Short-Term Effects of Ambient Particles on Mortality in the Elderly: Results from 28 Cities in the APHEA2 Project

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Short-term effects of ambient particles on mortality in the elderly: results from 28 cities in the APHEA2 project


ABSTRACT: Within the framework of the APHEA2 (Air Pollution on Health: a European Approach) project, the effects of ambient particles on mortality among persons ≥ 65 yrs of age were investigated. Daily measurements for particles with a 50% cut-off aerodynamic diameter of 10 µm (PM10) and black smoke (BS), as well as the daily number of deaths among persons ≥ 65 yrs of age, from 29 European cities, have been collected. Data on other pollutants and meteorological variables, to adjust for confounding effects and data on city characteristics, to investigate potential effect modification, were also recorded. For individual city analysis, generalised additive models extending Poisson regression, using a locally weighted regression (LOESS) smoother to control for seasonal effects, were applied. To combine individual city results and explore effect modification, second stage regression models were applied. The per cent increase (95% confidence intervals), associated with a 10 µg m⁻³ increase in PM10, in the elderly daily number of deaths was 0.8% (0.7–0.9%) and the corresponding number for BS was 0.6% (0.5–0.8%). The effect size was modified by the long-term average levels of nitrogen dioxide (higher levels were associated with larger effects), temperature (larger effects were observed in warmer countries), and by the proportion of the elderly in each city (a larger proportion was associated with higher effects).

These results indicate that ambient particles have effects on mortality among the elderly, with relative risks comparable or slightly higher than those observed for total mortality and similar effect modification patterns. The effects among the older persons are of particular importance, since the attributable number of events will be much larger, compared to the number of deaths among the younger population.

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2.9% with increasing ambient levels of NO₂, nonsignificantly by 2.1% with BS in adults (15–64 yr); significantly by 7.5% with SO₂ and by 8% in cold seasons with NO₂, and nonsignificantly by 3% with BS in children <15 yrs.

Spix et al. [17], from the quantitative pooling of local analyses on five West European cities, found a significant increase of daily admissions for respiratory diseases (adults of 15–64 yrs and elderly of ≥65 yrs) with elevated levels of O₃. This finding was stronger in the elderly, had a rather immediate effect, and was homogeneous over cities. The elderly were affected more during the warm season. The effect of BS was significantly stronger with high NO₂ levels on the same day. O₃ results were in good agreement with the results of similar USA studies.

Zmirou et al. [18], from a meta-analysis on 10 large European cities, found that daily deaths from cardiovascular conditions increased 2% with BS, 2% with O₃ and 4% with SO₂; the analogous figures for respiratory diseases were 4, 6 and 5%, respectively. This occurred in Western but not in Central European cities.

Some papers [19–21] summarised and commented on the APHEA findings and considered the theoretical and practical aspects of a monitoring system and made recommendations concerning the minimum data-set required, the methods of statistical analysis and presentation, and Europe-wide coordination of monitoring.

One intriguing finding was that the effects were lower in Central-Eastern European cities. Samoli et al. [22] reanalysed through generalised additive models the original data by restricting to days with pollutant concentration <150 μg·m⁻³. The new estimates for increase in mortality, only in Central-Eastern European cities, were larger than the ones published previously: by 69% for BS and 55% for SO₂. Thus, part of the heterogeneity in the estimates of air pollution effects had been caused by the statistical approach and lack of threshold for pollutant levels.

Overall, through the APHEA study, the existence of an association between daily variations in the levels of urban air pollution and adverse health effects was confirmed in Europe. This association is weak, but it involves the whole resident population, so it is a major cause of concern from the public health point of view.

APHEA methodology has been discussed and utilised by other investigators, as well [23–33].

The APHEA (Air Pollution on Health: a European Approach) project

During the last decade consistent results from several epidemiological studies have indicated that current concentrations of ambient particulate matter (PM) have adverse health effects including increases in daily mortality [34, 14]. Important evidence was added to these results by multicentre studies such as the APHEA project in Europe [1–22] and the National Mortality Morbidity and Air Pollution Study (NMMAPS) in the USA [35], which included data from several cities collected and analysed using a standardised protocol. The above results influenced the revisions of air quality standards in the USA and in Europe [36, 37].

Recently, attention has shifted to understanding, among other issues, which particular population groups are more sensitive to these effects [38]. The elderly, which are proportionally increasing in Europe, are a group of special interest.

The APHEA2 project was implemented, as a continuation of the APHEA project, based on a more extended database, with objectives to address the consistency of associations, to identify sensitive subpopulations and specific particle characteristics, and to explore confounding and effect modification [39, 40].

The estimated increase in the daily number of deaths for all ages for a 10 μg·m⁻³ increase in daily particles with a 50% cut-off aerodynamic diameter of 10 μm (PM10) or BS concentrations was 0.6%, whereas for the elderly it was slightly higher [39]. There were important effect modifications for several variables: e.g. in a city with low versus one with high average NO₂, the estimated increase was 0.19 versus 0.80%; in a relatively cold versus one with warm climate 0.29 versus 0.82%; in a city with low versus one with high standardised mortality rate 0.80 versus 0.43%. For the same pollutants increase, Atkinson et al. [40] found increase in daily hospital admission for: asthma (0–14 yrs) of 1.2%, asthma (15–64 yrs) of 1.1%, and COPD plus asthma and all-respiratory (≥65 yrs) of 1.0 and 0.9%. In the ≥65 groups PM10 estimates were positively associated with annual mean concentrations of O₃, Zanobetti et al. [41] analysed the mortality displacement issue, i.e. if it is due solely to the deaths of frail individuals, which are brought forward by only a brief period of time. They fit a Poisson regression model and a polynomial distributed lag model with up to 40 days of delay in each city. They found that the overall effect of PM10 per 10 μg·m⁻³ for the fourth-degree distributed lag model is a 1.61% increase in daily deaths (95% confidence interval (CI): 1.02–2.20), whereas the mean of PM10 on the same day and the previous day is associated with only a 0.70% increase in deaths (95% CI: 0.43–0.97). Thus, the effect size estimate for airborne particles more than doubles when longer-term effects are considered, which has important implications for risk assessment.

This paper reports the results of the APHEA2 project on the effects of daily PM on mortality among persons ≥65 yrs, in 28 European cities.

Data and methods

Data was collected from 28 cities across Europe: Athens, Barcelona, Basel, Bilbao, Birmingham, Budapest, Cracow, Dublin, Geneva, Helsinki, Ljubljana, Lodz, London, Lyon, Madrid, Marseille, Milano, Paris, Poznan, Prague, Rome, Stockholm, Tel-Aviv, Teplice, Torino, Valencia, Wroclaw, Zurich with a total population exceeding 43 million. The study period was ~5 yrs for most cities, within the nineties. The health outcome in the present analysis was the daily number of deaths (excluding deaths from external causes, International Classification of Diseases (ICD)9 ≥800) among persons ≥65-yrs-old, which ranged, in the different cities, from 4–139 on average per day. PM10 concentrations were contributed for the whole or part of the period (or could be estimated based on other studies) from 21 cities: the 24 hr concentrations ranged from 15 μg·m⁻³ to 66 μg·m⁻³ on average. Fourteen cities contributed daily BS measurements; these ranged 10–64 μg·m⁻³ (24 h concentrations). Measurements of air pollutants were provided by monitoring networks established in each town. The selection criteria for monitors to be included in the study (based on completeness of measurements) and the methods for replacing the few remaining missing values are described elsewhere [39]. Data was also collected on potential confounders: other pollutants (specifically SO₂, NO₂, O₃, carbon monoxide), meteorological variables (daily temperature and relative humidity), influenza epidemics. Day of the week, national and school holidays, seasonality and long-term trends were also adjusted for. Since significant heterogeneity between individual city estimates had been observed before [14], the present authors collected information on potential effect modifiers characterising the
city with respect to the pollutant mix, the status of health of the population, climate and geography [39]. A two-stage analysis was applied. In the first stage, city-specific regression models were fitted and their results were used in a second stage analysis to provide overall estimates and to investigate effect modification. Days with PM10 or BS levels >150 μg·m⁻³ were excluded. These days did not exceed 5% of the total number of days. Generalised additive models, extending Poisson regression were applied allowing for over-dispersion. Local nonparametric locally weighted regression (LOESS) smoothers were used to control for seasonal patterns and long-term trends. Temperature, humidity, day of the week, holidays, unusual events and influenza epidemics were also appropriately controlled for [39]. For PM10 and BS, the holidays, unusual events and influenza epidemics were also (LOESS) smoothers were used to control for seasonal patterns and the investigation of the role of potential effect modifiers in explaining observed heterogeneity. Fixed and random effects models were used as appropriate. More details on the data and methods have been reported elsewhere [39].

**Results**

In figure 1 the individual city as well as the pooled effect estimates for the daily number of deaths among the elderly, associated with a PM10 increase of 10 μg·m⁻³ are shown. The individual city effect estimates are positive for all cities except one. They range from an increase in the daily number of deaths of 0–1.7%, associated with 10 μg·m⁻³ increase in daily PM10 concentrations. In figure 2 the corresponding effect estimates for a similar increase in BS are shown. BS effects in individual cities range from 0–1.6% increase in the daily number of deaths associated with a daily increase of 10 μg·m⁻³ in BS concentrations. In table 1 the pooled estimated effect from fixed and random effects models for the elderly and those for all ages (for comparison) are shown. It should be noted that published estimates for all ages mortality included one more city, Erfurt in Germany, in which the daily number of deaths for the elderly was not available [39]. For reasons of comparability, the present authors calculated here the combined estimates without Erfurt. The pooled effects remain practically the same since Erfurt had little weight in the combined analysis, i.e. the combination of results across cities, meta-regression models were used. These allowed the estimation of combined effects and the investigation of the role of potential effect modifiers in explaining observed heterogeneity. Fixed and random effects models were used as appropriate. More details on the data and methods have been reported elsewhere [39].

![Figure 1](image1.png)

**Figure 1.** Estimated per cent increase and 95% confidence intervals in the daily number of deaths of persons ≥65-yr-olds associated with an increase of 10 μg·m⁻³ in the levels of black smoke for individual cities and overall. The size of the data point is inversely proportional to its variance. #: fixed effect; #: random effect.

![Figure 2](image2.png)

**Figure 2.** Estimated per cent increase and 95% confidence intervals in the daily number of deaths of persons ≥65-yr-olds associated with an increase of 10 μg·m⁻³ in the levels of black smoke for individual cities and overall. The size of the data point is inversely proportional to its variance. #: fixed effect; #: random effect.

<table>
<thead>
<tr>
<th>Mortality</th>
<th>PM10</th>
<th>BS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Among ≥65-yr-olds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed effects model</td>
<td>0.79 (0.66–0.92)</td>
<td>0.63 (0.49–0.78)</td>
</tr>
<tr>
<td>Random effects model</td>
<td>0.74 (0.52–0.95)</td>
<td>0.68 (0.43–0.92)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed effects model</td>
<td>0.71 (0.60–0.83)</td>
<td>0.51 (0.39–0.64)</td>
</tr>
<tr>
<td>Random effects model</td>
<td>0.67 (0.47–0.87)</td>
<td>0.58 (0.32–0.84)</td>
</tr>
</tbody>
</table>

Data are presented as per cent increase (95% confidence interval).
The effects of black smoke (BS) on the daily number of natural deaths among persons ≥65 yrs old

Table 2. Results of the second stage regression models investigating the role of potential effect modifiers of the estimated effects of particles with a 50% cut-off aerodynamic diameter of 10 μm (PM10) on the daily number of natural deaths among persons ≥65 yrs old

<table>
<thead>
<tr>
<th>Effect modifier in model</th>
<th>Mean over the study period 25th, 75th percentiles</th>
<th>Increase in the daily number of deaths associated with an increase of 10 μg m⁻³ in PM10 concentrations, at levels of effect modifier equal to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>25th percentile</td>
</tr>
<tr>
<td>24 h NO₂ μg·m⁻³</td>
<td>40, 70</td>
<td>0.30 (0.07–0.53)</td>
</tr>
<tr>
<td>24 h temperature °C</td>
<td>9, 15</td>
<td>0.44 (0.25–0.64)</td>
</tr>
<tr>
<td>24 h relative humidity %</td>
<td>66, 77</td>
<td>0.98 (0.82–1.14)</td>
</tr>
<tr>
<td>Age standardised annual mortality rate per 100,000</td>
<td>666, 972</td>
<td>0.93 (0.77–1.09)</td>
</tr>
<tr>
<td>Proportion of individuals ≥65 yrs %</td>
<td>13, 17</td>
<td>0.67 (0.50–0.83)</td>
</tr>
<tr>
<td>Geographical region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northwest/Central-East</td>
<td></td>
<td>0.81 (0.63–0.98)</td>
</tr>
<tr>
<td>Northwest/South</td>
<td></td>
<td>0.81 (0.63–0.98)</td>
</tr>
</tbody>
</table>

Data are presented as estimated per cent increase (95% confidence interval) unless otherwise stated. *These are variables characterising each city. Only effect modifiers reducing the heterogeneity by >10% are presented; †The effect modifiers were included alternatively in the model. NO₂: nitrogen dioxide.

Table 3. Results of the second stage regression models investigating the role of potential effect modifiers of the estimated effects of black smoke (BS) on the daily number of natural deaths among persons ≥65 yrs old

<table>
<thead>
<tr>
<th>Effect modifier in model</th>
<th>Mean over the study period 25th, 75th percentiles</th>
<th>Increase in the daily number of deaths associated with an increase of 10 μg m⁻³ in BS concentrations, at levels of effect modifier equal to:</th>
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<tr>
<td>24 h relative humidity %</td>
<td>66, 77</td>
<td>0.65 (0.51–0.80)</td>
</tr>
<tr>
<td>Proportion of individuals ≥65 yrs %</td>
<td>13, 17</td>
<td>0.59 (0.45–0.73)</td>
</tr>
<tr>
<td>Geographical region</td>
<td></td>
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<tr>
<td>Northwest/Central-East</td>
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</tbody>
</table>

Data are presented as estimated per cent increase (95% confidence interval) unless otherwise stated. *These are variables characterising each city. Only effect modifiers reducing the heterogeneity by >10% are presented; †The effect modifiers were included alternatively in the model. NO₂: nitrogen dioxide.

Other important effect modifying variables are the temperature and relative humidity levels (PM10 effects are higher in warmer and drier cities), the age-standardised annual mortality rate (higher mortality is associated with lower PM10 effects), the proportion of the elderly (a higher proportion of elderly is associated with higher PM10 effects) and geographical region (effects are highest in Southern and lowest in the Central-Eastern cities). It should be noted that these effect modifying variables were included in the models alternatively and the effects reported may be partly due to their intercorrelations. The effect modification pattern for BS effects is similar to that for PM10. When three effect modifiers were included in one model (the most important ones from each category, i.e. NO₂, temperature and age-standardised mortality rate or the proportion of the elderly) the p-value for the remaining heterogeneity was >0.20.

**Discussion**

The present study estimated the effect of daily ambient particulate matter concentrations on the number of deaths among the elderly (persons ≥65-yrs-old) in 28 European cities, using the database compiled within the APHEA2 project [39]. The effect estimates were consistently larger, by 10–20%, than those estimated for all age mortality from an identical database. The effects of two different ambient particle measures, PM10 and BS, were comparable.

In the studied cities elderly mortality comprised 67–88% of the total number of deaths, thus playing a predominant role in determining the magnitude of all age mortality. In other studies in which the effect of particles on mortality has been investigated, the age distribution of those who died on any given day was different. Thus, in a study in Sao Paolo, Brazil [42], the percentage of deaths among those ≥65 yrs was only 49%. In that study, the effect of a daily change of 10 μg·m⁻³ in PM10 on the daily number of deaths from all causes among the elderly was found to be a 0.5% increase, which is comparable to the one reported from the present analysis, but slightly smaller. The difference in size may be due to the use of a one day PM measurement in the Brazilian study, whilst in APHEA2 the average of lags 0 and 1 was used. It has been shown that longer time averages result in higher estimates [43]. This difference may also be attributable to a higher mean age of death in the APHEA2 populations compared to Sao Paolo. If older age groups are consistently at higher risk of death from air pollution, then it will be expected that, in a population where the mean age is higher, larger PM effects...
will be observed. In studies conducted in places where the age-
distribution of the population is similar to that in Europe, the
results were close to those reported here. Thus, in a study in
Canada [44] the increase in mortality among the elderly
associated with a 10 μg·m⁻³ increase in PM10 was found to be
0.69% for lag0 and 0.79% for lag1 whilst that for all ages was
0.67% for lag0 and 0.36% for lag1. In the USA NMMPAPs
[35] the increase in the daily number of deaths for all ages
associated with a 10 μg·m⁻³ change in PM10 was 0.5%.

The city specific estimates in the current study were hetero-
geneous, as were those reported before for all age total and
cause-specific mortality [14, 18, 39]. One objective of the
APHEA2 project was to investigate the reasons for this
heterogeneity. In this analysis important effect modifiers have
been identified. They are generally consistent to those
reported for the all age mortality [39]. Thus, higher long-term average
NO2 concentrations are associated with larger PM effects.

Since NO2 is mainly an indicator of pollution originating
from traffic and it is likely that in locations with high NO2
are in line with this hypothesis.

risks and the health status of the population and is consistent
smaller, in relative terms. This may be a result of competing
standardised mortality rate, PM effects on the elderly are
higher exposure to outdoor air pollution of populations living
warmer and drier climates. This finding may be due to a
harmful to human health. Higher PM effects are found in
cities with higher age-
standardised mortality rate, PM effects on the elderly are
smaller, in relative terms. This may be a result of competing
risks and the health status of the population and is consistent
with the results published by GOUVEIA and FLETCHER [42].

It is also found that in cities with higher age-
standardised mortality rate, PM effects on the elderly are
smaller, in relative terms. This may be a result of competing
risks and the health status of the population and is consistent
with the results published by GOUVEIA and FLETCHER [42].

An interesting finding in the present context, is that the
proportion of the elderly appears as modifying the PM effect
on elderly mortality. This implies that the PM effect is not
constant across different age subgroups among those ≥65 yrs.
The average PM effect in an elderly population, thus, probably
depends on the mean age of this population. It is plausible to
expect that in cities with a larger proportion of elderly, the
population group of those ≥65 will also have a higher mean age.
In this case, if PM effects increase with age, then higher
mean age would result in larger effect estimates. The present
authors’ result and that reported by GOUVEIA and FLETCHER
[42] are in line with this hypothesis.

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References

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