

# Premature mortality due to air pollution in European cities: a health impact assessment



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## Summary

**Background** Ambient air pollution is a major environmental cause of morbidity and mortality worldwide. Cities are generally hotspots for air pollution and disease. However, the exact extent of the health effects of air pollution at the city level is still largely unknown. We aimed to estimate the proportion of annual preventable deaths due to air pollution in almost 1000 cities in Europe.

**Methods** We did a quantitative health impact assessment for the year 2015 to estimate the effect of air pollution exposure (PM<sub>2.5</sub> and NO<sub>2</sub>) on natural-cause mortality for adult residents (aged ≥20 years) in 969 cities and 47 greater cities in Europe. We retrieved the cities and greater cities from the Urban Audit 2018 dataset and did the analysis at a 250 m grid cell level for 2015 data based on the global human settlement layer residential population. We estimated the annual premature mortality burden preventable if the WHO recommended values (ie, 10 µg/m<sup>3</sup> for PM<sub>2.5</sub> and 40 µg/m<sup>3</sup> for NO<sub>2</sub>) were achieved and if air pollution concentrations were reduced to the lowest values measured in 2015 in European cities (ie, 3·7 µg/m<sup>3</sup> for PM<sub>2.5</sub> and 3·5 µg/m<sup>3</sup> for NO<sub>2</sub>). We clustered and ranked the cities on the basis of population and age-standardised mortality burden associated with air pollution exposure. In addition, we did several uncertainty and sensitivity analyses to test the robustness of our estimates.

**Findings** Compliance with WHO air pollution guidelines could prevent 51213 (95% CI 34036–68682) deaths per year for PM<sub>2.5</sub> exposure and 900 (0–2476) deaths per year for NO<sub>2</sub> exposure. The reduction of air pollution to the lowest measured concentrations could prevent 124729 (83332–166535) deaths per year for PM<sub>2.5</sub> exposure and 79435 (0–215165) deaths per year for NO<sub>2</sub> exposure. A great variability in the preventable mortality burden was observed by city, ranging from 0 to 202 deaths per 100000 population for PM<sub>2.5</sub> and from 0 to 73 deaths for NO<sub>2</sub> per 100000 population when the lowest measured concentrations were considered. The highest PM<sub>2.5</sub> mortality burden was estimated for cities in the Po Valley (northern Italy), Poland, and Czech Republic. The highest NO<sub>2</sub> mortality burden was estimated for large cities and capital cities in western and southern Europe. Sensitivity analyses showed that the results were particularly sensitive to the choice of the exposure response function, but less so to the choice of baseline mortality values and exposure assessment method.

**Interpretation** A considerable proportion of premature deaths in European cities could be avoided annually by lowering air pollution concentrations, particularly below WHO guidelines. The mortality burden varied considerably between European cities, indicating where policy actions are more urgently needed to reduce air pollution and achieve sustainable, liveable, and healthy communities. Current guidelines should be revised and air pollution concentrations should be reduced further to achieve greater protection of health in cities.

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## Introduction

Ambient air pollution is a major environmental cause of morbidity and mortality worldwide. Long-term exposure to ambient particulate matter (PM) with diameter less than or equal to 2·5 µm (PM<sub>2.5</sub>) was estimated to cause between 4 and 9 million premature deaths in 2015 globally, ranking PM<sub>2.5</sub> as the fifth greatest risk factor for global mortality in the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2015.<sup>1,2</sup>

In Europe, levels of air pollution are decreasing below the EU and WHO air quality guidelines.<sup>3</sup> The EU directive sets the annual mean limits of ambient pollution at

25 µg/m<sup>3</sup> for PM<sub>2.5</sub> and 40 µg/m<sup>3</sup> for NO<sub>2</sub>, whereas the WHO recommendations are set at 10 µg/m<sup>3</sup> for PM<sub>2.5</sub> and 40 µg/m<sup>3</sup> for NO<sub>2</sub>.<sup>3,4</sup> Nevertheless, studies have reported associations between air pollution and mortality at concentrations below these guidelines, with no evidence of a safe exposure threshold.<sup>5–8</sup> Reductions in air pollution below the values set by both guidelines are expected to offer a greater protection of population health, particularly for NO<sub>2</sub>, for which the WHO guideline and EU limit have been shown to be inadequate for protecting health in previous studies.<sup>7–9</sup> Accordingly, it was estimated that, in 2016, more than 400000 deaths (equating to

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### Research in context

#### Evidence before this study

We searched the PubMed and Google Scholar databases, without language or publication date restrictions, for estimates of the effects of air pollution exposure on health. Our search terms were: "air pollution" OR "PM<sub>2.5</sub>" OR "NO<sub>2</sub>" or "particulate matter" OR "nitrogen dioxide" AND "mortality" OR "premature mortality" OR "health impact" OR "risk" AND "city" OR "cities" OR "Europe". We included only health impact assessment and burden of disease studies specifically on air pollution up to the year 2019 and for the European region. We excluded any epidemiological studies from the search (ie, cohort studies, case-control studies, and cross-sectional studies). Previous studies, such as the Global Burden of Disease, Injuries, and Risk Factors Study 2017, have assessed the adverse health effects associated with air pollution exposure at the global and country level. However, this level of analysis provided little indication for cities where actions are more urgently needed to reduce air pollution and its adverse health outcomes. City-level estimates are needed for more targeted policy actions as cities offer a good opportunity for policy change because of direct local accountability, better responsiveness than national governments, and faster actions than national governments. In addition, cities are generally hotspots for air pollution and disease due to high level of motorised traffic and local fuel combustion. However, the exact extent of the effects of air pollution on health at the city level are still largely unknown. Previously, a few studies estimated the health effects of air pollution exposure for several selected cities in Europe, such as Barcelona (Spain), Vienna (Austria), and Bradford (UK). Only one large city-level study estimated the health effects of PM<sub>2.5</sub> exposure in 250 major cities worldwide. Nevertheless, this study did not consider city-specific mortality rates and used cruder air pollution estimates at 10 km resolution scale.

#### Added value of this study

To our knowledge, this study is the first to estimate the premature mortality burden due to air pollution in nearly 1000 cities in Europe. The main strengths of the study include the use of a fine resolution scale of 250 m, city-specific mortality rates, the inclusion of uncertainty, and a considerable number of sensitivity analyses and the inclusion of a wide range of European cities, particularly in eastern Europe where research is scarce. Our results indicate that a considerable proportion of premature deaths in European cities could be avoided annually by decreasing air pollution concentrations, particularly below WHO guidelines. Notably, we show that the preventable mortality burden varies greatly by city, reaching up to 15% for PM<sub>2.5</sub> and 7% for NO<sub>2</sub> of annual premature mortality. In addition, our sensitivity analyses show that the results are particularly sensitive to the choice of the exposure response function, but less so to the choice of baseline mortality values and exposure assessment method.

#### Implications of all the available evidence

Our study estimated higher preventable mortality burdens for PM<sub>2.5</sub> and NO<sub>2</sub> compared with previous EU-wide and country assessments. Additionally, we highlight local differences in the preventable mortality burden that have not been accounted for by previous national-level estimates. Our findings have great implications for policy implementations in cities, as we provide local administrations with comprehensive local estimates of the effects of air pollution on health, allowing for more targeted actions to reduce air pollution concentrations. Further research at the city level is needed to estimate the effects of distinct adverse environmental and lifestyle exposures prevalent in cities (eg, air pollution, noise, shortage of green spaces, heat, and sedentary behaviour) in Europe and globally.

7% of annual mortality) in Europe were attributable to PM<sub>2.5</sub> exposure and more than 70 000 deaths (equating to 1% of annual mortality) were attributable to NO<sub>2</sub> exposure. Moreover, these mortality estimates were when concentrations of air pollution were below the recommendations given in the EU and WHO guidelines.<sup>3</sup>

Most of the estimates of the health effects of air pollution exposure are calculated on a global or country level.<sup>1-3</sup> However, this level of analysis provides little indication of where actions are more urgently needed to reduce the adverse health outcomes associated with air pollution. There is a need for local estimates that are more relevant for targeted policy action, and cities could represent a more appropriate unit of analysis. Cities are home to 72% of the European population<sup>10</sup> and offer a good opportunity for policy change because of direct local accountability, better responsiveness than national governments, and faster actions than national governments.<sup>11</sup> In addition, cities are often hotspots for air

pollution and air pollution-related disease.<sup>12</sup> In cities, motorised traffic is a major contributor to high outdoor levels of air pollution.<sup>12</sup> In Europe, the contribution of traffic to urban PM<sub>2.5</sub> concentrations is estimated at an average of 14% of total urban PM<sub>2.5</sub> concentrations, going up to 39% for particular cities, and to NO<sub>2</sub> concentrations of 47%, reaching up to 70% for particular cities.<sup>13,14</sup> In addition, local fuel combustion (eg, household heating, industrial combustion, and wood burning) also contributes to high PM<sub>2.5</sub> concentrations, with an average contribution to urban PM<sub>2.5</sub> concentrations of 13%, reaching up to 48% in several eastern European cities.<sup>14,15</sup>

We did a quantitative health impact assessment (HIA) to estimate the annual preventable premature mortality burden in 969 European cities and 47 greater cities in 31 European countries if WHO-recommended air pollution concentrations for PM<sub>2.5</sub> and NO<sub>2</sub> were achieved. In addition, because of the association between air pollution and mortality at levels below WHO air quality

guidelines, we evaluated the annual premature mortality burden preventable if feasibly lower levels of air pollution were attained. Our goal was to provide local mortality estimates for more targeted and health preserving urban and transport planning policies to promote sustainable, liveable, and healthy communities in European cities.

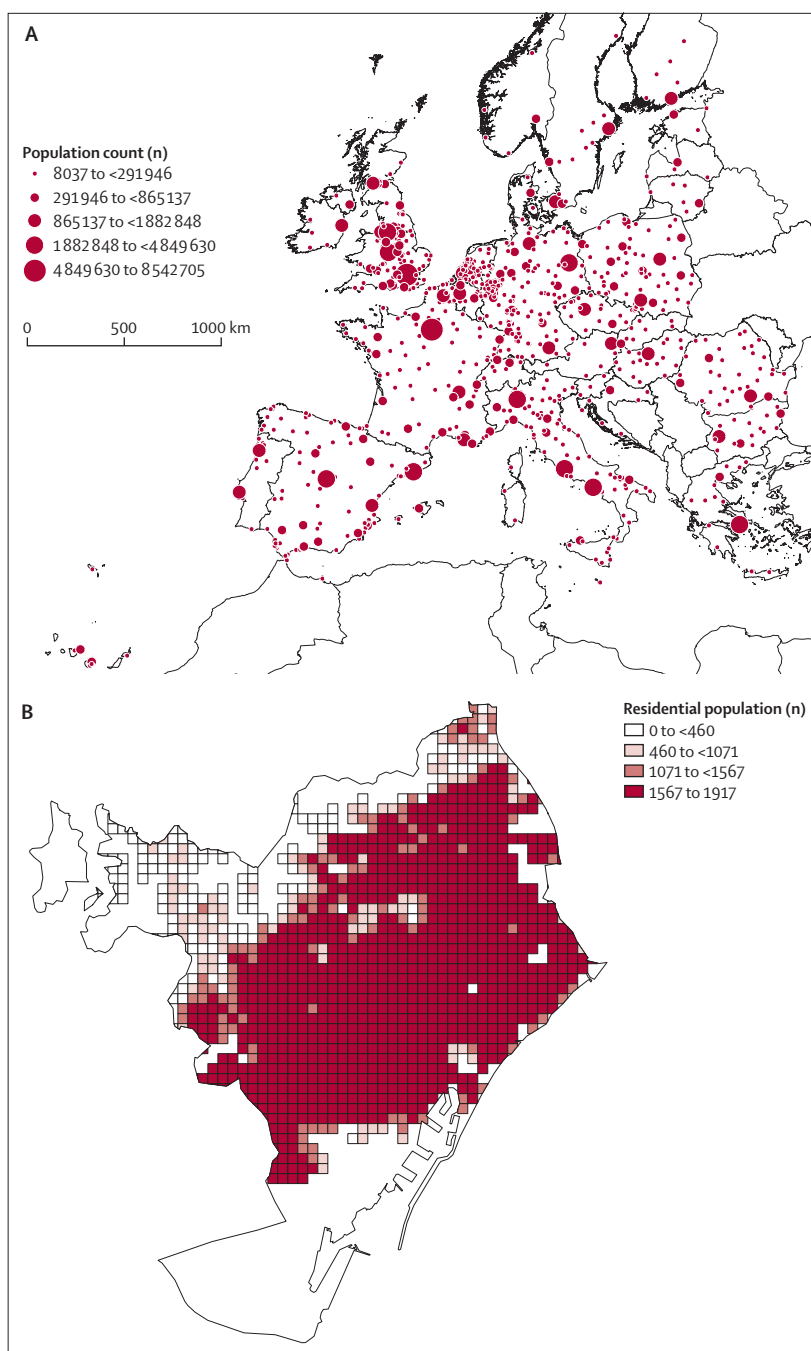
## Methods

### City definition

We retrieved the European cities for the HIA from the Urban Audit 2018 dataset (appendix p 2).<sup>16</sup> This dataset contained 980 cities and 49 greater cities in 31 European countries. The 49 greater cities covered 160 cities either by representing a city of larger area than the defined city or by constituting a combination of several cities. We excluded Saint Denis (Réunion) and Fort-de-France (Martinique) because of their location out of the European study area. Nine cities and two greater cities located in Madeira (Portugal), the Azores (Portugal), and the Canary Islands (Spain) were excluded because no air pollution estimates were available. The analysis was done for the remaining 969 cities and 47 greater cities (figure 1A).

### Quantitative HIA

We did a quantitative HIA at 250 m by 250 m grid cell level for 2015, based on the global human settlement layer (GHSL) residential population (figure 1B, appendix pp 2–4).<sup>17</sup> The analysis estimated the effect of air pollution exposure ( $PM_{2.5}$  and  $NO_2$ ) on natural-cause mortality for adult residents who were aged 20 years or older from the 969 cities and 47 greater cities. We followed the methods used for the Urban and Transport Planning Health Impact Assessment, which are based on the comparative risk assessment approach.<sup>18–21</sup> We retrieved exposure response functions (ERFs) from several studies quantifying the strength of association between air pollution exposure and mortality (appendix p 10). We set as counterfactual scenarios the WHO recommended values (ie,  $10 \mu\text{g}/\text{m}^3$  for  $PM_{2.5}$  and  $40 \mu\text{g}/\text{m}^3$  for  $NO_2$ ) and the lowest measured values among the European cities in 2015 (ie,  $3.7 \mu\text{g}/\text{m}^3$  for  $PM_{2.5}$  and  $3.5 \mu\text{g}/\text{m}^3$  for  $NO_2$ ).<sup>4,22</sup> The steps were as follows: (1) we estimated the baseline levels of air pollution exposure for 2015; (2) we determined the difference in level exposure between the 2015 levels and counterfactual levels; (3) we used the ERFs to compute the relative risk associated to the exposure difference and; (4) we calculated the population attributable fraction for each exposure difference. We obtained point estimates and CIs in our final estimations by propagating the uncertainties in the ERFs using Monte Carlo simulations (appendix pp 8–9). We added up the results by city and greater city and calculated the preventable age-standardised mortality per 100 000 population on the basis of the European standard population<sup>23</sup> and the percentage of annual preventable premature deaths for



**Figure 1:** Location and population size of the 969 cities and 47 greater cities defined in the Urban Audit 2018 and included in the health impact assessment analysis (A). An example of the Global Human Settlement Layer residential population grid is shown for Barcelona (Spain; B)

$PM_{2.5}$  and  $NO_2$ . To complement the premature mortality estimates, we calculated the years of life lost due to the premature deaths (appendix p 9). Given that the best available meta-analyses are based on single-pollutant models and because  $PM_{2.5}$  and  $NO_2$  are generally spatially correlated, the deaths associated with  $PM_{2.5}$  and  $NO_2$  exposures were not added up but instead were

See Online for appendix

City count (n)	City examples	Median air pollution ( $\mu\text{g}/\text{m}^3$ )	Preventable age-standardised mortality per 100 000 population: WHO scenario (95% CI)	Preventable age-standardised mortality per 100 000 population: lowest concentrations scenario (95% CI)	% preventable annual mortality: WHO scenario (95% CI)	% preventable annual mortality: lowest concentrations scenario (95% CI)	YLL per 100 000 population: WHO scenario (95% CI)	YLL per 100 000 population: lowest concentrations scenario (95% CI)	
<b>PM<sub>2.5</sub> clusters</b>									
1	38	Milan (IT), Warsaw (PL), Turin (IT), Ostrava (CZ), Kraków (PL)	23.2	99 (70–135)	144 (102–194)	9% (6–11)	12% (8–16)	1353 (952–1831)	1961 (1388–2636)
2	106	Budapest (HU), Bucharest (RO), Athens (GR), Sofia (BG), Ljubljana (SI)	17.1	64 (45–87)	116 (82–158)	5% (3–7)	9% (6–12)	776 (542–1056)	1405 (988–1900)
3	225	Vienna (AT), Brussels (BE), Prague (CZ), Berlin (DE), Barcelona (ES)	13.9	30 (21–42)	76 (53–103)	3% (2–4)	7% (5–9)	405 (282–553)	1012 (709–1374)
4	309	Hamburg (DE), Munich (DE), Madrid (ES), Copenhagen (DK), Lisbon (PT)	12.6	17 (11–23)	57 (40–77)	2% (1–2)	6% (4–8)	220 (153–301)	760 (532–1034)
5	180	Helsinki (FI), Dublin (IE), Stockholm (SE), London (UK), Reykjavik (IS)	9.2	1 (1–1)	35 (24–47)	0%	3% (2–5)	10 (7–14)	448 (312–612)
<b>NO<sub>2</sub> clusters</b>									
1	6	Madrid (ES), Antwerp (BE), Paris (FR), Milan (IT), Barcelona (ES)	39.4	4 (0–10)	58 (0–164)	0.4% (0–1)	7% (0–18)	49 (0–143)	798 (0–2276)
2	32	Brussels (BE), Cologne (DE), Rotterdam (NL), Warsaw (PL), Athens (GR)	34.5	1 (0–3)	60 (0–172)	0.1% (0–0.3)	6% (0–15)	14 (0–40)	806 (0–2309)
3	344	Prague (CZ), Berlin (DE), London (UK), Budapest (HU), Bucharest (RO)	25.7	0	45 (0–131)	0%	4% (0–11)	1 (0–3)	598 (0–1728)
4	476	Helsinki (FI), Dublin (IE), Stockholm (SE), Vilnius (LT), Reykjavik (IC)	19.0	0	29 (0–85)	0%	3% (0–8)	0	381 (0–1107)

AT=Austria. BE=Belgium. BG=Bulgaria. CZ=Czech Republic. DE=Germany. DK=Denmark. ES=Spain. FI=Finland. FR=France. GR=Greece. HU=Hungary. IE=Ireland. IS=Iceland. IT=Italy. LT=Lithuania. NL=Netherlands. PL=Poland. PT=Portugal. RO=Romania. SE=Sweden. SI=Slovenia. YLL=years of life lost.

**Table 1: City clusters for PM<sub>2.5</sub> and NO<sub>2</sub>**

considered independently.<sup>24,25</sup> The analysis was done in R-3.5.1, Python (version 3.7), and PostGIS (version 2.4).

**Natural-cause mortality**

City-specific all-cause mortality counts for 2015 were available through Eurostat.<sup>26</sup> City-specific mortality, rather than country-specific mortality, was chosen because of the difference and considerable variability (ie, with a median variance of  $\pm 22\%$  and an IQR of 9–32%) in the city-specific mortality (appendix p 6). Overall, 127 cities and 15 greater cities had missing mortality counts. In these instances, all-cause mortality counts were estimated with the corresponding Nomenclature of Territorial Units for Statistics (NUTS) 3 (n=131), NUTS2 (n=1), or country-level (n=10) all-cause age-specific mortality rates (appendix p 4).<sup>27,28</sup> To calculate the number of natural-cause deaths by age group for each city and greater city we retrieved NUTS3-level mortality

counts by age group, NUTS2, and country-level mortality counts by age and cause of death.<sup>27,28</sup> We calculated the external deaths fractions (defined by the International Classification of Diseases 10 mortality codes V01–Y89) by age group and estimated the proportion of deaths by natural causes by age group at the NUTS3-level. These proportions were applied to the corresponding city-level total all-cause mortality counts (appendix p 4).

**Baseline levels of air pollution exposure**

We used three air pollution models to estimate baseline annual mean PM<sub>2.5</sub> and NO<sub>2</sub> concentrations at 250 m grid cell level for the year 2015. For 802 cities and 46 greater cities, annual mean PM<sub>2.5</sub> and NO<sub>2</sub> estimates were retrieved from land use regression (LUR) models developed on a 100 m by 100 m grid cell scale for 2010 as part of the Effects of Low-Level Air Pollution: a Study in Europe (ELAPSE) project (appendix pp 11–16).<sup>29</sup> For 167 cities and one greater

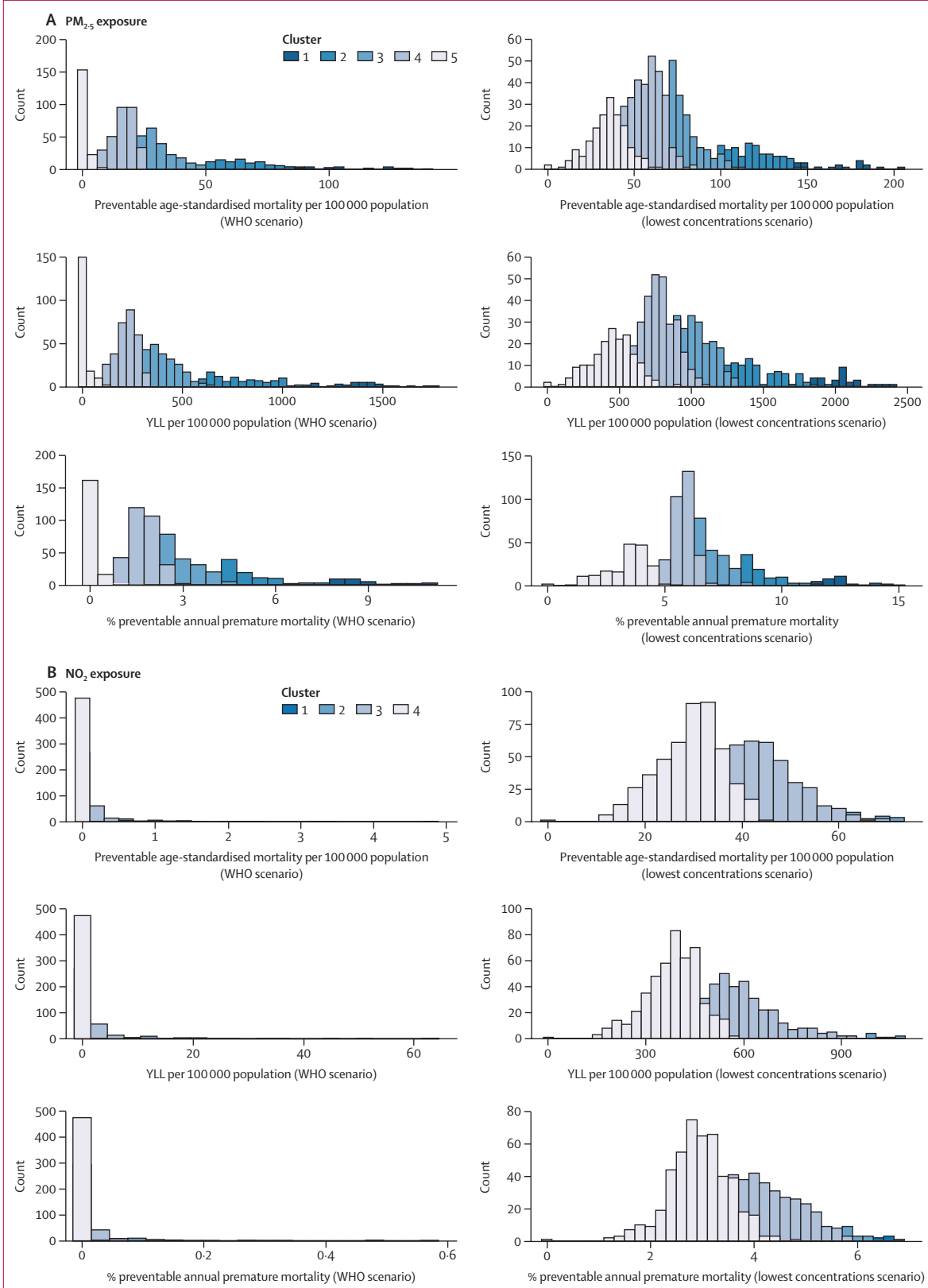


Figure 2: Histograms showing the variability in the estimated preventable mortality burden associated with PM<sub>2.5</sub> (A) and NO<sub>2</sub> (B) exposures by city and greater city. The mortality parameters are shown for the WHO and the lowest levels air pollution reduction scenarios  
YLL=years of life lost.

	PM <sub>2.5</sub> population weighted mean (µg/m <sup>3</sup> )	PM <sub>2.5</sub> range (min–max; µg/m <sup>3</sup> )	Preventable number of deaths: WHO scenario (95% CI)	Preventable number of deaths: lowest concentrations scenario (95% CI)	Preventable age-standardised mortality per 100 000 population: WHO scenario (95% CI)	Preventable age-standardised mortality per 100 000 population: lowest concentrations scenario (95% CI)
(1) Brescia (IT)	27.5	21.9–30.4	232 (156–308)	309 (209–407)	127 (90–172)	170 (121–227)
(2) Bergamo (IT)	26.1	20.1–28.6	137 (92–182)	186 (126–246)	133 (94–179)	181 (128–242)
(3) Karviná (CZ)	22.7	22.2–23.5	52 (35–70)	76 (51–101)	138 (97–187)	202 (143–272)
(4) Vicenza (IT)	26.5	22.2–27.9	124 (83–164)	167 (113–221)	115 (81–155)	156 (111–209)
(5) Górnośląsko-Zagłębiowska Metropolia (PL)	22.4	19.3–23.4	1739 (1163–2320)	2564 (1728–3399)	122 (86–166)	181 (128–243)
(6) Ostrava (CZ)	23.0	21.1–23.8	270 (181–360)	392 (264–519)	133 (93–180)	193 (136–259)
(7) Jastrzębie-Zdrój (PL)	23.3	21.7–23.6	71 (48–95)	102 (69–136)	127 (89–172)	183 (129–246)
(8) Saronno (IT)	27.1	25.8–28.6	46 (31–60)	61 (41–80)	105 (74–141)	140 (100–188)
(9) Rybnik (PL)	23.1	22.3–23.4	113 (76–151)	164 (111–217)	125 (88–169)	181 (128–244)
(10) Havírov (CZ)	22.6	22.3–23.2	67 (44–89)	98 (66–129)	126 (88–170)	185 (131–249)
(1) Reykjavík (IS)	3.3	2.5–3.6	0	0	0	0
(2) Tromsø (NO)	3.6	2.3–4.8	0	0	0	0
(3) Umeå (SE)	5.0	2.0–6.5	0	10 (6–13)	0	9 (6–12)
(4) Oulu (FI)	5.8	3.1–7.2	0	16 (11–22)	0	11 (8–15)
(5) Jyväskylä (FI)	5.9	3.2–7.2	0	13 (8–18)	0	11 (7–15)
(6) Uppsala (SE)	6.0	3.0–7.1	0	24 (16–32)	0	15 (10–20)
(7) Trondheim (NO)	6.0	3.6–8.0	0	20 (13–27)	0	15 (10–20)
(8) Lahti (FI)	5.8	3.8–7.0	0	16 (11–22)	0	14 (10–19)
(9) Örebro (SE)	5.9	3.4–7.1	0	20 (13–28)	0	15 (11–21)
(10) Tampere (FI)	6.2	3.6–7.7	0	29 (19–40)	0	15 (10–20)

CZ=Czech Republic. FI=Finland. IS=Iceland. IT=Italy. NO=Norway. PL=Poland. SE=Sweden.

**Table 2: Preventable number of deaths and preventable age-standardised annual mortality in the ten European cities with the highest (top) and lowest (bottom) PM<sub>2.5</sub> mortality burden**

city for which the ELAPSE model was unavailable, the annual mean PM<sub>2.5</sub> values were extracted from the Ensemble model developed on a 10 km by 10 km scale for the year 2015.<sup>30</sup> Annual mean NO<sub>2</sub> estimates were retrieved from the global LUR model for NO<sub>2</sub> developed on a 100 m by 100 m grid cell scale for the year 2011 (appendix pp 17–20).<sup>31</sup> The modelled values were contrasted with measured time series air pollution data for the year 2015 from the European air quality database (AirBase)<sup>22</sup> and temporal adjustments were done when appropriate (appendix pp 11–20). Model comparisons showed high correlations between the three models ( $r=0.94$  for PM<sub>2.5</sub> and  $r=0.81$  for NO<sub>2</sub>); however, the ELAPSE estimates were higher overall by 4–5% (appendix p 20).

### Uncertainty analyses

We did uncertainty analyses for 15 selected cities to evaluate the effect on the CIs of our estimates of the uncertainty distributions of the parameters included in the quantitative HIA analysis (ie, city-specific mortality, city population age structures, air pollution models, and ERFs [appendix pp 28–35]). We then constructed uncertainty distributions for these variables and obtained

point estimates and CIs in our final estimations using Monte Carlo simulations (appendix pp 28–29). We did the first round of Monte Carlo sampling while considering the uncertainty in all four variables. Afterwards, we did a new round of Monte Carlo sampling considering the uncertainty in only one of the four variables simultaneously.

### Sensitivity analyses

We did sensitivity analyses to evaluate the effect of changes in input model variables on the magnitude of our final mortality estimations (appendix pp 36–64). We tested the effects of using distinct ERFs (appendix p 36),<sup>32–34</sup> distinct air pollution estimates, country-level mortality rates (instead of city-level mortality rates), average city-level population weighted air pollution concentrations (instead of 250 m grid cell values), and finally, European Environment Agency (EEA) HIA model assumptions (appendix pp 36–64).

### City comparisons

For city comparisons, we first did a cluster analysis to identify clusters of cities with similar preventable

	% preventable annual mortality: WHO scenario (95% CI)	% preventable annual mortality: lowest concentrations scenario (95% CI)	YLL per 100 000 population: WHO scenario (95% CI)	YLL per 100 000 population: lowest concentrations scenario (95% CI)
(1) Brescia (IT)	11% (7–15)	15% (10–20)	1730 (1222–2332)	2304 (1638–3083)
(2) Bergamo (IT)	10% (7–14)	14% (9–18)	1740 (1228–2348)	2370 (1683–3176)
(3) Karviná (CZ)	8% (5–11)	12% (8–16)	1530 (1075–2073)	2239 (1584–3012)
(4) Vicenza (IT)	11% (7–14)	14% (10–19)	1572 (1110–2121)	2126 (1510–2848)
(5) Górnośląsko-Zagłębiowska Metropolia (PL)	8% (5–11)	12% (8–16)	1630 (1145–2209)	2404 (1700–3235)
(6) Ostrava (CZ)	8% (6–11)	12% (8–16)	1466 (1031–1986)	2129 (1507–2863)
(7) Jastrzębie-Zdrój (PL)	9% (6–11)	12% (8–16)	1446 (1017–1958)	2085 (1476–2804)
(8) Saronno (IT)	11% (7–14)	15% (10–19)	1497 (1057–2019)	2006 (1426–2685)
(9) Rybnik (PL)	8% (6–11)	12% (8–16)	1424 (1001–1928)	2063 (1460–2774)
(10) Havírov (CZ)	8% (5–11)	12% (8–16)	1394 (979–1889)	2048 (1449–2755)
(1) Reykjavík (IS)	0%	0%	0	0
(2) Tromsø (NO)	0%	0%	0	1 (1–1)
(3) Umeå (SE)	0%	1% (0–1)	0	112 (78–154)
(4) Oulu (FI)	0%	1% (1–2)	0	140 (97–192)
(5) Jyväskylä (FI)	0%	1% (1–2)	0	150 (104–206)
(6) Uppsala (SE)	0%	2% (1–2)	0	165 (115–227)
(7) Trondheim (NO)	0%	2% (1–2)	0	162 (112–222)
(8) Lahti (FI)	0%	1% (1–2)	0	202 (141–277)
(9) Örebro (SE)	0%	1% (1–2)	0	203 (141–278)
(10) Tampere (FI)	0%	2% (1–2)	0	198 (138–272)

CZ=Czech Republic. FI=Finland. IS=Iceland. IT=Italy. NO=Norway. PL=Poland. SE=Sweden. YLL=years of life lost.

**Table 3: Percentage of preventable annual mortality and YLL per 100 000 population in the ten European cities with the highest (top) and lowest (bottom) PM<sub>2.5</sub> mortality burden**

mortality patterns (appendix pp 65–67). Cluster analysis was chosen over a simple city ranking because of the sensitivity of the cities' position in the ranking to the air pollution model data, air pollution reduction scenario, and the mortality variables chosen to score the cities (ie, different rankings are obtained depending on the variable chosen to score the cities). To avoid the repetition of cities that overlapped with the greater cities, we kept the greater cities and excluded the smaller size cities that corresponded to them. Overall, the clustering was done for 811 cities and 47 greater cities. We used the K-means clustering algorithm<sup>35,36</sup> and established the optimal number of clusters at five clusters for PM<sub>2.5</sub> and at four clusters for NO<sub>2</sub> (appendix p 66). The clusters were ordered from highest to lowest mortality burden (table 1). To compare the cities within each cluster, we ranked the cities according to a mortality burden score, which was calculated through a principal component analysis on the mortality variables associated with air pollution exposure (appendix pp 72, 106–57).

#### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the

study and had final responsibility for the decision to submit for publication.

#### Results

City population counts ranged from 8307 (Suwalki, Poland) to 8542705 (London, UK), with a median population size of 127 002 inhabitants (appendix pp 75–105). In total, 168180047 adults aged 20 years or older resided in the 969 European cities and 47 greater cities, representing 32% of the population in the 31 European countries. Overall, at the 250 m grid cell level, PM<sub>2.5</sub> concentrations ranged from 0.7 µg/m<sup>3</sup> to 30.8 µg/m<sup>3</sup>, with a median value of 12.3 µg/m<sup>3</sup>. NO<sub>2</sub> concentrations, at the 250 m grid cell level, varied between 0.7 µg/m<sup>3</sup> and 84.5 µg/m<sup>3</sup>, with a median value of 20.7 µg/m<sup>3</sup> (appendix pp 106–57). The correlation between both air pollutants was  $r=0.50$ .

Across all cities, 84% of the population were exposed to PM<sub>2.5</sub> concentrations above the WHO guideline and 9% of the population were exposed to NO<sub>2</sub> concentrations above the WHO guideline. Compliance with the WHO air pollution guideline could prevent 51213 (95% CI 34036–68682) annual premature deaths (ie, 2% [1–3%] of annual mortality) for PM<sub>2.5</sub> exposure and 900 (0–2476) annual premature deaths (ie, 0.04% [0–0.1] of annual mortality) for NO<sub>2</sub> exposure. The reduction of air pollution to the lowest measured concentrations could

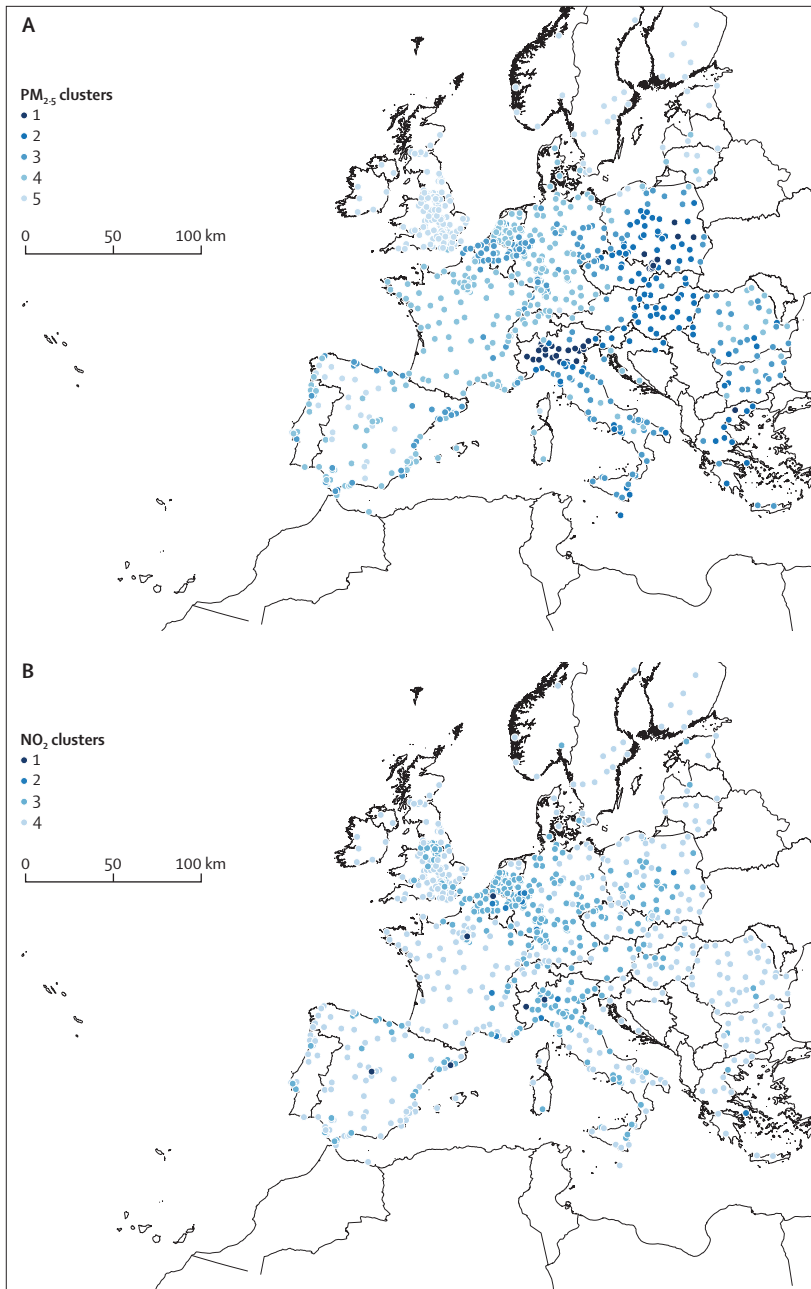


Figure 3: Cities' categorisation by clusters for  $PM_{2.5}$  (A) and  $NO_2$  (B) exposures

prevent 124729 (83332–166535) annual premature deaths (ie, 6% [4–7] of annual mortality) for  $PM_{2.5}$  exposure and 79435 (0–215165) annual premature deaths (ie, 4% [0–10] of annual mortality) for  $NO_2$  exposure. The estimated preventable mortality burden showed highest positive correlation with  $PM_{2.5}$  and  $NO_2$  concentrations (ie,  $r \approx 0.9$  [the  $r$  value is approximate because it is based on the correlations of various outcome measures, such as mortality rates and percentage of mortality and years of life lost for the WHO scenario and lowest concentrations

scenarios, with air pollution concentrations and baseline mortality]), and a moderate positive correlation with city-level mortality (ie,  $r \approx 0.4$ ).

A great variability in the preventable mortality burden was observed by city. At the city level, compliance with WHO air pollution guidelines could prevent between 0 and 138 deaths per 100 000 population (ie, 0–11% of annual mortality), with an average of 26 (95% CI 18–36) deaths per 100 000 population for  $PM_{2.5}$  exposure, and between 0 and 5 deaths per 100 000 population (ie, 0–1% of annual mortality), with an average of 0.1 (0–0.3) deaths per 100 000 population for  $NO_2$  exposure. The reduction of air pollution to the lowest measured concentrations could prevent between 0 and 202 deaths per 100 000 population (ie, 0 to 15% of annual mortality), with an average of 68 (48–93) deaths per 100 000 population for  $PM_{2.5}$  exposure, and between 0 and 73 deaths per 100 000 population (ie, 0 to 7% of annual mortality), with an average of 37 (0–107) deaths per 100 000 population for  $NO_2$  exposure (figure 2). The correlation between the estimated preventable mortality burden associated with  $PM_{2.5}$  exposure and  $NO_2$  exposure by city and greater city varied between  $r=0.36$  and  $r=0.56$ , depending on the outcome measure (appendix p 27).

For  $PM_{2.5}$ , the uncertainty analysis indicated that the primary source of uncertainty was the variability in the age structure of the city populations, followed by the city-specific mortality, the ERF, and the  $PM_{2.5}$  model data (appendix pp 29–31). For  $NO_2$ , the uncertainty analysis indicated that the main source of uncertainty was the uncertainty in the ERF, followed by the age structure of the city populations, city-specific mortality rates, and ultimately, the  $NO_2$  model data (appendix pp 32–35). Notably, for cities with low  $PM_{2.5}$  and  $NO_2$  concentrations, the analysis showed that not accounting for the uncertainty in the air pollution model estimates can lead to underestimations in the final outcome (appendix pp 30–33).

The sensitivity analyses indicated greatest changes in our final estimations upon changes in the ERFs. For  $PM_{2.5}$ , the use of the European Study of Cohorts for Air Pollution Effects ERF and the global exposure mortality model led to almost a doubling in the estimated preventable mortality burden (appendix pp 36–43). The use of ensemble  $PM_{2.5}$  or  $NO_2$  global LUR models resulted in lower estimated preventable mortality burdens (appendix pp 44–47). The use of single 2015 and 2018 AirBase measurements or city-level averages led to greatest reductions in the estimated preventable mortality burden for  $NO_2$  in the WHO scenario (appendix pp 48–53, 58–61). The adoption of EEA HIA model assumptions led to an increase in the estimated preventable mortality burden for  $PM_{2.5}$  and to a decrease for  $NO_2$  (appendix pp 62–64). Finally, the use of country-level mortality rates led to slightly higher estimated preventable mortality burdens for  $PM_{2.5}$  and  $NO_2$  (appendix pp 54–57). In addition, the use of country-level



	NO <sub>2</sub> population weighted mean (µg/m <sup>3</sup> )	NO <sub>2</sub> range (min-max; µg/m <sup>3</sup> )	Preventable number of deaths: WHO scenario (95% CI)	Preventable number of deaths: lowest concentrations scenario (95% CI)	Preventable age-standardised mortality per 100 000 population: WHO scenario (95% CI)	Preventable age-standardised mortality per 100 000 population: lowest concentrations scenario (95% CI)
(1) Madrid (ES)	39.2	12.3–82.4	206 (0–565)	2380 (0–6373)	5 (0–14)	57 (0–161)
(2) Antwerp (BE)	39.7	19.7–66.2	22 (0–61)	307 (0–822)	5 (0–14)	66 (0–188)
(3) Turin (IT)	40.8	23.0–53.0	34 (0–94)	673 (0–1803)	3 (0–10)	67 (0–190)
(4) Paris (FR)	39.7	15.3–78.7	185 (0–508)	2575 (0–6894)	3 (0–10)	46 (0–131)
(5) Milan (IT)	38.0	19.8–69.5	103 (0–285)	2271 (0–6094)	2 (0–7)	54 (0–155)
(6) Barcelona (ES)	38.9	15.1–63.9	82 (0–226)	1883 (0–5048)	2 (0–7)	56 (0–160)
(7) Mollet del Vallès (ES)	40.6	29.3–54.4	1 (0–3)	24 (0–65)	2 (0–6)	49 (0–140)
(8) Brussels (BE)	37.3	16.8–66.6	18 (0–49)	530 (0–1424)	2 (0–6)	64 (0–183)
(9) Herne (DE)	35.2	23.0–68.7	2 (0–6)	114 (0–307)	1 (0–4)	72 (0–206)
(10) Argenteuil–Bezons (FR)	37.6	26.7–68.6	1 (0–4)	46 (0–123)	2 (0–5)	53 (0–151)
(1) Tromsø (NO)	3.4	0.7–8.4	0	0	0	0
(2) Umeå (SE)	9.5	0.9–23.2	0	13 (0–36)	0	12 (0–34)
(3) Oulu (FI)	11.8	1.4–32.0	0	18 (0–50)	0	12 (0–35)
(4) Kristiansand (NO)	11.8	3.8–26.5	0	8 (0–23)	0	13 (0–39)
(5) Pula (HR)	10.1	3.8–16.9	0	8 (0–21)	0	16 (0–47)
(6) Linköping (SE)	11.2	1.8–22.9	0	20 (0–55)	0	14 (0–41)
(7) Galway (IE)	11.3	2.9–18.6	0	8 (0–21)	0	15 (0–45)
(8) Jönköping (SE)	11.4	2.0–25.0	0	19 (0–53)	0	14 (0–41)
(9) Alytus (LT)	10.7	5.4–13.6	0	10 (0–27)	0	15 (0–45)
(10) Trondheim (NO)	12.4	3.3–23.3	0	22 (0–60)	0	15 (0–45)

BE=Belgium. DE=Germany. ES=Spain. FI=Finland. FR=France. HR=Croatia. IE=Ireland. IT=Italy. LT=Lithuania. NO=Norway. SE=Sweden.

**Table 4:** Preventable number of deaths and preventable age-standardised annual mortality in the ten European cities with the highest (top) and lowest (bottom) NO<sub>2</sub> mortality burden

mortality rates led to changes in the ranking position for the studied cities, particularly those with more central positions (appendix p 72).

For PM<sub>2.5</sub>, cluster 1 contained 38 cities with the highest mortality burden, including cities in the Po Valley (northern Italy), southern Poland, and eastern Czech Republic (table 1, figures 3A, appendix pp 106–31). Among these cities, the top ten cities with the highest burden were: (1) Brescia (Italy), (2) Bergamo (Italy), (3) Karviná (Czech Republic), (4) Vicenza (Italy), (5) Górnośląsko-Zagłębiowska Metropolia (Poland), (6) Ostrava (Czech Republic), (7) Jastrzębie-Zdrój (Poland), (8) Saronno (Italy), (9) Rybnik (Poland), and (10) Havírov (Czech Republic; tables 2, 3). For NO<sub>2</sub>, cluster 1 included six cities with the highest mortality burden due to exceedances in the WHO guideline and cluster 2 included 32 cities with the highest mortality burden due to exposures below the WHO recommendation. These clusters generally included large cities and capital cities in western and southern Europe, as well as smaller cities located in their vicinity (figure 3B, table 1, appendix pp 132–57). Among these cities, the top ten cities with the highest burden were: (1) Madrid (Spain), (2) Antwerp (Belgium), (3) Turin (Italy), (4) Paris (France), (5) Milan (Italy), (6) Barcelona (Spain), (7) Mollet del Vallès (Spain), (8) Brussels (Belgium),

(9) Herne (Germany), and (10) Argenteuil–Bezons (France; tables 4, 5).

Generally, the cities with the lowest mortality burden due to air pollution were located in northern Europe. The cities with the lowest PM<sub>2.5</sub> mortality burden (ie, those grouped in cluster 5) were: (1) Reykjavík (Iceland), (2) Tromsø (Norway), (3) Umeå (Sweden), (4) Oulu (Finland), (5) Jyväskylä (Finland), (6) Uppsala (Sweden), (7) Trondheim (Norway), (8) Lahti (Finland), (9) Örebro (Sweden), and (10) Tampere (Finland; figure 3A, tables 2, 3, appendix pp 106–31). Finally, the cities with the lowest NO<sub>2</sub> mortality burden (ie, cluster 4) were: (1) Tromsø (Norway), (2) Umeå (Sweden), (3) Oulu (Finland), (4) Kristiansand (Norway), (5) Pula (Croatia), (6) Linköping (Sweden), (7) Galway (Ireland), (8) Jönköping (Sweden), (9) Alytus (Lithuania), and (10) Trondheim (Norway; figure 3B, tables 4, 5, appendix pp 132–57).

## Discussion

To our knowledge, this is the first study to estimate the premature mortality burden due to air pollution at a city level in Europe. Previously, the effects of air pollution exposure on health have been mainly evaluated on a global or country level.<sup>1–3</sup> Our results indicate that a considerable proportion of premature deaths in European cities could be avoided annually by lowering air pollution

	% preventable annual mortality: WHO scenario (95% CI)	% preventable annual mortality: lowest concentrations scenario (95% CI)	YLL per 100 000 population: WHO scenario (95% CI)	YLL per 100 000 population: lowest concentrations scenario (95% CI)
(1) Madrid (ES)	0.6% (0-1.5)	7% (0-17)	63 (0-185)	730 (0-2079)
(2) Antwerp (BE)	0.5% (0-1.3)	7% (0-18)	63 (0-184)	863 (0-2461)
(3) Turin (IT)	0.3% (0-1.0)	7% (0-18)	51 (0-150)	1010 (0-2879)
(4) Paris (FR)	0.5% (0-1.3)	7% (0-18)	46 (0-134)	639 (0-1821)
(5) Milan (IT)	0.3% (0-0.8)	6% (0-17)	35 (0-103)	770 (0-2200)
(6) Barcelona (ES)	0.3% (0-0.8)	6% (0-17)	34 (0-99)	776 (0-2215)
(7) Mollet del Vallès (ES)	0.3% (0-0.8)	7% (0-18)	27 (0-80)	670 (0-1909)
(8) Brussels (BE)	0.2% (0-0.6)	6% (0-17)	24 (0-70)	704 (0-2012)
(9) Herne (DE)	0.1% (0-0.3)	6% (0-16)	22 (0-65)	1082 (0-3098)
(10) Argenteuil – Bezons (FR)	0.2% (0-1.0)	6% (0-17)	20 (0-60)	680 (0-1944)
(1) Tromsø (NO)	0%	0%	0	1 (0-2)
(2) Umeå (SE)	0%	1% (0-3)	0	147 (0-429)
(3) Oulu (FI)	0%	2% (0-4)	0	151 (0-442)
(4) Kristiansand (NO)	0%	2% (0-4)	0	152 (0-445)
(5) Pula (HR)	0%	1% (0-4)	0	178 (0-520)
(6) Linköping (SE)	0%	1% (0-4)	0	178 (0-522)
(7) Galway (IE)	0%	1% (0-4)	0	170 (0-497)
(8) Jönköping (SE)	0%	2% (0-4)	0	190 (0-555)
(9) Alytus (LT)	0%	1% (0-4)	0	216 (0-633)
(10) Trondheim (NO)	0%	2% (0-5)	0	170 (0-498)

BE=Belgium. DE=Germany. ES=Spain. FI=Finland. FR=France. HR=Croatia. IE=Ireland. IT=Italy. LT=Lithuania. NO=Norway. SE=Sweden. YLL=years of life lost.

**Table 5: Percentage of preventable annual mortality and YLL per 100 000 population in the ten European cities with the highest (top) and lowest (bottom) NO<sub>2</sub> mortality burden**

levels, particularly below WHO guidelines. Notably, we show that the mortality burden varies considerably between European cities, reaching up to 15% for PM<sub>2.5</sub> and 7% for NO<sub>2</sub> of annual premature mortality in the cities with the highest pollution concentrations. In addition, we show that our results are mainly sensitive to the choice of the ERF, but less so to the choice of baseline mortality values and exposure assessment method.

Compared with previous studies, the estimated average preventable mortality for PM<sub>2.5</sub> in the cities included in our study was higher than the EU region. The EEA estimated an average 74 deaths per 100 000 population among the EU28 countries for the year 2017, equating to 7% of annual premature mortality.<sup>3</sup> Our sensitivity analyses with the EEA model's assumptions resulted in an average of 99 deaths per 100 000 population, equating to 8% of annual premature mortality, showing a higher PM<sub>2.5</sub> mortality burden in urban areas. In addition, the preventable mortality burden varied considerably by country and city within each country. We estimated the highest PM<sub>2.5</sub> mortality burden for cities in Italy, Czech Republic, Poland, Greece, Hungary, Slovakia, Slovenia, Croatia, Bulgaria, Romania, and Malta. We thus identified similar regions to the EEA as the ones bearing the highest burden (ie, primarily cities within eastern Europe).<sup>3</sup> However, we additionally

highlight local differences in the mortality burden that are not accounted for by national-level estimates. For instance, we estimated the highest mortality burden for cities in northern Italy, although country-level estimates did not place Italy among the countries with the highest mortality burden due to PM<sub>2.5</sub> exposure.<sup>3</sup>

Similarly, the GBD study also identified mainly eastern European countries as those bearing the highest mortality burden due to PM<sub>2.5</sub>.<sup>1</sup> Nevertheless, GBD country-level mortality estimates were overall lower than our results (eg, 45 vs 92 deaths per 100 000 population for Italy and 57 vs 114 deaths per 100 000 population for Poland),<sup>37</sup> probably because we accounted for all natural-cause deaths instead of six specific causes of mortality as done in GBD and used a higher resolution for the exposure assessment (ie, 250 m vs 10 km scale). Because of the absence of city-level cause-specific mortality data, we could not assess the effect of GBD model assumptions on our results. Nevertheless, Burnett and colleagues<sup>34</sup> showed that using the global exposure mortality mode, which accounts for all non-communicable causes of deaths, leads to a more than doubling in the health burden estimates compared with the integrated exposure response used by GBD. In addition, lower resolutions tend to underestimate exposure by averaging concentrations from high and low exposure areas, thus leading to

underestimations in mortality burden.<sup>38</sup> Accordingly, the large city-level study by Anenberg and colleagues,<sup>39</sup> which followed the GBD approach, using country-specific mortality data and cruder air pollution estimates (ie, at 10 km resolution) also estimated a smaller mortality burden range due to PM<sub>2.5</sub> (ie, 13–125 deaths vs 0–202 deaths per 100 000 population), even though they included cities with higher annual mean PM<sub>2.5</sub> concentrations than those reported in Europe.

As for NO<sub>2</sub>, the EEA estimated an average of 13 deaths per 100 000 population among the EU28 countries, corresponding to 1% of annual premature mortality.<sup>3</sup> In our sensitivity analyses with EEA model assumptions we estimated a higher preventable mortality burden for NO<sub>2</sub> in urban areas (ie, 26 deaths per 100 000 population, equating to 2% of annual premature mortality), possibly due to a higher resolution (ie, 250 m vs 1 km scale) and higher NO<sub>2</sub> concentrations in urban areas. Reductions below the EEA counterfactual scenario of 20 µg/m<sup>3</sup> resulted in an even larger preventable mortality burden of 37 deaths per 100 000 population. Given the evidence, there is no basis to assume that there is no risk of mortality below 20 µg/m<sup>3</sup>.<sup>7,8</sup> Thus, testing the effects of air pollution reductions to the lowest measured concentrations provides a more comprehensive overview of the mortality burden associated with NO<sub>2</sub> exposure. In addition, a fine exposure resolution is relevant for a pollutant with strong local source influences, such as NO<sub>2</sub>.<sup>25</sup> NO<sub>2</sub> has larger small-scale spatial contrast with higher concentrations near sources (eg, major roads) than PM<sub>2.5</sub>.<sup>25</sup> Thus, by using a fine resolution, we were able to account for the extent and local variability in the mortality burden that is not accounted for by lower resolutions.<sup>3</sup>

We estimated the highest preventable mortality burden for cities that had the highest air pollution concentrations, consistent with the highest positive correlation found between air pollution concentrations and the estimated preventable mortality burdens for PM<sub>2.5</sub> and NO<sub>2</sub>. For PM<sub>2.5</sub>, we estimated the highest mortality burden for cities in northern Italy, southern Poland, and eastern Czech Republic. Ambient PM<sub>2.5</sub> originates from diverse sources, including fossil fuel combustion and biomass burning.<sup>25</sup> In European cities, the main contributors to PM<sub>2.5</sub> are traffic (ie, on average by 14% and up to 39% of all contributors of PM<sub>2.5</sub>), domestic fuel burning (ie, on average by 13% and up to 48%), and industrial activities (ie, on average by 20% and up to 47%).<sup>14</sup> In addition, the average city contribution to PM<sub>2.5</sub> concentration is estimated at 26% of all potential spatial source contributors (eg, regional, national, and transboundary pollution sources), stressing the importance of not only local source contributions but also regional and national source contributions.<sup>14</sup> In northern Italy, the Po Valley is a highly urbanised area characterised by high emissions from traffic and industries and frequently stagnant meteorological conditions related to the valley, leading to

increased PM<sub>2.5</sub> concentrations in the region.<sup>40</sup> The southern Poland and eastern Czech Republic regions are characterised by coal mining industry, and domestic coal burning is frequent throughout the winter for heat production, contributing to high PM<sub>2.5</sub> concentrations.<sup>41</sup> The high mortality burden due to PM<sub>2.5</sub> for cities located in the Po Valley, southern Poland, and eastern Czech Republic is thus consistent with the higher degree of anthropogenic emissions and unfavourable climatic conditions in these areas.

For NO<sub>2</sub>, we estimated the highest mortality burden for large cities and capital cities in western and southern Europe. NO<sub>2</sub> is an important surrogate for traffic emissions.<sup>25</sup> The contribution of road transport to NO<sub>2</sub> concentrations in European cities has an average of 47% and goes up to 70% of total NO<sub>2</sub>.<sup>13</sup> NO<sub>2</sub> concentrations are highly dependent on city design, traffic density, and vehicle fleet (ie, the type of vehicles driven). Generally, densely populated cities with high traffic volumes tend to have high NO<sub>2</sub> concentrations.<sup>42</sup> Accordingly, the mortality burden due to NO<sub>2</sub> was the highest for the cities that were highly populated and capital cities, such as Paris, Madrid, Barcelona, Milan, Brussels, and Antwerp, as well as for smaller size cities located in their vicinity with potentially increased car use for commuting from smaller to bigger size cities.

In addition, although air pollution concentrations had the highest correlation with the estimated preventable mortality burden for PM<sub>2.5</sub> and NO<sub>2</sub>, the baseline mortality and age structure of the city populations should also be considered as relevant variables influencing the preventable mortality burden estimates. We found a modest positive correlation between the estimated preventable mortality burden and increasing baseline mortality rates. In addition, our uncertainty analyses showed that the main sources of uncertainty were the variability in underlying city-level age structures and mortality rates. Thus, changes in city age structures and baseline mortality are likely to have an effect on adverse health burden estimations.

The main strengths of our study include the use of a fine spatial scale of 250 m, the use of city-specific mortality rates, the inclusion of uncertainty, and a considerable number of sensitivity analyses and the inclusion of a large proportion of eastern European cities, for which there has been little research. HIA studies at the city level promote targeted evidence-based policies for healthy urban environments<sup>43</sup> and their advantages have been described elsewhere.<sup>18,19,21</sup> We used the best available and most recent data for all cities and we believe that our estimates provide a robust indication of the magnitude and variability of the adverse health effects associated with air pollution exposure among European cities.

Nevertheless, our study also has several limitations. Because of limitations in the availability of data, we could not assess air pollution exposure for a more recent year

than 2015. Our sensitivity analyses with 2018 Airbase data suggested a slight decrease from 2015 to 2018 in the mortality burden associated with changes in  $PM_{2.5}$  and  $NO_2$  exposure concentrations; thus, slight overestimation in our results is possible compared with more recent years. In addition, although we did uncertainty analyses for selected cities, we did not propagate all sources of error to our final point estimates and CIs for all cities. As a result, the uncertainty in our results is somewhat underestimated. Furthermore, we used three distinct air pollution models and used temporal adjustments to estimate air pollution concentrations. Although all three models were contrasted with the air pollution concentrations from 2015 and adjusted accordingly when appropriate, model comparisons indicated that ELAPSE estimates were overall 4–5% higher than the ensemble and global LUR model estimates. The ensemble model had a considerably lower spatial scale (ie, 10 km vs 250 m), which potentially led to the underestimation of  $PM_{2.5}$  concentrations,<sup>38</sup> whereas the global LUR model was constructed only using global predictors (eg, distance to major roads),<sup>31</sup> thus, not accounting for local predictors within the European region (eg, local traffic density and land use) that could better describe  $NO_2$  concentrations and spatial variability.<sup>42</sup> Accordingly, our sensitivity analyses showed a lower estimated preventable mortality burden for  $PM_{2.5}$  and  $NO_2$  with the ensemble and global LUR models than the ELAPSE models. Given these methodological issues, direct city-to-city comparisons should be done with caution. As shown in the sensitivity analyses, it is likely that the mortality burden due to air pollution exposure, although indicative of the extent, was underestimated for the cities for which the ensemble and global LUR models were used. For city comparisons, city clusters should be considered first. Variation within the proposed city ranking is plausible upon the use of more homogeneous air pollution data. However, we found robust agreement in the cities' classification by cluster upon the use of distinct air pollution models, indicating the higher reliability of cities' categorisation by clusters (appendix pp 68–69).

Moreover, we could not account for mortality and age structure variability within cities. Although population counts were available through the GHSL at 250 m resolution,<sup>17</sup> no such layer was available for death counts or age groups. Accordingly, our sensitivity analyses with city-level population weighted air pollution concentrations led to almost identical estimations as those using the 250 m grid cells, with the exception of the preventable mortality burden associated with  $NO_2$  exposure, for which resolving small-scale spatial contrasts is relevant because of local source contributions. Despite these results, the continued use of a fine scale resolution for city-level HIAs is important, particularly when mortality and age-structure data become available at a finer scale and can be incorporated into the HIA models for more refined results. In addition, the use of city-level mortality

rates adds an additional level of precision in relation to previous HIAs done on a large scale, for which country-level mortality rates were generally used.<sup>13,39,44</sup> Our results showed considerable variability between city-level and country-level mortality rates, as well as an effect of the use of country-level mortality rates instead of city-level ones on health burden estimations and city comparisons (appendix p 72).

Finally, further insights into the ERFs that relate air pollution with premature mortality are needed, particularly for  $NO_2$ . As shown in our sensitivity analyses, the ERF has the greatest effect on the final outcome, indicating the importance of the ERF choice. We chose our ERFs based on WHO recommendations (for  $PM_{2.5}$ ) and most recent and best available meta-analysed evidence (for  $NO_2$ ).<sup>24,25</sup> Nevertheless, both ERFs were pooled ERFs for non-accidental mortality, assuming equivalent mortality risk for diverse settings and populations. Risk estimate extrapolation to other settings has a potential for bias as the true ERF might vary from sub-population to sub-population, particularly if cause of death composition varies greatly between locations used to derive the concentration response associations and those where estimates are applied. As of June, 2020, there were no specific meta-analysed ERFs for distinct age, sex, or socioeconomic status categories for the European region. Nevertheless, previous research has suggested differential exposure to air pollution based on the socioeconomic group<sup>45,46</sup> and greater adverse health effects for people aged older than 65 years.<sup>3</sup> Further research is needed so that future HIAs can account for the differential health effects that are based on region, age, sex, and socioeconomic status. Such analyses will provide a deeper understanding on how adverse health effects vary within the population and will inform more targeted policy actions where they are needed the most.

To conclude, we estimated the local mortality burden due to air pollution for a wide range of European cities for, to our knowledge, the first time, providing local administrations with estimates for more targeted urban and transport planning policies for health preservation. Notably, the mortality burden varied greatly by city, reaching up to 15% of annual premature mortality for  $PM_{2.5}$  and 7% of annual premature mortality for  $NO_2$ , showing where more urgent actions are needed. Further health benefits could be achieved by lowering air pollution concentrations below WHO guidelines. Research supports the association between air pollution and mortality at concentrations below WHO recommendations with no evidence of a safe exposure threshold. Thus, current guidelines should be revised and air pollution concentrations should be reduced further to achieve a greater protection of health in cities.

#### Contributors

MN conceptualised the study idea. SK and MC worked on the study design and data collection. SK and EP-B did the data analysis. SK, EP-B, MC, NM, and MN contributed to data interpretation. NM and

DR-R provided input on the health impact assessment methods. JB-G provided help with all statistical analyses and wrote the R script for the uncertainty analyses. KdH and GH contributed to the development of the ELAPSE models and provided input on air pollution exposure estimations. SK wrote the manuscript. SK, MC, and EP-B accessed and verified the data. All authors reviewed the manuscript and provided feedback on the study design, data analysis, and interpretation of results.

#### Declaration of interests

We declare no competing interests.

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