the Department of Environmental Affairs (DEA) VTAPA network run by South African Weather Service (SAWS). All data were accessed through SAAQIS (http://www.saaqis.org.za/), which is run and hosted by SAWS. In total, missing data amount for 0.00% and 15.3% of the mortality and PM air pollution, respectively. We thank the Statistics South Africa for providing the mortality data, and cities of Johannesburg and Tshwane, DEA, SAAQIS, and SAWS for providing the air pollution and environmental data.

South Korea

We collected data from 7 cities between 1st of January 1992 and 31st of December 2015. Daily mortality was obtained from the Korea National Statistics Office for each city in Korea, and is represented by counts of deaths for all causes and for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚C) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements. Measures of inhalable particles (PM_{10}, in μg/m^3), carbon monoxide (CO, in ppm), ozone (O_3, in ppb), nitrogen dioxide (NO_2, in ppb), and sulfur dioxide (SO_2, in ppb) were available in the period 1999-2015 from the National Institute of Environmental Research. Daily level of pollutants were computed as the 24-hour mean based on hourly measurements. In total, missing data amount for 0.86% and 1.40% of the mortality and air pollution series, respectively. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3).

Spain

We collected data from the 48 capital cities between 1st of January 2001 and 31st of December 2014. Daily mortality, obtained from Spain National Institute of Statistics, is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in °C), computed as the 24-hour average based on hourly measurements, and was obtained from Spain National Meteorology Agency. A single weather station, located within the urban area or at the near airport, was selected for each city. Single-day missing values were imputed as the average of the days before and after. For periods longer than two days no imputation was done. Measures of hourly air pollution data from the free national repository (Magrama). For each sampler, selected as "valid days" for those having at least 18 out of the 24 hourly values (75%) and averaged the hourly data values within a day to obtain daily values; we dropped each daily value over 10SD to the mean for the whole period. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), carbon monoxide (CO, in μg/m^3), ozone (O_3, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), and sulfur dioxide (SO_2, in μg/m^3) were available in the same period, but for some pollutants the period started later. In the present study, all concentration units were unified to μg/m^3 expect for CO (mg/m^3). In total, missing data amount for 0.00% and 6.54% of mortality and PM air pollution, respectively.

Sweden

We collected data from the county of Stockholm between 1st of January 1994 and 31st of December 2010. Daily mortality, obtained from the Swedish Cause of Death Register at the Swedish National Board of Health and Welfare, is represented by counts of deaths for all causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-hour average based on hourly measurements, were obtained from the Environment and Health Administration. A single weather station, located at Torkel Knutssongatan in Central Stockholm, was selected. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), ozone (O_3, in μg/m^3) and nitrogen dioxide (NO_2, μg/m^3), and carbon monoxide (CO, mg/m^3) were available in the same period. Daily level of pollutants were calculated as the 24-h averaged measurements except for O_3 as 8-h maximum. In total, missing data amount for 0.00% and 6.93% of mortality and PM air pollution, respectively.

Switzerland

We collected data from 8 cities (Basel, Bern, Zurich, Geneva, Lausanne, Lucerne, Lugano, St. Gallen) between 1st January 1995 to 31st December 2013. Lugano also includes the small municipalities around the main city of Lugano with similar altitude. Daily mortality, provided by the Federal Office of Statistics (Switzerland), is represented by counts of non-external deaths with accidents included (International Classification of Diseases, 10th revision (ICD-10) codes A00-R99,). Daily data on several meteorological indicators were collected from the IDAWEB database (a service provided by MeteoSwiss, the Swiss Federal Office of Meteorology and Climatology). A single weather station located within or near the urban area was selected for each city. The meteorological indicators were: mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the 24-hour average based on hourly measurements. Daily measurements of inhalable particles (PM_{10}, μg/m^3), fine particles ($PM_{2.5}$, μg/m^3) nitrogen dioxide (NO_2, μg/m^3), sulfur dioxide (SO_2, in μg/m^3), and ozone (O_3, in μg/m^3) were provided by the Immissionsdatenbank Luft (IDB, Federal Office of the Environment, Bern, Switzerland) from urban monitoring stations and computed as 24-h average for the former four, and from urban and sub-urban monitoring stations for O_3 as 8h-maximum. In total, missing data amount for 0.00% and 1.04% of the mortality and air pollution series, respectively.

Taiwan

We collected data in Kaohsiung, Taipei and Taichung between 1st of January 1994 and 31st of December 2014 from the Department of Health in Taiwan. Daily mortality is represented by counts of deaths for all causes and for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %) were computed as the 24-hour average based on hourly measurements. Measures of carbon monoxide (CO, in mg/m^3), ozone (O_3, in μg/m^3), nitrogen dioxide (NO_2, in μg/m^3), inhalable particles (PM_{10}, in μg/m^3) and sulfur dioxide (SO_2, in μg/m^3) were available for the same period. Fine particles measures ($PM_{2.5}$, in μg/m^3) were available only in 2005–2007. Daily level of pollutants were computed as the 24-hour mean based on hourly measurements. Data were pooled from 1 meteorological station and 11 air quality monitoring stations in Kaohsiung, 2 meteorological station and 5 air quality monitoring stations in Taichung, and 3 meteorological station and 15 air quality monitoring stations in Taipei, respectively. In total, missing data amount for 0.03% and 0.03% of the mortality and air pollution series, respectively.

Thailand

We collected data from 19 provinces between 1st of January 1999 and 31st of December 2008. Daily mortality, obtained from the Ministry of Public Health, Thailand, is represented by counts of deaths for all causes (ICD-10: A00-R99). Mean daily temperature (in ˚**C**) and relative humidity (in %), computed as the average between daily minimum and maximum, were obtained from the Meteorological Department, Ministry of Information and Communication Technology, Thailand. Measures of inhalable particles (PM_{10}, in μg/m^3), carbon monoxide (CO, in ppm), ozone (O_3, in ppb), nitrogen dioxide (NO_2, in ppb), and sulfur dioxide (SO_2, in ppb) were obtained from the Pollution Control Department, Ministry of Natural Resources and Environment for 18 provinces during 1999–2008 (Air Quality and Noise Management Bureau 2010).

Monitoring air pollution data started from 2004 for Chachoengsao, and from 2000 for Nakhon sawa. For each province and air pollutant, daily concentration was averaged by fixed air quality monitoring stations within the province. If monitored data for an individual pollutant were insufficient to calculate a daily average, all measurements from that day were excluded for that pollutant and monitor. In the present study, all concentration units were unified to $\mu g/m^3$ expect for CO (mg/m^3) in the present study. In total, missing data amount for 0.00% and 10.6% of the mortality and air pollution series, respectively.

United Kingdom

We collected data from 15 cities between 1st of January 1993 and 31st of December 2006. All data were downloaded from the UK Air Quality Archive, which reports results from the network of monitoring stations operated by the UK government. Daily mortality is represented by counts of deaths for all causes and for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚**C**) and relative humidity (in %) were obtained from the Meteorological Department obtained from British Atmospheric Data Centre. Series for each city daily mean temperatures were similarly constructed from all meteorological stations providing data for at least 75% of days. Measures of inhalable particles (PM_{10}, in $\mu g/m^3$), and ozone (O_3, in $\mu g/m^3$) were available in the same period. In total, missing data amount for 0.00% and 5.52% of the mortality and air pollution series, respectively.

United States

We collected data from 142 cities between 1st of January 1987 and 31st of December 2006. Daily mortality is represented by counts of deaths for non-external causes (ICD-9: 0-799; ICD-10: A00-R99), cardiovascular causes (ICD-10: I00-I99) and respiratory disease causes (ICD-10: J00-J99). Mean daily temperature (in ˚C, computed as the 24-hour average based on hourly measurements) was obtained from the National Climatic Data Center (NCDC) of the National Oceanic and Atmospheric Administration (NOAA). The air pollutant measurements were generated using input from the U.S. Environmental Protection Agency (EPA) Air Quality System (AQS). Estimates for each "city" are based on a county or set of contiguous counties. The dataset contains urban/suburban areas. Measures of inhalable particles (PM_{10}, in μg/m^3), fine particles ($PM_{2.5}$, in μg/m^3), ozone (O_3, in μg/m^3), sulfur dioxide (SO_2, in μg/m^3), and nitrogen dioxide (NO_2, μg/m^3), and carbon monoxide (CO, mg/m^3) were available in the same period. In total, missing data amount for 0.00% and 1.12% of mortality and PM air pollution, respectively.

2. Results

2.1 Descriptive Statistics

This study included 652 urban cities from 24 countries/regions and covered the period from 1986 to 2015, with different years of data for different countries/regions (Table S1). This analysis included 59.6 million deaths from total or non-external causes, including 20.1 million from cardiovascular diseases and 5.6 million from respiratory diseases, based on the cities where such data were available.

Table S3 shows descriptive statistics on the trimmed exposure data in our study. On average, annual-mean daily PM_{10} concentration in 598 cities was 56.0 μg/m^3 [median: 44.3 μg/m^3; range: 11.0 to 295.0 μg/m^3; interquartile range (IQR): 37.9 to 70.1 μg/m^3]. China had the highest level of annual-mean PM_{10} pollution (89.2 μg/m^3). For $PM_{2.5}$, annual-mean daily concentration in 499 cities was 37.5 μg/m^3 on average (median: 31.9 μg/m^3; range: 4.1 to 116.9 μg/m^3; IQR: 21.5 to 43.5 μg/m^3), with the highest level in one city of China (116.9 μg/m^3) and the lowest level in one city of Canada (6.0 μg/m^3). There were only 52 cities with annual-mean daily $PM_{2.5}$ concentrations below the WHO Air Quality Guideline for $PM_{2.5}$ (annual-mean: 10 μg/m^3)[11]. On average, annual-mean daily concentrations of O_3, NO_2, SO_2, and CO across all cities were 65.4 μg/m^3, 30.4 μg/m^3, 20.2 μg/m^3, and 1.0 mg/m^3, respectively. PM_{10} was strongly correlated with $PM_{2.5}$ with a Pearson coefficient of 0.78 on average. Pearson correlations of PM_{10} were 0.20 with O_3, 0.38 with SO_2, and 0.405 with CO. $PM_{2.5}$'s correlations were 0.22 with O_3, 0.40 with SO_2, and 0.45 with CO. $PM_{2.5}$ was more correlated with NO_2 than PM_{10} (Pearson correlation coefficient = 0.48 and 0.46, respectively). There were marked variations in climatic conditions among cities, with an average annual-mean temperature of 15.2°C (ranging from –3.1°C to 29.3°C) and an average annual-mean relative humidity of 69% (ranging from 33% to 91%). On average, PM_{10}'s Pearson correlation coefficient was –0.23 with daily mean temperature and was –0.21 with relative humidity. $PM_{2.5}$'s Pearson correlation coefficient was –0.25 with daily mean temperature and was –0.17 with relative humidity.

Table S3. Descriptive statistics on annual-mean daily levels (mean ± SD) of particulate matter, weather conditions and gaseous pollutants in each country or region throughout the study period. *

Country/Region	PM_{10} (μg/m^3)	$PM_{2.5}$ (μg/m^3)	O_3 (μg/m^3)	NO_2 (μg/m^3)	SO_2 (μg/m^3)	CO (mg/m^3)	Temperature (°C)	Humidity (%)
Australia	19.0 ± 5.5	6.9 ± 3.8	30.4 ± 11.5	21.6 ± 9.2	5.0 ± 6.9	0.5 ± 0.4	18.3 ± 4.3	69.4 ± 11.1
Brazil	42.5 ± 15.5	NA	83.0 ± 40.5	91.9 ± 37.5	11.8 ± 6.2	2.1 ± 1.1	20.4 ± 3.4	73.4 ± 10.5
Canada	19.7 ± 10.8	9.3 ± 6.0	43.0 ± 20.0	32.0 ± 13.2	8.3 ± 5.9	0.6 ± 0.3	7.4 ± 9.8	73.0 ± 11.8
Chile	52.5 ± 25.7	28.1 ± 21.6	27.5 ± 13.8	25.5 ± 13.8	NA	0.8 ± 0.7	14.0 ± 4.3	60.2 ± 13.5
China	89.2 ± 37.2	52.3 ± 27.0	78.9 ± 36.9	31.0 ± 13.2	29.0 ± 18.8	1.1 ± 0.5	15.3 ± 8.9	68.3 ± 13.9
Colombia	64.4 ± 18.1	NA	25.4 ± 10.1	34.5 ± 12.0	18.9 ± 9.9	NA	13.9 ± 0.9	NA
Czech Republic	33.4 ± 16.2	NA	74.1 ± 35.3	31.8 ± 9.9	12.8 ± 15.6	NA	9.3 ± 8.0	76.1 ± 12.7
Estonia	16.1 ± 7.9	7.8 ± 5.2	51.4 ± 17.5	12.9 ± 7.4	2.9 ± 4.2	NA	6.3 ± 9.1	82.2 ± 11.7
Finland	18.0 ± 11.0	15.3 ± 9.4	52.2 ± 16.2	8.3 ± 5	8.3 ± 6.2	0.3 ± 0.1	6.4 ± 8.8	76.6 ± 14.1
France	19.7 ± 6.8	NA	69.3 ± 29.9	NA	NA	NA	12.3 ± 6.5	NA

Greece	41.9 ± 14.8	22 ± 8.1	77.0 ± 28.2	51.6 ± 14.9	NA	2.1 ± 1.2	18.9 ± 7.4	64.4 ± 14.8
Italy	30.3 ± 12.1	NA	NA	NA	NA	NA	16.5 ± 7.0	NA
Japan	18.1 ± 7.4	13.6 ± 6.3	56.9 ± 21.8	20.5 ± 9.8	6.2 ± 3.5	NA	15.7 ± 8.3	69.4 ± 12.1
Mexico	56.6 ± 20.2	26.1 ± 9.2	26.4 ± 8.6	NA	NA	NA	18.3 ± 3.8	56.3 ± 14.9
Portugal	30.4 ± 13.8	12.9 ± 7.3	45.5 ± 18.7	29.1 ± 14.7	4.3 ± 4.3	0.3 ± 0.2	16.0 ± 4.6	NA
South Africa	59.3 ± 27.0	30.5 ± 15.4	NA	NA	NA	NA	16.3 ± 4.9	NA
South Korea	49.3 ± 18.7	NA	47.7 ± 22.1	50.8 ± 18.5	16.7 ± 7.1	0.7 ± 0.3	13.7 ± 9.6	63.4 ± 15.5
Spain	27.8 ± 9.6	11.3 ± 5.4	50.8 ± 17.9	27.7 ± 9.8	5.5 ± 2.4	0.4 ± 0.2	15.5 ± 6.3	NA
Sweden	14.1 ± 5.9	7.7 ± 4.0	64.3 ± 19.7	27.9 ± 10.8	NA	1.2 ± 0.7	7.8 ± 8.1	76.1 ± 13.0
Switzerland	23.6 ± 11.0	18.2 ± 9.4	75.9 ± 36.4	33.2 ± 12.1	5.4 ± 5.1	NA	10.9 ± 7.4	73.9 ± 11.9
Taiwan	61.5 ± 24.2	34.5 ± 14.9	77.6 ± 36.1	47.6 ± 16.3	16.5 ± 8.4	0.8 ± 0.3	24.1 ± 4.7	75.1 ± 7.5
Thailand	47.9 ± 19.1	NA	38.5 ± 17.8	26.1 ± 11.1	11.0 ± 6.3	0.7 ± 0.3	27.6 ± 2.2	74.0 ± 8.3
United Kingdom	25.2 ± 8.9	NA	51.4 ± 22.3	NA	NA	NA	10.6 ± 5.1	73.7 ± 12.5

United States	25.6 ± 10.5	12.4 ± 6.6	53.8 ± 20.4	34.4 ± 14.2	13.8 ± 11.0	1.0 ± 0.6	14.5 ± 8.5	NA
Total	56.0 ± 23.1	35.6 ± 18.4	65.4 ± 28.6	30.4 ± 12.7	20.2 ± 13.2	1.0 ± 0.4	15.2 ± 7.9	69.0 ± 13.2

* Values shown are 10 percent trimmed means, as described in the Method section.

Abbreviations: SD, standard deviation; PM_{10}, particulate matter with an aerodynamic diameter less than or equal to 10 µm; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 µm; O_3, ozone; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; CO, carbon monoxide.

2.2 Lag structure

The choice of 2-day moving average (lag 0–1 days) for PM and 4-day moving average (lag 0–3 days) for temperature generated the smallest average GCV scores (Tables S4 and S5), and were then applied in subsequent analyses.

Table S4. Effect estimates and average scores of generalized cross validation on different lag days of PM_{10} and $PM_{2.5}$ at the global level.

Pollutants	Lags of PM	Effect estimates	GCV
PM_{10}	Lag 0	0.36 (0.31, 0.40)	1.3708
	Lag 1	0.26 (0.22, 0.30)	1.3714
	Lag 2	0.10 (0.07, 0.13)	1.3719
	Lag 0–1	0.44 (0.39, 0.50)	1.3677
	Lag 0–2	0.42 (0.36, 0.48)	1.3766
$PM_{2.5}$	Lag 0	0.53 (0.45, 0.61)	1.4274
	Lag 1	0.39 (0.33, 0.45)	1.4280
	Lag 2	0.09 (0.04, 0.14)	1.4315
	Lag 0–1	0.68 (0.59, 0.78)	1.4222
	Lag 0–2	0.59 (0.50, 0.68)	1.4300

Abbreviations: PM, particulate matter; PM_{10}, particulate matter with an aerodynamic diameter less than or equal to 10 μm; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; GCV, generalized cross validation.

Notes: Lag 0, the present day; lag 1, the previous day; lag 2, the previous 2 day; lag 0–

1, moving average of the present and the previous day; lag 0–2, moving average of the present and the previous 2 days. The effect estimates were presented as percentage changes and related 95% confidence intervals in daily total mortality per 10 μg/m^3 increase of PM concentrations.

Table S5. Effect estimates of PM_{10} and $PM_{2.5}$ and average scores of generalized cross validation at the global level, with adjustment for different lag days of temperature.

Pollutants	Lags of temperature	Effect estimates	GCV
PM_{10}	Lag 0	0.30 (0.25, 0.34)	1.3708
	Lag 0 and lag 1	0.27 (0.22, 0.32)	1.3859
	Lag 0–3	0.44 (0.39, 0.50)	1.3603
	Lag 0 and lag 1–3	0.22 (0.17, 0.27)	1.3821
	Lag 0–7	0.48 (0.43, 0.54)	1.3706
	Lag 0–14	0.49 (0.43, 0.55)	1.3705
	Lag 0–21	0.52 (0.46, 0.58)	1.3762
$PM_{2.5}$	Lag 0	0.42 (0.34, 0.51)	1.4268
	Lag 0 and lag 1	0.41 (0.33, 0.49)	1.4443
	Lag 0–3	0.68 (0.59, 0.78)	1.4214
	Lag 0 and lag 1–3	0.32 (0.24, 0.40)	1.4405
	Lag 0–7	0.67 (0.57, 0.76)	1.4244
	Lag 0–14	0.66 (0.56, 0.75)	1.4257

Lag 0–21	0.70 (0.60, 0.79)	1.4316

Abbreviations as in Table S4.

Notes: Lag 0, the present day; lag 0 and lag 1, the present day and the previous day; lag 0–3, moving average of the present day and the previous 3 days; lag 0 and lag 1–3, the present day and the mean of 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. The effect estimates were presented as percentage changes and related 95% confidence intervals in daily total mortality per 10 μg/m^3 increase of 2-day moving average PM concentrations.

2.3 Results for cause-specific associations

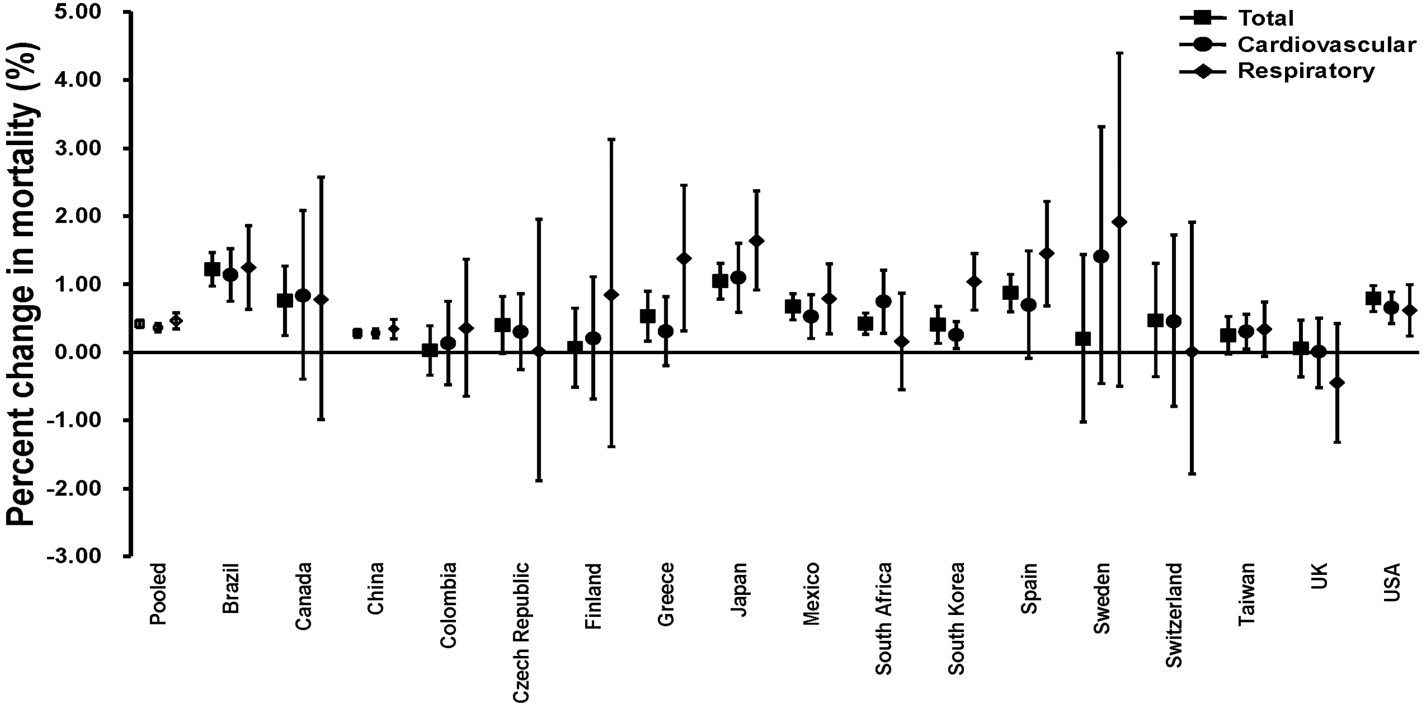

Figure S1. Percent change (pooled estimate and 95% confidence intervals) in daily total, cardiovascular, and respiratory mortality associated with a 10 μg/m^3 increase in two-day average concentrations of inhalable particulate matter (PM_{10}) in 528 cities. Effect estimates were pooled using a random effect model within a country/region or at the global level.

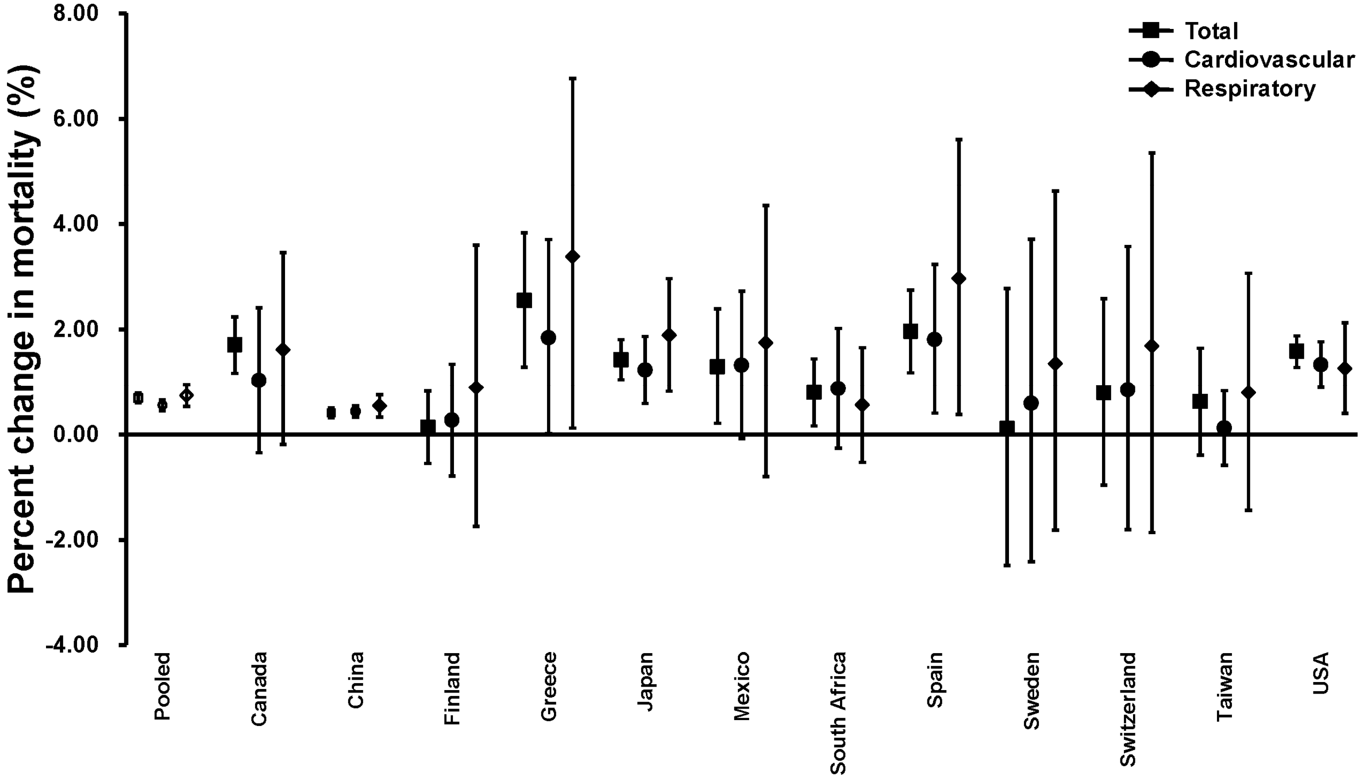

Figure S2. Percent changes (pooled estimate and 95% confidence intervals) in daily total, cardiovascular, and respiratory mortality associated with a 10 μg/m^3 increase in two-day average concentrations of fine particulate matter ($PM_{2.5}$) in 488 cities. Effect estimates were pooled using a random effect model within a country/region or at the global level.

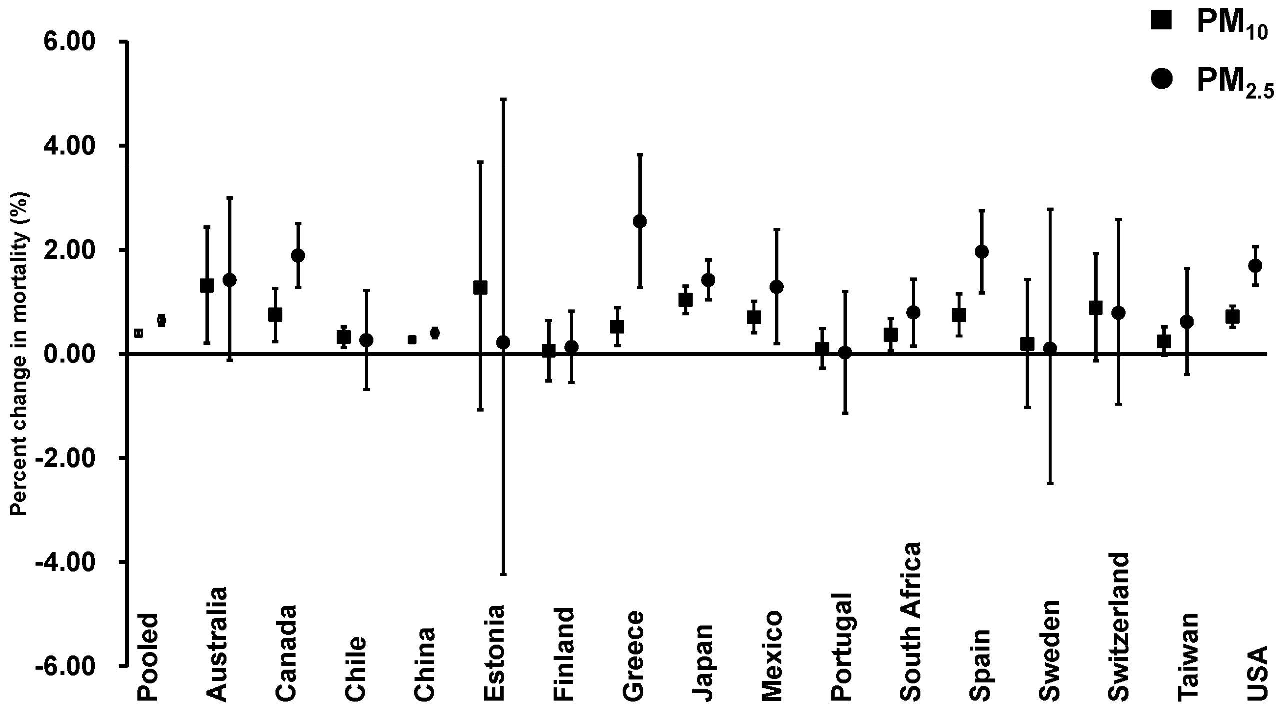

Figure S3. Percent change (pooled estimate and 95% confidence intervals) in daily total mortality associated with a 10 μg/m^3 increase in two-day averaging concentrations of inhalable particulate matter (PM_{10}) and fine particulate matter ($PM_{2.5}$) in 445 cities of 16 countries/regions with both PM_{10} and $PM_{2.5}$ data. Effect estimates were pooled using a random effect model within a country/region or at the global level.

2.4 Results for heterogeneity and effect modification analyses

Among all cities, the PM-mortality association was significantly heterogeneous with an I^2 of 46% for PM_{10} and 43% for $PM_{2.5}$. The within-country heterogeneity was generally smaller, with the I^2 ranging from 0% to 68.7% (median: 16.4%) for the PM_{10}'s association, and from 0% to 71.8% (median: 2.2%) for the $PM_{2.5}$'s association.

In regional analyses (Table S6), the associations between both PM_{10} and $PM_{2.5}$ and daily mortality were stronger in the Region of the Americas and were smaller in the Western Pacific Region.

Table S6. Effect estimates of PM_{10} and $PM_{2.5}$ classified by different regions and *p*-values for testing difference among regions.

Classification	Regions	PM_{10}		$PM_{2.5}$	
		Estimates	*p*-value	Estimates	*p*-value
WHO	WPRO	0.34 (0.29, 0.40)	<0.001	0.48 (0.38, 0.57)	<0.001
	EURO	0.46 (0.31, 0.61)		0.94 (0.47, 1.40)	
	AMRO	0.73 (0.59, 0.88)		1.47 (1.23, 1.72)	
GDP	1	0.33 (0.27, 0.39)	<0.001	0.43 (0.34, 0.52)	<0.001
	2	0.53 (0.41, 0.64)		1.38 (1.07, 1.68)	
	3	0.75 (0.58, 0.91)		1.50 (1.25, 1.76)	

Abbreviations as in Table S3.

Note: The Region for Africa (ROA) was excluded from regional analysis classified by WHO because this region only included one country (South Africa). The effect estimates were presented as percentage changes and related 95% confidence intervals in daily total mortality per 10 $\mu g/m^3$ increase of 2-day moving average PM concentrations. *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. A *p*-value < 0.05 was considered statistically significant for regional differences.

In meta-regression models, we observed stronger associations of PM_{10} and $PM_{2.5}$ in locations with lower annual-mean levels of PM and higher annual-mean levels of temperature (all *p*-values < 0.001). To be specific, the PM_{10}-mortality association increased by 0.025% (95%CI: 0.011%, 0.040%) in areas with a 10 ˚C higher annual-mean temperature, and increased by 0.004% (95%CI: 0.002%, 0.006%) in areas with a 10 μg/m^3 lower long-term PM_{10} level. As for $PM_{2.5}$, the association increased by 0.029% (95%CI: 0.001%, 0.057%) and 0.012% (95%CI: 0.005%, 0.019%) in areas with a 10 ˚C higher annual-mean temperature, and a 10 μg/m^3 lower long-term $PM_{2.5}$ level, respectively. There were no significant effect modifications by annual levels of co-pollutants (all p-values>0.05), latitude (p=0.873), WHO region (p=0.592), missing rate of mortality (p=0.561), missing rate of PM_{10} (p=0.755), missing rate of $PM_{2.5}$ (p=0.705), and GDP per capita (p=0.262).

2.5 Country-specific concentration-response curves

As shown in Figure S4 and Figure S5, the shape of curves differed appreciably by country/region. In most cases, the shapes appeared linear in the full range, and nearly so in low- and middle- concentration ranges, but excess relative rate seemed to be smaller (i.e., the exposure-response relation seemed to flatten) at high ranges. In some cases, the shapes tended to be flat, for example, the PM_{10}-mortality curve for France, Sweden, Switzerland, and UK; and the $PM_{2.5}$-mortality curve for Sweden.

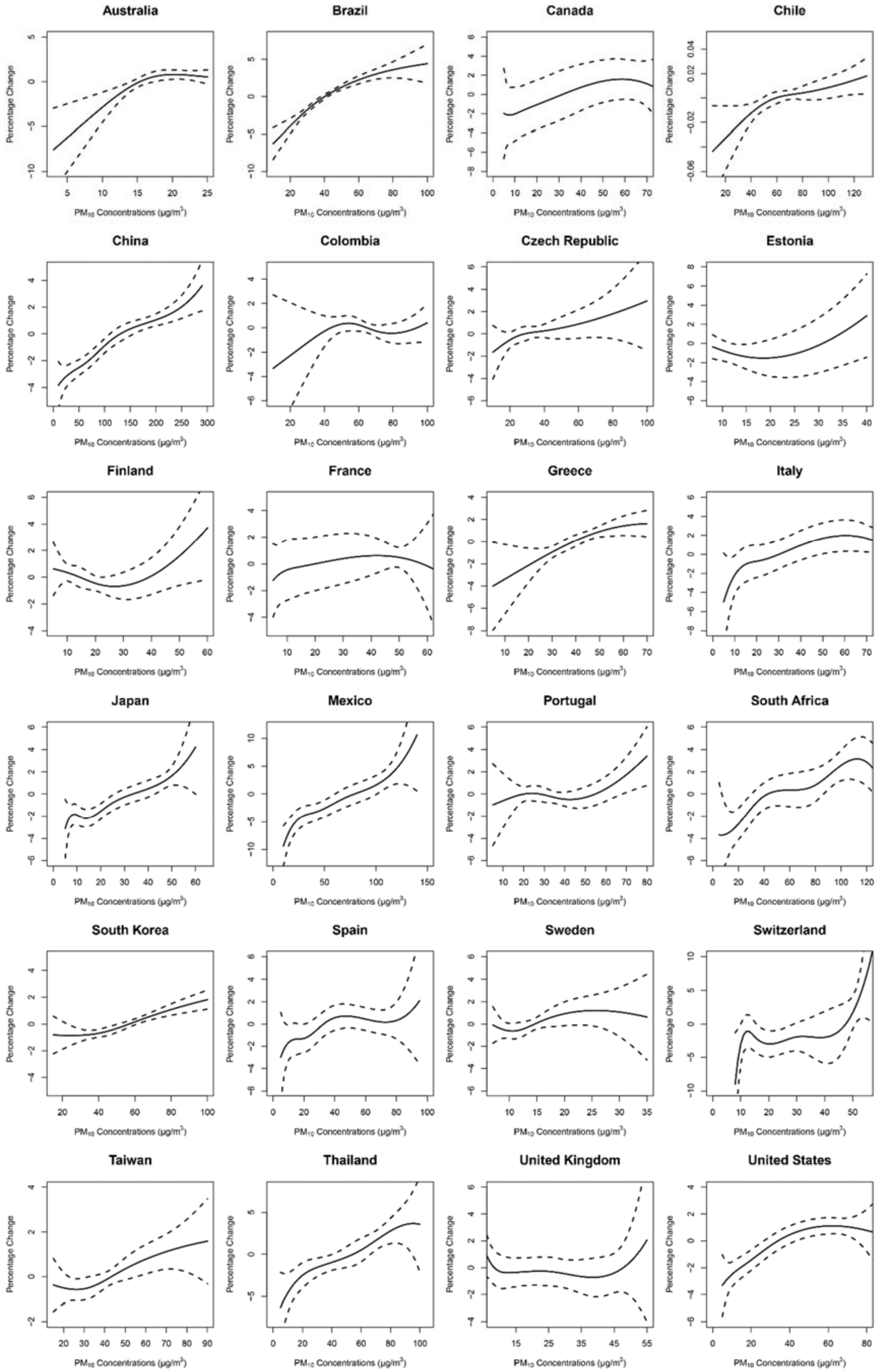

Figure S4. Concentration–response curves between PM_{10} concentrations (lag 0–1)

and daily total mortality in 24 countries/regions. The y-axis can be interpreted as the relative change from the mean effect of PM_{10} on mortality; the fraction of the curve below zero denotes a smaller estimate compared with the mean effect.

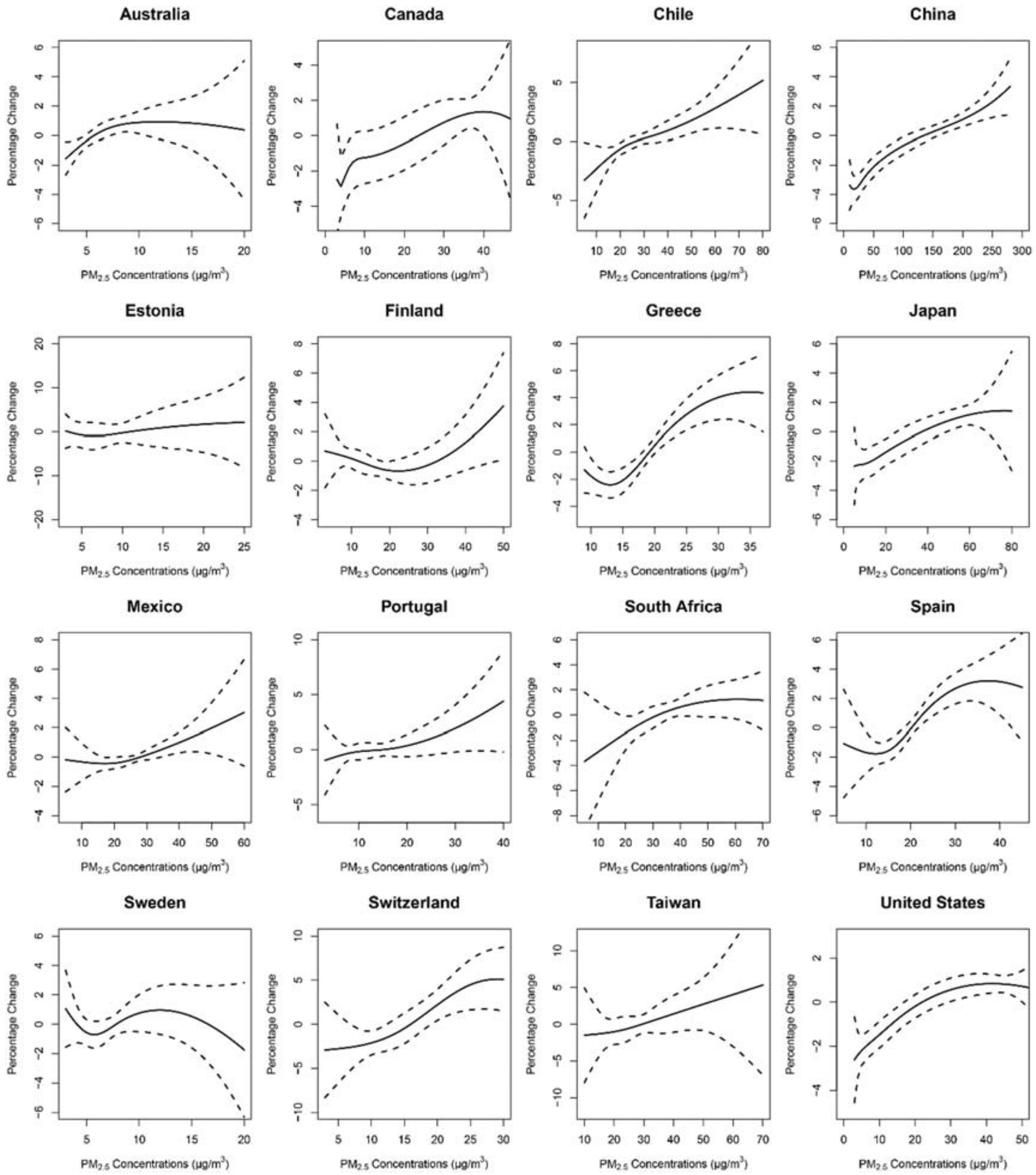

Figure S5. Concentration–response curves between $PM_{2.5}$ concentrations (lag 0–1) and daily total mortality in 16 countries/regions. The y-axis can be interpreted as the relative change from the mean effect of $PM_{2.5}$ on mortality; the fraction of the curve below zero denotes a smaller estimate compared with the mean effect.

2.6 Sensitivity analyses

Sensitivity analyses confirmed our main results. The use of alternative knots did not substantially change the shape of the C–R curves (Figure S6 and Figure S7). There were no significant changes after adjustment for humidity (Table S7).

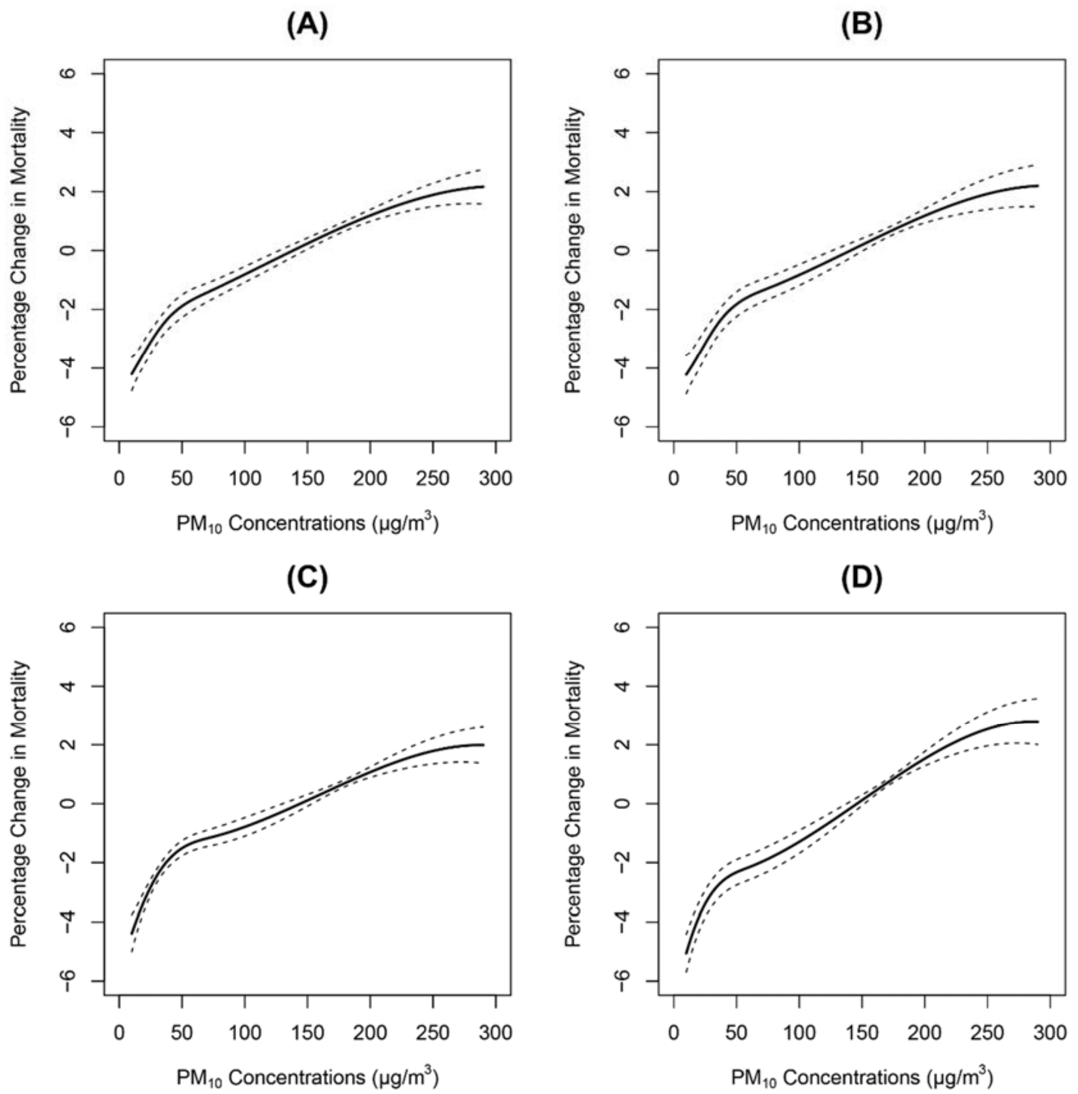

Figure S6. Pooled concentration–response curves at the global level between PM_{10} concentrations (lag 0–1) and total mortality using alternative knots. The y-axis can be interpreted as the relative change from the mean effect of PM_{10} on mortality; the fraction of the curve below zero denotes a smaller estimate compared with the mean effect. (A) knots at (35, 70) μg/m³ (main analysis); (B) knots at (35, 75) μg/m³; (C) knots at (30, 75) μg/m³; and (D) knots at (30, 80) μg/m³.

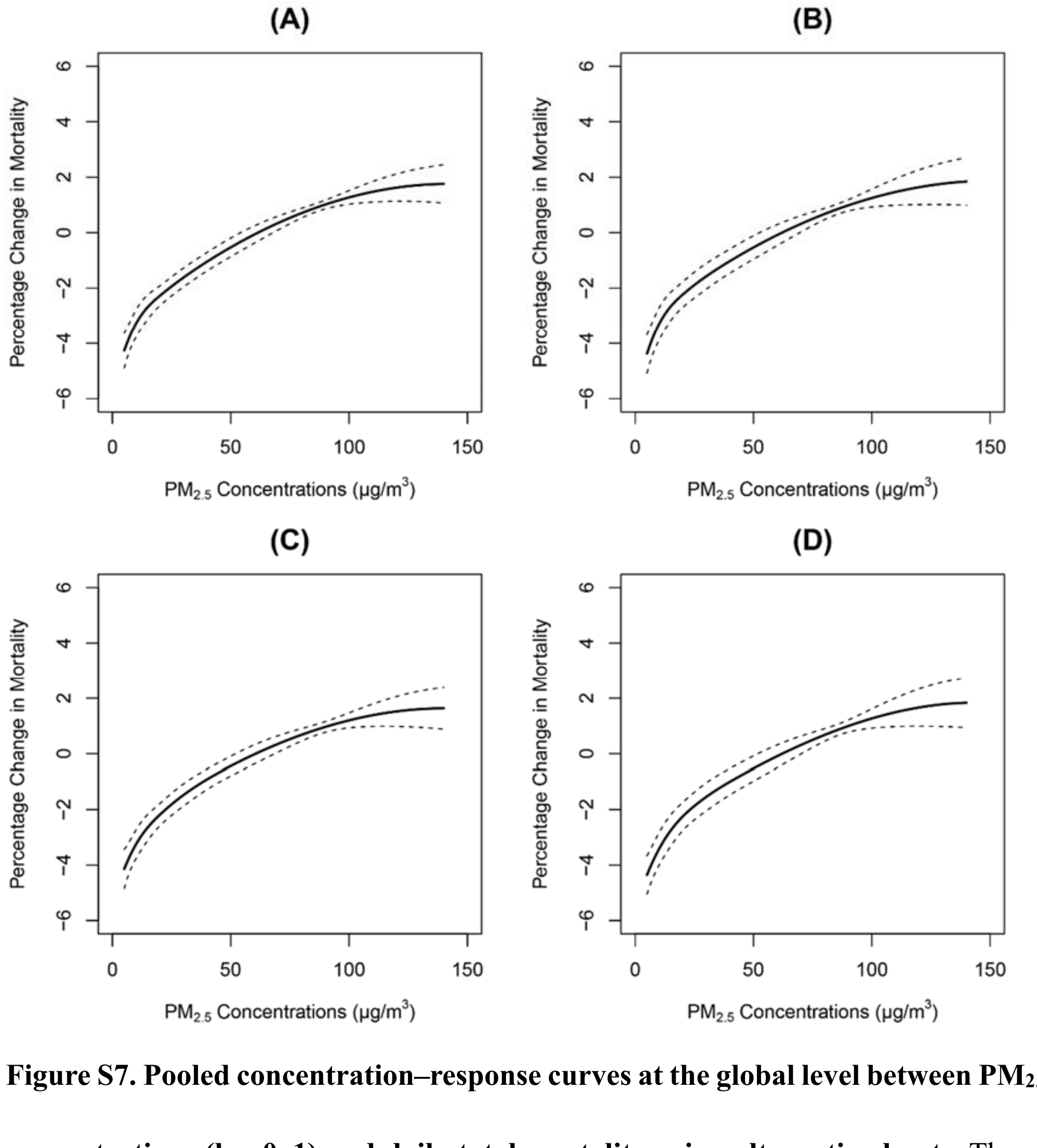

Figure S7. Pooled concentration–response curves at the global level between $PM_{2.5}$ concentrations (lag 0–1) and daily total mortality using alternative knots. The y-axis can be interpreted as the relative change from the mean effect of $PM_{2.5}$ on mortality; the fraction of the curve below zero denotes a smaller estimate compared with the mean effect. (A) knots at (20, 45) μg/m^3 (main analysis); (B) knots at (20, 40) μg/m^3; (C) knots at (20, 50) μg/m^3; and (D) knots at (25, 45) μg/m^3.

Table S7. Effect estimates of PM_{10} and $PM_{2.5}$ at the global level with and without adjustment for relative humidity and *p*-values for difference.

Pollutants	N	Adjustment	Estimates	*p*-values
PM_{10}	403	With	0.36 (0.31, 0.42)	0.863
		Without	0.37 (0.32, 0.43)	
$PM_{2.5}$	363	With	0.53 (0.44, 0.62)	0.949
		Without	0.51 (0.42, 0.60)	

Notes: N denotes the number of cities that have the data on humidity. The effect estimates were presented as percentage changes and related 95% confidence intervals in daily total mortality per 10 μg/m^3 increase of 2-day moving average PM concentrations. *P*-values for difference was calculated by evaluating a binary variable (with and without the adjustment for humidity) in a paired Z-test with both model estimates. A *p*-value < 0.05 was considered statistically significant for differences.

2.7 Results of complete exposure data

Table S8. Percent change (pooled estimate and 95% confidence intervals) in total mortality associated with a 10 μg/m^3 increase in two-day average concentrations of inhalable particulate matter (PM_{10}) and fine particulate matter ($PM_{2.5}$) using complete exposure data.*

Country/Region	PM_{10}		$PM_{2.5}$	
	N	Estimates	N	Estimates
Australia	3	0.88 (0.26, 1.49)	3	0.71 (–1.00, 2.45)
Brazil	1	1.07 (0.87, 1.27)	0	NA
Canada	13	0.79 (0.18, 1.41)	25	1.57 (1.20, 1.95)
Chile	4	0.28 (0.13, 0.43)	4	0.25 (–0.29, 0.79)
China	272	0.21 (0.16, 0.26)	272	0.26 (0.19, 0.33)
Colombia	1	0.05 (–0.29, 0.39)	0	NA
Czech Republic	1	0.20 (–0.08, 0.49)	0	NA
Estonia	4	–0.52 (–1.26, 0.22)	3	–0.62 (–1.90, 0.69)
Finland	1	–0.25 (–0.69, 0.18)	1	–0.28 (–0.79, 0.24)
France	18	0.50 (0.10, 0.89)	0	NA
Greece	1	0.36 (0.11, 0.61)	1	1.55 (0.64, 2.47)
Italy	18	0.62 (0.39, 0.84)	0	NA
Japan	47	1.04 (0.84, 1.23)	47	1.49 (1.24, 1.75)
Mexico	8	0.74 (0.50, 0.98)	3	1.44 (1.15, 1.75)
Portugal	2	0.02 (–0.20, 0.24)	1	–0.17 (–0.90, 0.57)

South Africa	6	0.21 (0.08, 0.34)	5	0.48 (0.01, 0.95)
South Korea	7	0.18 (0.12, 0.24)	0	NA
Spain	45	0.50 (0.24, 0.76)	19	1.01 (0.49, 1.52)
Sweden	1	–0.07 (–0.94, 0.80)	1	1.03 (–0.01, 2.07)
Switzerland	8	0.61 (0.12, 1.11)	4	–0.51 (–2.12, 1.13)
Taiwan	3	0.21 (0.09, 0.34)	3	0.25 (–0.45, 0.96)
Thailand	19	0.57 (0.24, 0.90)	0	NA
United Kingdom	15	–0.20 (–0.54, 0.14)	0	NA
United States	100	0.65 (0.51, 0.79)	107	1.11 (0.89, 1.33)
Total	598	0.35 (0.31, 0.40)	499	0.52 (0.45, 0.59)

* This analysis were based on non-trimmed PM data. This table was moved from the main text because some results might be implausible, likely due to the inaccuracies driven by the outlying PM data.

Abbreviations as in Table S3. N, number of cities with available data.

3. Discussion

3.1 Concentration-response curves

The pooled C–R curves were consistently increasing without obvious thresholds between PM and daily mortality at the global level. For both curves, extreme concentration ranges are characterized by wider CIs, with some uncertainty on the actual mortality risk at such values. In the current study, there were 16 cities (out of 598 cities) with annual-average daily concentration of PM_{10} over 150 μg/m^3, and 33 cities (out of 499 cities) with annual-average $PM_{2.5}$ levels over 75 μg/m^3. We should also be cautious that the pooled concentration-response curves were somewhat heterogeneous in nature because they were merged from cities or countries with diverse PM ranges, population susceptibility and data quality/representability.

3.2 Heterogeneity and effect modifications

We found significant evidence of spatial heterogeneity in associations between PM and daily mortality across countries and regions. A number of factors could contribute to this variability, including different PM components, long-term air pollution levels, population susceptibility, and different lengths of study periods. As shown in Figure S1-S2, The point estimates in some countries (e.g., France, Finland, Sweden and United Kingdom) were smaller and not statistically significant. Similarly, in these countries, nearly non-increasing concentration-response curves were also observed (Figure S4, S5). The non-significant or non-increasing associations may be due to the following reasons: (1) These estimates generally occurred in countries with smaller number of cities included and shorter time periods evaluated, which increased the statistical uncertainty in effect estimation; (2) these countries are generally located in areas with low annual-mean temperature, which may decrease the PM-mortality association as showed in our meta-regression analyses; (3) compared with classic risk factors, short-term exposure to air pollution typically showed weak health effects, so non-positive associations are more probable to occur (especially in such a global analysis) in a random manner that depends on the study period and number of cities and populations included; and (4) one advantage of this global analysis is to avoid publication bias by reporting all results (including non-increasing associations) based on the largest dataset to date. Nevertheless, this study has great power to show a robust association between short-term PM exposure and increased mortality at the global level.

3.3 Limitations

Another limitation of the current study is some missingness in exposure and health data. This issue is not likely to produce appreciable influences on our estimates due to the following reasons. First, the missing data (mostly for air pollution series) mainly occurred in periods of consecutive days that are entirely missing, more than in isolated days. This is often due to problems with the monitoring equipment or data logging error, more than any more complex pathways. Therefore, this kind of missingness is likely to be independent from any other predictors and especially the outcome. Second, even if there really exists some collinearity of missing rates with time (e.g., induced by seasonality) in some countries or cities, it can be properly accounted for by the smooth function of time in our time-series models. Third, the missing rates at city level were generally low for daily mortality (mean: 0.52%; median: 0.00%, range: 0.00%– 9.90%), for PM_{10} concentrations (mean: 5.2%, median: 1.3%, range: 0.0% – 20.5%), and for $PM_{2.5}$ concentrations (mean: 2.0%, median: 0.6%, range: 0.0% – 20.1%), so the influence, if it really exists, may be not substantial to our pooled estimates.

We conducted two additional analyses to further check the influences on our results. First, we performed a multivariable linear regression model (Table S9), which did not indicate significant relationships of missingness in both pollutant and mortality data with potential country-level modifiers (including regions defined by WHO, numbers of cities included, GDP per capita, and annual-average temperature levels). Second, we added two separate variables of "missing rate of mortality data" and "missing rate of PM data" in our multivariable meta-regression models, and still found there were no significant impacts of the missingness on city-specific estimates (see the above results in Appendix Section 2.4).

In conclusion, the amount of missingness from both mortality and PM data was small, and both missingness did not produce substantial biases into our main effect estimates.

Table S9. Associations (coefficients and p-values) of missing rates in mortality and PM data with country-level covariates in multivariable linear regression models.

Covariates	Mortality	PM_{10}	$PM_{2.5}$
Region	0.365 (0.547)	-0.095 (0.829)	0.534 (0.238)
City number	-0.115 (0.115)	0.005 (0.249)	0.001 (0.997)

GDP	-0.001 (0.163)	0.001 (0.067)	0.001 (0.167)
Temperature	0.136 (0.151)	0.036 (0.644)	0.059 (0.405)

Notes: Missing rates of mortality, PM_{10}, $PM_{2.5}$ were included in the linear regression model as dependent variables. Country-level covariates include: Region (classified by WHO); City number, the number of cities in each country; GDP, gross domestic product per capita of each country; Temperature, annual-mean temperature of each country.

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