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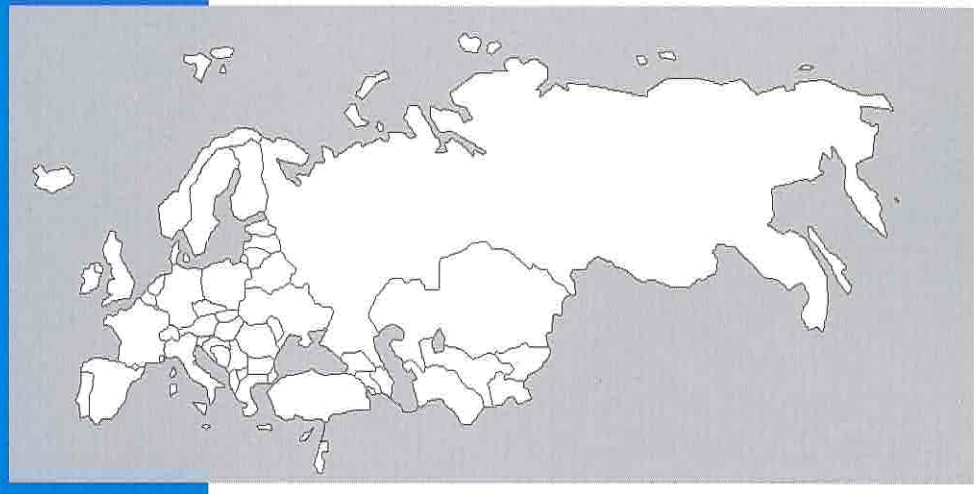

Prepared by: **H. Ross Anderson, Richard W. Atkinson, Janet L. Peacock, Louise Marston and Kostas Konstantinou**

Meta-analysis of time-series studies and panel studies of Particulate Matter (PM) and Ozone (O_3)

Report of a WHO task group

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Report of a WHO task group

This report was prepared by: H. Ross Anderson, Richard W. Atkinson, Janet L. Peacock, Louise Marston and Kostas Konstantinou, all at the Department of Community Health Sciences, Epidemiology, St. George's Hospital Medical School, London, United Kingdom as part of the WHO project "Systemic Review of Health Aspects of Air Quality in Europe"

ABSTRACT

Quantitative health impact assessment has become increasingly important in the development of air quality policy. For such analysis it is important to have accurate information on the concentration-response relationships for the effects investigated, for example on the relationship between changes in daily air pollution and its impact on health. Therefore, a quantitative meta-analysis of peer reviewed studies was conducted to obtain summary estimates for certain health effects linked to the exposure to particulate matter (PM) and ozone. This work was done as part of the WHO project "Systematic review of health aspects of air pollution in Europe", which is funded by the European Commission and is intended to provide input to the Clean Air For Europe (CAFE) programme. The data for these analyses came from a database of time-series studies (ecological and individual) developed at St. George's Hospital Medical School at the University of London. The meta-analysis was also performed at St. George's Hospital according to a protocol that was agreed upon by a WHO Task Group in advance of the work. This analysis confirmed statistically significant relationships between levels of PM and ozone in ambient air with mortality, using data from several European cities. Updated risk coefficients in relation to ambient exposure to PM and ozone were obtained for all-cause (relative risk for a 10 $\mu g/m^3$ increase in PM_{10}: 1.006 (1.004, 1.008) and ozone: 1.003 (1.001, 1.004), respectively) and cause-specific mortality and hospital admissions for respiratory and cardiovascular causes. In addition, possible publication bias was investigated and revised summary estimates were calculated. Also panel studies were analyzed to derive summary estimates for coughs and medication use in individuals with underlying respiratory disease.

Keywords

META-ANALYSIS
AIR POLLUTANTS – adverse effects
ENVIRONMENTAL EXPOSURE
OZONE
RISK ASSESSMENT

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1. Background

The WHO project *"Systematic Review of Health Aspects of Air Quality in Europe"*, which is financially supported by the European Commission, aims to provide the *Clean Air for Europe* (CAFE) programme of the Commission's DG Environment with a systematic, periodic and scientifically independent review of the health aspects of air pollution in Europe.

As part of this review process WHO/Europe convened a working group to provide answers to a set of twelve questions in relation to the health effects of particulate matter, ozone and nitrogen dioxide. The report from this working group provided a comprehensive description of the hazards related to these pollutants, but no detailed guidance on risk assessment (WHO 2003). Therefore, the working group recommended conducting a quantitative meta-analysis of existing studies which could be used subsequently for health impact assessments. The data for these analyses came from a database of time-series studies (ecological and individual) developed at St. George's Hospital Medical School at the University of London. The meta-analysis of these data will be used to update risk coefficients for selected health endpoints in relation to ambient exposure to particulate matter and ozone.

2. Process

A WHO task group was established to perform the meta-analysis. The analysis was carried out at St. George's Hospital Medical School at the University of London. The members of the task group are listed in Annex 1.

This report describes the work undertaken for this meta-analysis and presents both the summary estimates and the raw data used in their calculation. It details the assumptions made in order to select the studies for inclusion in the calculation of the summary estimates. The Task Group agreed on these assumptions at a meeting in London on 8 April 2003. The minutes from this meeting are attached as Annex 2. At this meeting it was decided to investigate a number of different health outcomes and to conduct sensitivity analyses. However, because of the large number of permutations of health outcomes and exposure measures, a core set of analyses was subsequently agreed with the task group: According to this agreement, meta-analytical estimates for the effects of particles (PM_{10}, $PM_{2.5}$, black smoke (BS) and coarse fraction) and ozone were estimated for the following health outcomes:

- daily number of deaths from all causes (excluding accidents), from respiratory causes and from cardiovascular causes as categorised by the WHO International Classification of Diseases;
- daily number of hospital admissions (incl. emergency department and emergency room admissions) for respiratory diseases (subdivided by ages 0–14, 15–64 and 65+ years) and for cardiovascular disease (for ages 65+);
- cough in individuals with underlying respiratory disease (for children and adults separately);
- respiratory medication use in individuals with underlying respiratory disease (for children and adults separately).

3. Methods

3.1 Systematic review database

As part of a project to assist the Department of Health in the United Kingdom in their evaluation of the evidence of the adverse health effects of air pollution, a series of databases containing details of published studies was set up at St. George's Hospital Medical School. Search criteria were developed to identify the relevant studies indexed in the peer-reviewed literature. They aimed to identify time-series studies (both ecological and individual) of the short-term health effects of air pollution. Original numerical estimates of these effects, together with other relevant information were extracted from these studies and entered into the ACCESS databases. The APED (Air Pollution Epidemiology Databases) contain estimates of the effects of particles, nitrogen dioxide, sulphur dioxide, ozone and carbon monoxide. The outcomes studied were mortality, hospital admissions, use of medical services, respiratory symptoms and lung function. Results for subdivisions by diagnosis, age and season and for various lags were also recorded. Procedures for the validation and analysis of these data have been developed and periodic reviews of the literature are carried out to update the databases. Further details are given in Annex 3.

3.2 Selection of studies for meta-analysis

Studies can vary in many ways, for example in their definition of the health outcome, their choice of pollutant metric and their reporting of results. When more than one study has been conducted using the same population, further consideration of the study characteristics are required. They may have been published at different times and may have used different statistical methods. It was considered desirable that, for the purposes of health impact assessment, the results were not dominated by multiple analyses of single locations. Also, it was important that study selection was unbiased by knowledge of the result. Hence, guidelines for study selection were discussed and determined at a meeting of the WHO Task Group in London on 8 April 2003 (see also Annex 2). The minutes of the meeting outline the decisions taken and therefore only the key points are summarized below.

1. The number of estimates available for meta-analysis should not be a determining factor in selecting studies – that is, there should be no compromises on any of the criteria for study selection in order to raise the number of studies included in the analysis
2. It was decided to concentrate upon European studies. If there were insufficient studies to perform a meta-analysis then it may be necessary to consider the inclusion of studies from other parts of the world. However, this issue would need further consideration by the whole task group should it occur.
3. Only one estimate from each city should be used in a meta-analysis. A number of cities have been studied more than once and therefore a mechanism for selecting the appropriate estimate was needed. It was decided to select the latest study published or, if the study participated in a large multicity study, to use the multicity study result.
4. The initial analysis will focus upon single-pollutant model results based upon an all-year analysis.
5. The "selected" lag from the database would be used rather than specific lags or combinations of lags.

3.3 Selection issues specific to panel studies

For panel studies the same protocol was followed. In particular, summary estimates were only calculated where there were four or more individual estimates, and the analysis was confined to European studies.

As will be seen, the results were dominated by the PEACE study, which was a multicentre study conducted in 14 centres using a common protocol. Each centre had an urban and rural panel of symptomatic children, giving 28 panels (and estimates) in all. It must be pointed out that there is a degree of correlation between these panel studies because all were carried out during the same winter period when air pollution levels were correlated over a wide area of Europe. Also, the studies coincided with an influenza epidemic which could not be accounted for in the analysis (Roemer et al., 2000).

3.3.1 Patient group

The requirement was to include studies among individuals with chronic respiratory disease. Studies varied in their definitions of patient group and the following were included for children: asthmatic (mild, moderate, severe, on and not on medication), and chronic respiratory symptoms. In adults, the same two categories were included plus panels with chronic obstructive pulmonary (airway) disease or bronchial hyperresponsiveness. No subgroup analyses within asthmatic panels were used.

3.3.2 Outcomes

The task group wished to have one or two outcomes that reflected an exacerbation in asthmatic patients. Panel studies have recorded a large variety of symptoms and lung function measures. It was agreed to use “cough” and “medication use” as indicators of a worsening of respiratory health in symptomatic individuals. The following measures of cough were used: unspecified cough, cough in combination with wheeze and tight chest and night cough. Both incidence and prevalence measures were analysed and where both were reported, incidence estimates were used. Measures of medication use were bronchodilator or specific use of ß agonists.

3.4 Meta-analysis

Fixed- and random-effects summary estimates for each pollutant-outcome pair were calculated for an effect of 10 $\mu g/m^3$ increase in the pollutant (Der Simonian & Laird, 1986).

4. Results

Using studies catalogued in bibliographic databases up to February 2003, 629 ecological time-series studies and 160 individual or panel studies have been identified. 286 time-series and 124 panel studies have provided usable data. The two databases contain over 11 700 and 6400 effect estimates, respectively.

4.1 Summary estimates

Tables 1–4 show the random-effects summary estimate for each pollutant/outcome combination. The tables also give the number of estimates available for analysis. For some outcome/pollutant

combinations there were insufficient numbers of studies for meta-analysis (a minimum of four estimates were required for meta-analysis) and therefore, no summary estimates are given in the tables. Individual city results are given in the Annex 4.

Table 1. Summary relative risk estimates (and 95% confidence intervals) for a 10 µg/m^3 increase in pollutant for all-cause and cause specific mortality

Outcome/ Disease	*Age*	*PM_{10}*	*$PM_{2.5}$*	*CF*	*BS*	*Ozone (8-hour)*
All-Cause	All age	1.006 (1.004, 1.008) **33**[1]	NA **3**	NA **1**	1.006 (1.004, 1.008) **26**	1.003 (1.001, 1.004) **15**
Respiratory	All age	1.013 (1.005, 1.020) **18**	NA **1**	NA **1**	1.006 (0.998, 1.015) **18**	1.000 (0.996, 1.005) **12**
Cardio-vascular	All age	1.009 (1.005, 1.013) **17**	NA **1**	NA **2**	1.004 (1.002, 1.007) **18**	1.004 (1.003, 1.005) **13**

Notes:
1. Numbers in bold indicate number of European studies available.
2. NA – insufficient numbers available for meta-analysis (<4).

Table 2. Summary relative risk estimates (and 95% confidence intervals) for a 10 µg/m^3 increase in pollutant for respiratory and cardiovascular hospital admissions

Outcome/ Disease	*Age in years*	*PM_{10}*	*$PM_{2.5}$*	*CF*	*BS*	*Ozone (8-hour)*
Respiratory	0–14	NA **3**	NA **1**	NA **1**	NA **2**	NA **3**
Respiratory	15–64	NA **3**	NA **1**	NA **1**	1.006 (1.001, 1.010) **5**	1.001 (0.991, 1.012) **5**
Respiratory	65+	1.007 (1.002, 1.013) **8**	NA **1**	NA **1**	1.001 (0.993, 1.010) **6**	1.005 (0.998, 1.012) **5**
Cardio-vascular	65+	NA **2**	NA **0**	NA **0**	NA **2**	**NA 1**

Notes:
1. Numbers in bold indicate number of European studies available.
2. NA – insufficient numbers available for meta-analysis (<4).

Table 3. Summary odds ratios (95% confidence intervals) for a 10 µg/m^3 increase in pollutant for cough

Patient group	*Age in years*	*PM_{10}*	*$PM_{2.5}$*	*CF*	*BS*	*Ozone*
Symptomatic children	5–15	0.999 (0.987, 1.011) **34**	NA **1**	NA **1**	1.001 (0.982, 1.021) **33**	NA **1**
Symptomatic adults	16–70	NA **3**	No studies	No studies	NA **2**	NA **1**

Notes:
1. Numbers in bold indicate number of European studies available.
2. NA – insufficient numbers available for meta-analysis (<4).

Table 4. Summary odds ratio estimates (and 95% confidence intervals) for a 10 µg/m^3 increase in pollutant for medication use

Patient group	*Age in years*	*PM_{10}*	*$PM_{2.5}$*	*CF*	*BS*	*Ozone*
Symptomatic children	5–15	1.005 (0.981, 1.029) **31**	NA **1**	NA **1**	1.008 (0.970, 1.049) **31**	NA **1**
Symptomatic adults	16+	NA **3**	No studies	NA **1**	NA **2**	NA **1**

Notes:
1. Numbers in bold indicate number of European studies available.
2. NA – insufficient numbers available for meta-analysis (<4).

4.2 Time-series results

Mortality and particles
Estimates of the effect of PM_{10} on all-cause mortality were taken from 33 separate European cities or regions (Table A1, Appendix). The random-effects summary relative risk for these 33 results was 1.006 (95% CI: 1.004, 1.008) for a 10 µg/m^3 increase in PM_{10}. 21 of theses estimates were taken from the APHEA 2 (Air Pollution and Health: a European Approach 2) study (Katsouyanni et al, 2001) and hence the summary estimate derived from this review is dominated by this multicity study.

Cause-specific results for mortality are yet to be published from the APHEA 2 project. Hence, the numbers of estimates for cardiovascular and respiratory mortality are smaller than for all-cause mortality, 17 and 18 respectively. The corresponding summary estimates were 1.009 (1.005, 1.013) and 1.013 (1.005, 1.020) for a 10 µg/m^3 increase in PM_{10} (Tables A2 and A3). The majority of the estimates in these two categories come from multicity studies conducted in France, Italy and Spain.

The estimates for all-cause mortality and cause-specific mortality are comparable to those originally reported from the National Mortality, Morbidity and Air Pollution Study (NMMAPS) based upon the 20 largest cities in the United States (Samet et al., 2000). For a 10 µg/m^3 increase in PM_{10} they reported a 0.51% (0.07, 0.93) increase in daily mortality from all causes and for cardio-respiratory mortality the corresponding percentage change was slightly larger at 0.68% (0.2, 1.16). A recent re-analysis of the NMMAPS data, organized by the US Health Effects Institute (HEI) because of concern over the statistical procedures used in the original analyses, revised the NMMAPS summary estimates downwards to 0.21% for all-cause mortality and 0.31% for cardio-respiratory mortality (HEI, 2003). A similar re-analysis of the APHEA 2 mortality data revealed that the European results were more robust to the method of analysis. Depending upon the method of smoothing adopted, the summary estimate for PM_{10} and all-cause mortality reduced by 4% when "loess" smoothing with more stringent convergence criteria were used, reduced by 34% when natural splines were used instead of "loess" smoothing and reduced by 11% when penalized splines were used to smooth the time-series. The actual effect estimates, expressed as an increase in mortality associated with a 10 µg/m^3 increase in PM_{10}, under these three scenarios were: 0.6% using "loess", 0.4% using natural splines and 0.6% using penalized splines.

Very few European studies of all-cause and cause-specific mortality and fine particles were found. All-cause mortality and $PM_{2.5}$ were reported from Erfurt, Germany (Wichmann et al.,

2000), the Czech Republic (Peters et al., 2000) and the West Midlands conurbation in the United Kingdom (Anderson et al., 2001) (Table A9). Evidence from Europe of an effect of fine particles on daily mortality is therefore sparse. Of the five estimates from three studies available, none showed a statistically significant positive association and one was significantly negative. The West Midlands study was a systematic study of both mortality and hospital admissions with the specific aim of investigating associations between health outcomes and different particle measures and sizes. It covered a population in excess of 2 million. The health data were from the mid-1990s and the analysis followed the APHEA 2 methodology, which included an a priori hypothesis of lag0+1. It therefore seems an appropriate study from which to take the health effect estimates for fine particles. These estimates are listed in Table A9. For all-cause mortality the relative risk for an effect of $PM_{2.5}$ was 1.0034 (0.9915, 1.0154). This compares with 1.0057 (0.9980, 1.0136) and 0.9837 (0.9677, 0.9999) from studies in the Czech Republic and Erfurt respectively. For cause-specific mortality only the West Midlands study provides effect estimates (Tables A9).

In view of the paucity of data on $PM_{2.5}$ effects in Europe, and following the decisions of the task group on the meta-analysis protocol, we also looked for studies conducted outside of Europe. This analysis is fully described in Annex 5. The estimates for North American cities were larger than those for Europe and their summary estimates were statistically significant. While the transferability of the North American coefficients to Europe will increase the uncertainty and requires proper consideration of the differences and similarities of the two regions, these results also give confidence that the results from the large West Midlands study are likely to represent a positive association with daily mortality. In general it is difficult to be confident that three estimates are sufficient to characterize the European situation. Whatever estimate is chosen for Europe, it seems clear that any health impact assessment analysing effects of short term exposure to $PM_{2.5}$ will need to consider these as a source of uncertainty.

Black smoke (BS) is a measure of the blackness of particles with diameter under 4.5 μm. It is probably a reasonable indicator of primary fine particles originating from combustion sources.

There are numerous studies of black smoke and mortality from the European Region. Twenty-six estimates of the effect of black smoke on all-cause mortality were extracted from the database and they show an overall summary relative risk of 1.006 (1.004, 1.008) per 10 $\mu g/m^3$ increase in BS (Table A5). As for PM_{10}, estimates from APHEA 2 study dominate this group of results. Also, since it was the larger cities in Europe that participated in the APHEA 2 programme, the results from this meta-analysis closely match those from APHEA 2. The summary estimate derived from this review was 1.006 (1.004, 1.009) slightly larger than that calculated from the meta-analysis of the 14 APHEA 2 estimates at 1.005 (1.004, 1.006). The re-analysis of the black smoke results by Katsouyanni and colleagues found little change in the size and precision of the summary BS estimate from the APHEA 2 data (Katsouyanni et al., 2001).

For cause-specific mortality, 18 estimates were available for both cardiovascular mortality and respiratory mortality (Tables A5 and A6), most estimates deriving from multicity studies conducted in France, Poland and Spain. The summary relative risks per 10 $\mu g/m^3$ increase in BS for cardiovascular and respiratory mortality were 1.004 (1.002, 1.007) and 1.006 (0.998, 1.015) respectively. Cause-specific results for BS from the APHEA 2 project were not in print at the time of the review.

The evidence for an effect of coarse fraction particles in Europe is even less substantive than for fine particles. Only two European studies, the West Midlands study described above, and a study of cardiovascular admissions from Krakow 1979–1989, have examined the effect of coarse particles ($PM_{10–2.5}$) on daily mortality. The only study to show a statistically significant adverse effect of particles in the range $PM_{10–2.5}$ was conducted in Poland (Krzyzanowski & Wojtyniak, 1991). At this stage, no summary relative risks for health impact assessments of coarse particles can be given.

Hospital admissions and particles

Sufficient numbers of estimates (>3) of the effect of PM_{10} were available only for respiratory admissions in the 65+ age group. The relative risk for a 10 μg/m^3 increase in PM_{10} was 1.007 (1.002, 1.013) (Table 2) and was based upon 8 estimates (Table A4). Six of these eight estimates were provided by the APHEA 2 project (Atkinson et al., 2001). As for mortality, a re-analysis of the APHEA 2 data confirmed the robustness of the original results (HEI, 2003). Unfortunately, we were unable to use much of the recent published data on particles and daily admissions for respiratory disease from APHEA 2 because this study did not report all respiratory admissions in the younger age groups.

For the other two age categories, ages 0–14 and 15–64 years, results were available from three studies conducted in London (Atkinson et al., 1999), West Midlands (Bremner et al., 1999) and Rome (Michelozzi et al., 2000) (Tables A4). Together these cities represent a population in excess of 10 million people. A meta-analysis of results from these three cities gave summary estimates of 1.010 (0.998, 1.021) and 1.008 (1.001, 1.015) per 10 μg/m^3 increases in PM_{10} for respiratory admissions, ages 0–14 and 15–64 years respectively. It may be appropriate to reconsider the guideline on the number of estimates required for a meta-analysis given the small numbers available for some combinations of health outcome and pollutant.

For fine and coarse particles only the West Midlands study provided results for the respiratory outcomes. The relative risks for $PM_{2.5}$ for each of the three age categories, 0–14, 15–64 and 65+ years were 1.091 (0.9994, 1.0391), 0.9881 (0.9633, 1.0135) and 0.9926 (0.9732, 1.0125) respectively (Table A10). There were no estimates available from the 65+ years, cardiovascular admissions group. Results for coarse particles were similar to those for fine particles.

Results for BS and respiratory admissions in the over 65 were dominated by the APHEA 2 programme (Atkinson et al., 2001), all bar one of the six results coming from that project. Hence the summary estimate of the relative risk of 1.001 (0.993, 1.010) was almost identical at 1.001 (0.993, 1.009). The slightly wider confidence interval in the meta-analytical estimate reflected the addition of the result from Edinburgh (Prescott et al., 1998), a relatively small city. For respiratory admissions in adults aged 15–64 years the summary estimate was based upon the original APHEA 1 analysis of four cities (Amsterdam, London, Paris and Rotterdam) (Spix et al., 1998) together with the result from the West Midlands study. The summary relative risk was 1.006 (1.001, 1.010) per 10 μg/m^3 increase in BS. For admissions for respiratory disease in children aged 0–14 years only two results were available, one from London and one from the West Midlands (Table A8). A meta-analysis of these two results gave an estimate slightly closer to the London estimate because of the larger weight London has in the analysis due to its larger population. The choice of estimate for this group needs further consideration.

Two studies of BS and cardiovascular admissions in the elderly (65+ years) have been published – from London and Edinburgh. Because of the larger population in London the summary

estimate from the London study would be appropriate – relative risk 1.017 (1.008, 1.026), compared to 1.023 (0.981, 1.069) for Edinburgh. We were unable to use the recently published results from APHEA 2 (Le Tertre et al., 2002) because these described cardiac rather than cardiovascular admissions. The present analysis includes cerebrovascular disease in addition to cardiac disease. Most European evidence suggests that there is no relationship between air pollution and cerebrovascular disease, so in retrospect, it might have been better to choose this diagnostic group.

Mortality and ozone
Table 1 shows the summary estimates for the three mortality outcomes and ozone. There were 15, 13 and 12 estimates available for meta-analysis for all-cause, cardiovascular and respiratory mortality. Details of the individual estimates are given in Tables A11–A13. The relative risks per 10 μg/m^3 increases in ozone were 1.003 (1.001, 1.004), 1.004 (1.003, 1.005) and 1.000 (0.996, 1.005) for all-cause, cardiovascular and respiratory mortality respectively. In each group the estimates are based upon studies in France, Italy, the Netherlands, Spain and the United Kingdom. Results from the APHEA 2 project are not yet published.

Hospital Admissions and ozone
The numbers of available estimates were limited for respiratory and cardiovascular admissions. The original APHEA programme provided summary estimates for respiratory admissions in age ranges 15–64 and 65+ years. Combining these results with those from the West Midlands study gave summary relative risks of 1.001 (0.991, 1.012) and 1.005 (0.998, 1.012) respectively. Three estimates were available for respiratory admissions in children aged 0–14 years. A meta-analysis of these estimates gave a summary relative risk of 0.999 (0.987, 1.012). Only one estimate, from a study in London, was available for cardiovascular admissions. It showed a positive and statistically significant association with ozone, relative risk 1.007 (1.002, 1.011) per 10 μg/m^3 increase in mean 8-hour ozone.

The lack of matching of outcomes chosen for this meta-analysis with those for which published data are available – discussed above for particles – was also a problem for ozone. A further problem was that some studies reported only results for maximum one-hour ozone, not eight-hour ozone.

4.3 Panel Results

Cough and particles in symptomatic children
Thirty-four estimates were available for PM_{10} and cough in children (Table A15). Many of the estimates used for European panel studies are from the PEACE study. PEACE is a multicity panel study conducted in 14 centres using a common protocol. Each PEACE centre studied an urban and a rural panel of symptomatic children. Hence, for most outcome/pollutant combinations, PEACE provided 28 estimates.

The dominance of the results by the PEACE study deserves special mention. This study was carried out in children in 14 centres (one urban and one rural panel per centre) throughout Europe in one winter. This will have reduced the potential for heterogeneity because the exposure of the panels will tend to have been more similar than if they had been conducted in different years or seasons. There was a concurrent influenza epidemic which could not be accounted for in the analysis and the study period was somewhat too short to make adequate adjustment for time trends (Roemer et al., 2000).

The pooled odds ratio estimate is close to 1.0 with 95% confidence limits indicating non-statistical significance. There was only one estimate for $PM_{2.5}$. This was from Finland where 49 children aged 8–13 were followed for six weeks (OR 1.091 (95%CI 1.007, 1.182) (Table A16). There was a complementary estimate for coarse particles from the same study (OR 1.086 (1.023, 1.152) (Table A16). There were 33 studies of effects of black smoke. Once again, these included 28 estimates from the PEACE studies and so provide a wide representation of European cities. The pooled estimate was close to 1.0 and was not significant (Table A17).

Cough and ozone in symptomatic children
Only one estimate was available for this. This came from a Parisian study which included 82 children aged 7–15 years followed for three months. The odds ratio was 1.040 (0.920, 1.176) (Table A16).

Cough and particles in symptomatic adults
There were six estimates of PM_{10} available in total but only three were usable. Of the usable estimates, two were from the Netherlands and one was from Paris and the pooled estimate was 1.043 (1.005, 1.084). One further study from the Netherlands could not be combined with the others since the estimate was a relative risk rather than an odds ratio. This estimate was not significant, (Table A18). For a relatively common outcome such as cough, odds ratios and relative risks cannot be considered to be equivalent. The two remaining studies of PM_{10} were also Dutch studies and were not usable since the results had simply been quoted as "not significant" in the text with no estimates of effect size presented (Table A18).

No studies were found which examined effects of $PM_{2.5}$ or coarse particles on cough in adults. There were five estimates of effects of black smoke, of which two were usable. These included one Dutch and one Parisian study in 52 and 40 subjects followed respectively for three and six months. The pooled estimate was 1.05 (1.011, 1.101). Three further Dutch studies had to be excluded from meta-analysis due to the use of a relative risk estimate (one estimate, not significant, Table A18) and results simply presented as "not significant" with no effect sizes (two estimates, Table A18).

Cough and ozone in symptomatic adults
There were only two studies which estimated effects of ozone on cough in adults. One was a study from the United Kingdom with 75 subjects followed for one month and gave an odds ratio of 1.050 (0.910, 1.212). The other was a Dutch study in 60 subjects followed for three months which reported a significant protective effect as a relative risk (Table A18), making it not combinable with the odds ratio estimate.

Medication use and particles in symptomatic children
There were 31 studies analysing PM_{10} in children including 27 estimates from the PEACE studies, thus providing a wide representation of European cities. (One PEACE centre [Poland] only reported an estimate for the rural panel and hence there were 27 and not 28 PEACE estimates, Table A19). The pooled estimate was 1.005 and the 95% CI spanned 1.00. No studies were found for $PM_{2.5}$ or coarse fraction. As for PM_{10}, there were 31 studies that analysed black smoke in children including 27 estimates from the PEACE studies and so again, these provide a reasonable representation of European cities. The pooled estimate was 1.008 which was non-significant as for PM_{10} (Table A20).

Medication use and ozone in symptomatic children
Only one study was found for ozone in children. This was from a Parisian study in 82 children followed for three months and gave an odds ratio of 1.410 (1.050, 1.890) (Table A21).

Medication use and particles in symptomatic adults
There were four estimates for PM_{10}, all from the Netherlands. One estimate could not be combined with the odds ratios as it was a relative risk. The pooled estimate for the remaining three was 1.010 (0.990, 1.031). The three studies comprised 138, 128 and 32 subjects who were all followed for about three months. The unusable estimate was non-significant (Table A22).

There were no studies found of $PM_{2.5}$ and only one study of coarse fraction. This was from Germany and involved 67 subjects who were followed for six months and gave an odds ratio of 1.008 (0.958, 1.061). There were three estimates of black smoke and these all came from Dutch studies. There were two usable estimates from studies of 138 and 128 subjects followed for about three months. The pooled estimate was 0.993 (0.956, 1.031). The third estimate was from a study in 60 subjects followed for three months where the relative risk indicated a non-significant protective effect (Table A22).

Medication use and ozone in symptomatic adults
Two studies looked at ozone in relation to medication use. One was a study performed in the United Kingdom in 75 subjects followed for one month and gave an odds ratio of 1.440 (1.140, 1.810). The other was a Dutch study in 60 subjects followed for three months and which reported a non-significant relative risk (Table A22).

5. Discussion

There are sufficient European studies of the health effects of particulate matter measured as PM_{10} and BS, and of ozone on all-cause and cause-specific mortality to perform a meta-analysis and derive summary relative risks. The APHEA 2 project investigated cause-specific mortality also for ozone (in relation to both all-cause and cause-specific mortality) and results are likely to be published shortly. It may be appropriate to take consideration of the findings of this study independently of this review – the results are already published in a technical report to the European Commission.

There are insufficient studies of the health effects of fine and coarse particles on daily mortality from Europe to fulfil the criteria to calculate summary estimates agreed by the Task Group. The West Midlands study (Anderson et al., 2001) was designed specifically to study the health effects of size-fractionated particulate matter and would provide a consistent and uniform set of results for health impact assessment calculations. An alternative method to address the paucity of results is to include non-European studies. The applicability of results from non-European studies to European populations needs consideration however.

There are few studies generally of particulate matter and ozone and hospital admissions. Certain age groups tend to be more frequently studied than others. For example sufficient studies of admissions for respiratory diseases in those aged 65 years and over exist but not for younger age groups. This is mainly because admissions for specific respiratory causes tend to be studied in younger subjects, for example asthma. There may be little advantage in looking outside Europe

for further evidence as in the United States data on hospital admissions are routinely available only for individuals older than 65 years. Other countries may, however provide usable results.

There is a surprising lack of estimates for the diagnostic group of all cardiovascular admissions (ICD 9 390–459). There are a number of options to consider in seeking additional evidence. First admissions for cardiac disease, ICD 9 codes 390–429, could be included in the study selection protocol, thus enabling the inclusion of APHEA 2 published results for cardiac admissions. Furthermore, studies of cardiac/cardiovascular admissions for all ages, rather than just for those over 64 years of age, may be considered. Cardiovascular diseases are less common in children and early adult life and so little may be lost in combining these two age groups.

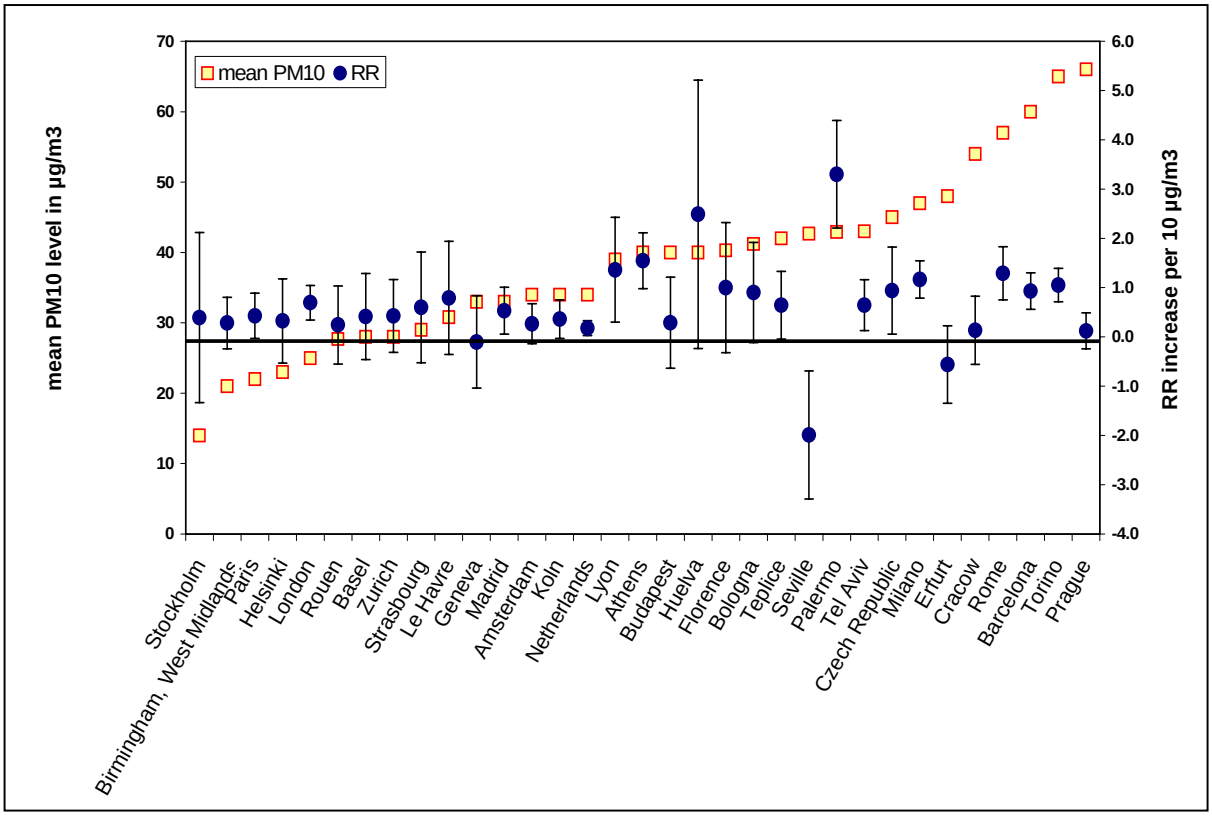
There were sufficient studies of effects of PM_{10} and BS on cough and medication use in symptomatic children to calculate overall pooled estimates. There were very few studies of effects on cough of fine particles, coarse particles or ozone in children and few studies overall for any pollutant in symptomatic adults. Summary values have been calculated in these situations. However although it would seem reasonable to accept these as best available estimates, they cannot be used with the same degree of confidence as those summary estimates based on larger numbers of studies.

5.1 Exploration of heterogeneity

This meta-analysis aimed at producing summary estimates for chosen pollutants and outcomes. It did not attempt to explain any heterogeneity in the estimates. Although there is the theoretical potential to use information about the causes of heterogeneity to tailor estimates to subregions of Europe, our knowledge is insufficient at present for this to be based on a solid foundation. However, because the database contains information on the annual mean level of pollutant for the cities concerned, it is relatively simple to produce a ranking of estimates according to the mean level of pollution (shown in the tables of individual city data). A relationship would be expected if a there was a threshold, or if another pollutant was an effect modifier. Fig. 1 gives an example by ranking estimates for all-cause mortality and PM_{10}, by the annual levels of PM_{10}.

It is seen that there is no apparent relationship, indicating that the relative risk estimates apply to a wide range of levels of PM_{10}.

Fig. 1. Ranking of PM_{10} estimates for all-cause mortality by annual average levels of PM_{10} (left y-axis: mean PM_{10} levels in µg/m^3; right y-axis: RR in total mortality of a 10 µg/m^3 increase of PM_{10})



5.2 Publication bias

Publication bias arises because there are more rewards for publishing positive or at least statistically significant findings. It is a common if not universal problem in our research culture (Sterling, 1959; Mahoney, 1977; Simes, 1986; Begg & Berlin, 1988 and 1989; Dickersin, 1997). In the case of time-series studies using routine data there are particular reasons why publication bias might occur. One is that the data are relatively cheap to obtain and analyse, so that there may be less determination to publish “uninteresting” findings. The other is that each study can generate a large number of results for various outcomes, pollutants and lags and there is quite possibly bias in the process of choosing amongst them for inclusion in a paper. In the field of air pollution epidemiology, the question of publication bias has only recently begun to be formally addressed (Anderson et al., 2002 and Peacock et al., 2002). A related source of bias is lag selection bias. These sources of bias are overcome by planned multicity studies (such as APHEA and NMMAPS) which have a commitment to publish and which may adopt an a priori lag specification.

There are methods of detecting publication bias but it should be noted that these are not without problems. One method is the “funnel plot” in which estimates are plotted against their standard error. If there is no publication bias, the resulting scatter should be symmetrically shaped like a funnel (Light & Pillemer, 1984). Evidence of asymmetry in the funnel plot can be tested by regressing the standardised effect size against the inverse of the standard error (Egger et al., 1997).

It is important to distinguish two different implications of publication bias. The first relates to hazard detection. Publication bias could lead to a false conclusion being drawn as to the association between air pollution and a health outcome, i.e. that there is an association when in fact there is none. The other implication is for health impact assessment because the publication bias could lead to inflation of the estimated magnitude of the health impacts. Therefore, it might be necessary to adjust for the bias before using the estimates in health impact assessments.

5.2.1 Time-series studies

The study results used in the calculation of the summary estimates in Tables 1 and 2 were investigated for evidence of asymmetry and therefore the possibility of publication bias. Asymmetry was assessed using both statistical procedures, Beggs test (Begg & Mazumdar, 1994) and Eggers test (Egger et al., 1997) and by graphical techniques using the funnel plot (Light & Pillemer, 1984). The "trim and fill" technique (Duval & Tweedie, 2000) was also applied both to further assess evidence for asymmetry and, where found, to calculate adjusted summary estimates.

For those pollutant-outcome pairs having sufficient numbers of estimates, the original and revised summary estimates are given in Tables 5 and 6. In all but one case there was evidence for asymmetry and possible publication bias. In some cases the evidence was strong with the graphical evidence concurring with the results of the significance tests. In others, e.g. PM_{10} and respiratory mortality, the evidence was less conclusive. In such cases the number of estimates "generated" by the trim and fill technique were small and the revised summary estimates little different to the originals.

Table 5. Original and revised summary relative risk estimates (for a 10 µg/m^3 increase) for selected pollutants and all-cause and cause-specific mortality. Revised estimates are calculated using the "trim and fill" technique. The total number of estimates used in the meta-analysis is indicated in bold.

Outcome/ Disease	*Age*	*Summary Estimate*	*PM_{10}*	*BS*	*Ozone (8-hour)*
All-Cause	All Age	Original (No. Estimates)	1.006 (1.004, 1.008) **33**	1.006 (1.004, 1.008) **26**	1.003 (1.001, 1.004) **15**
		Revised (No. Estimates)	1.006 (1.004, 1.008) **33**	1.004 (1.002, 1.007) **33**	1.002 (1.000, 1.003)[1] **20**
Respiratory	All Age	Original (No. Estimates)	1.013 (1.005, 1.020) **18**	1.006 (0.998, 1.015) **18**	1.000 (0.996, 1.005) **12**
		Revised (No. Estimates)	1.010 (1.001, 1.018) **20**	0.999 (0.990, 1.008) **24**	0.999 (0.995, 1.004) **15**
Cardio-vascular	All Age	Original (No. Estimates)	1.009 (1.005, 1.013) **17**	1.004 (1.002, 1.007) **18**	1.004 (1.003, 1.005) **13**
		Revised (No. Estimates)	1.005 (1.001, 1.010) **23**	1.004 (1.001, 1.006) **22**	1.004 (1.003, 1.005) **17**

[1] 1.0020 (1.0005, 1.0035).

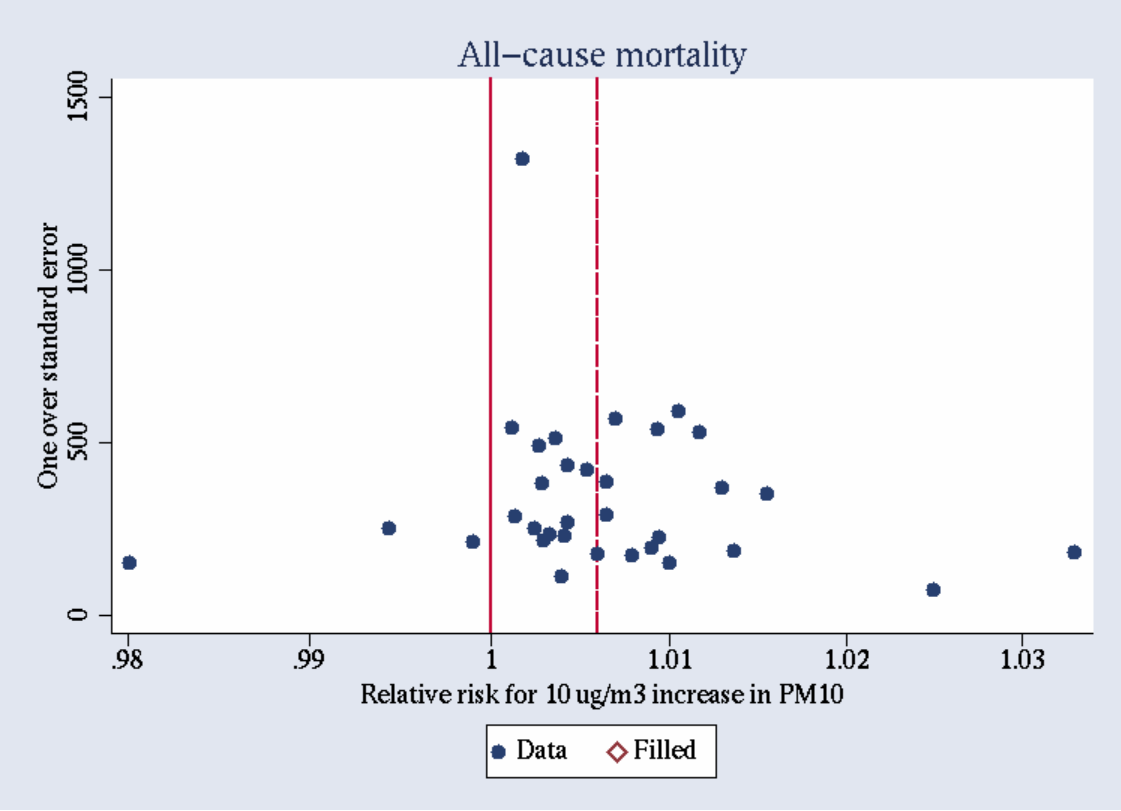
Table 6. Original and revised summary relative risk estimates (for a 10 µg/m^3 increase) for selected pollutants and respiratory hospital admissions. Revised estimates are calculated using the "trim and fill" technique. The total number of estimates used in the meta-analysis is indicated in bold.

Outcome/ Disease	*Age*	*Summary Estimate*	*PM_{10}*	*BS*
Respiratory	65+	Original (No. Estimates)	1.007 (1.002, 1.013) **8**	1.001 (0.993, 1.010) **6**
		Revised (No. Estimates)	1.006 (1.000, 1.011) **10**	1.001 (0.993, 1.009) **7**

Figures 2–12 show the funnel plots for each of the eleven pollutant-outcome pairs. These plots show the individual estimates plotted, as filled circles, against the reciprocal of the standard error (measure of estimate precision). The estimates "generated" by the "trim and fill" technique are shown as open diamonds. The original (long-dash line) and revised (short-dash line) summary estimates are also shown.

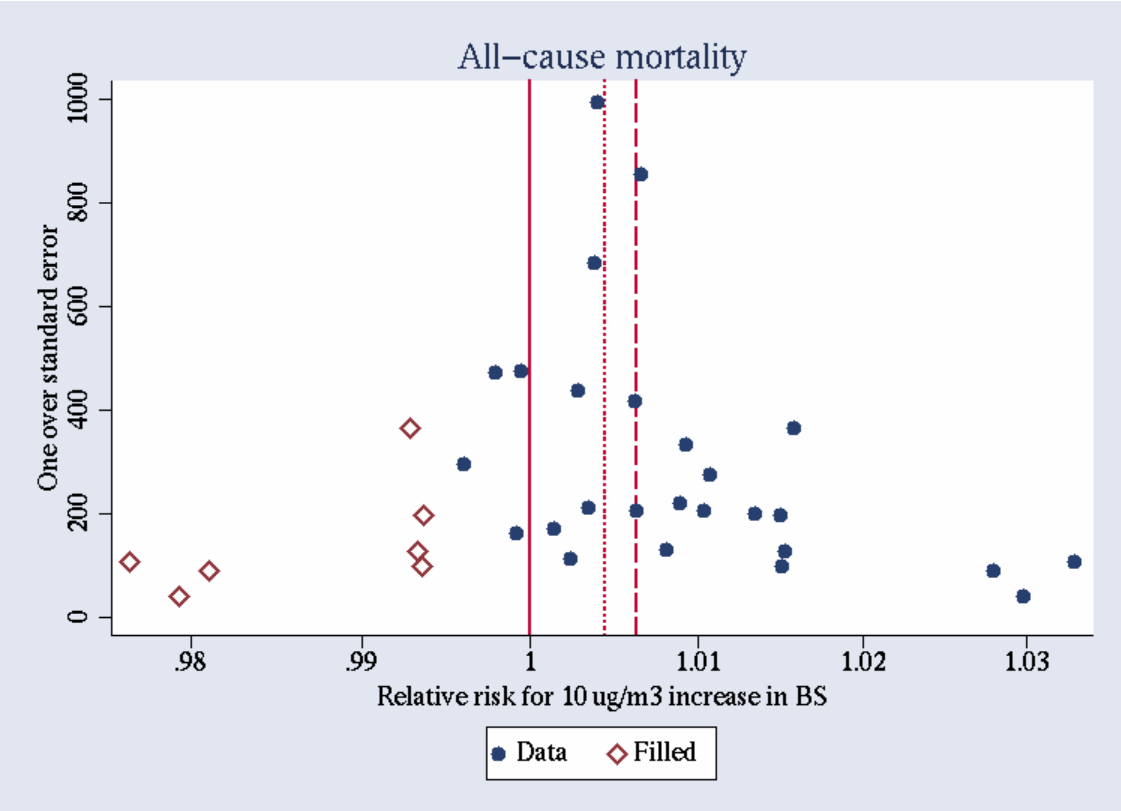
As previously noted the detection and adjustment for asymmetry and possible publication bias is not without its problems. There is evidence of asymmetry in most cases and that adjustment for this asymmetry leads to smaller summary effect estimates. However, the overall conclusions remain unaltered – that of small but statistically significant associations between air pollution measures and indicators of daily mortality and morbidity.

Fig. 2. Funnel plot of estimates for all-cause mortality and PM_{10}



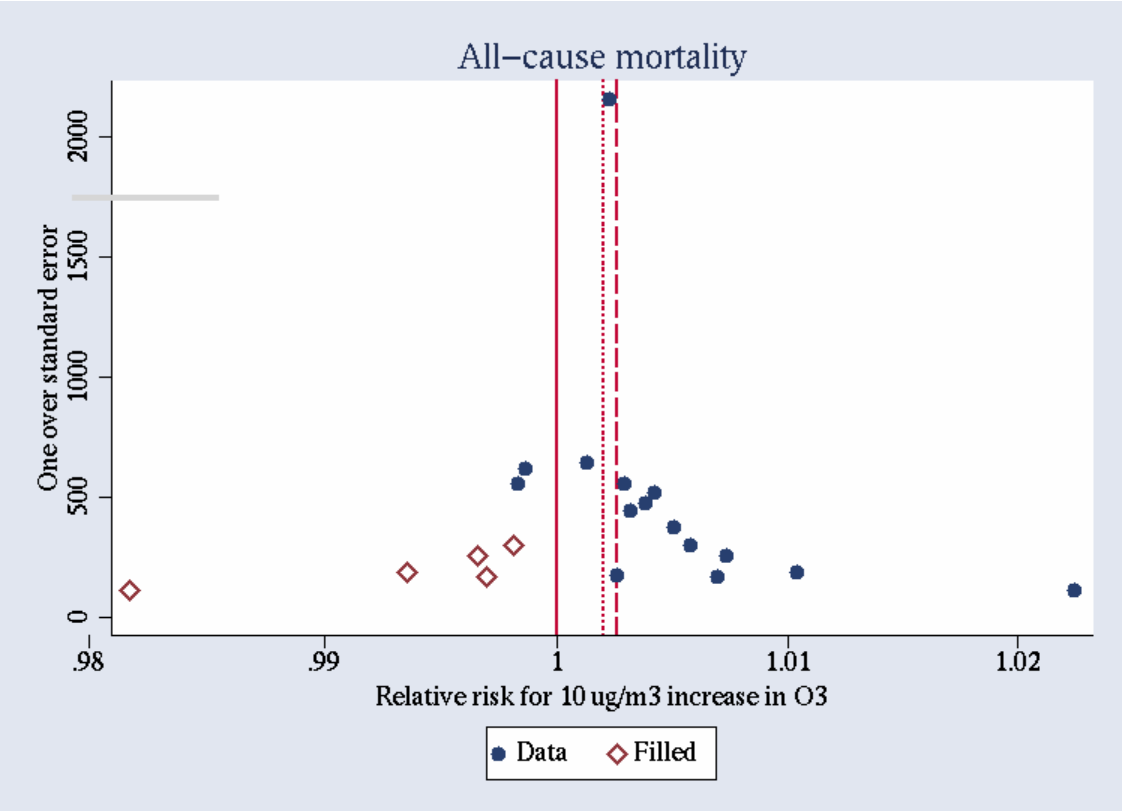
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 3. Funnel plot of estimates for all-cause mortality and black smoke



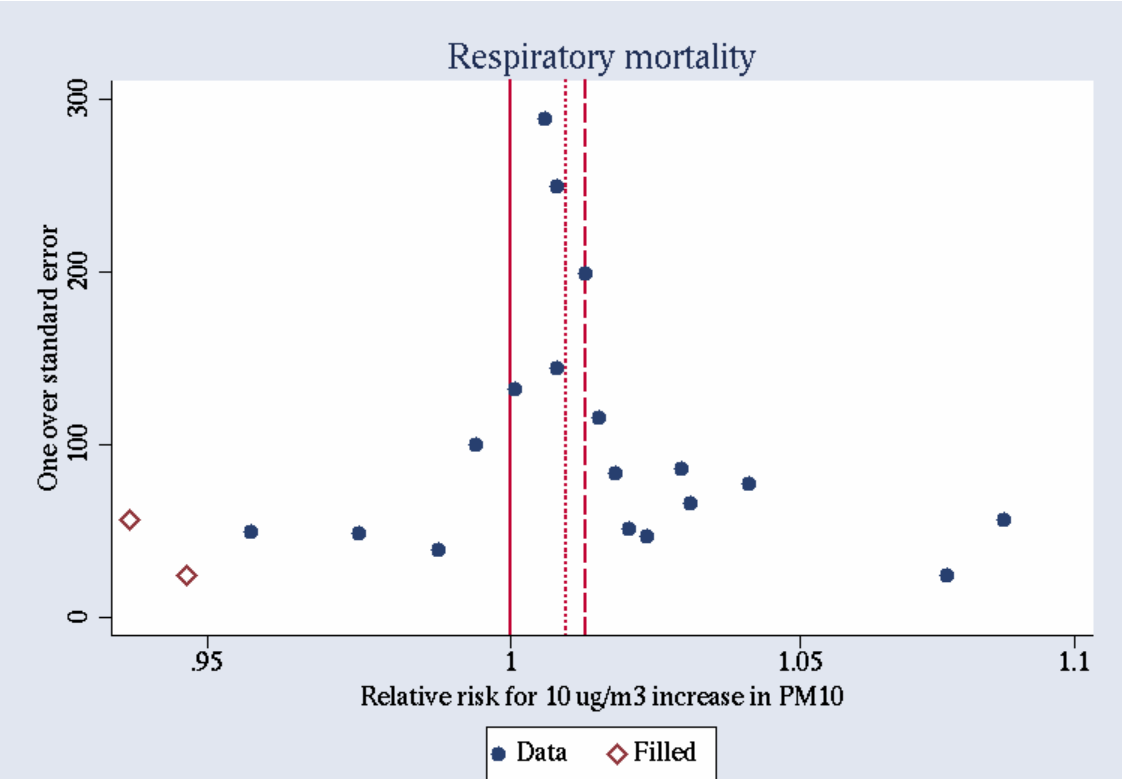
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 4. Funnel plot of estimates for all-cause mortality and ozone



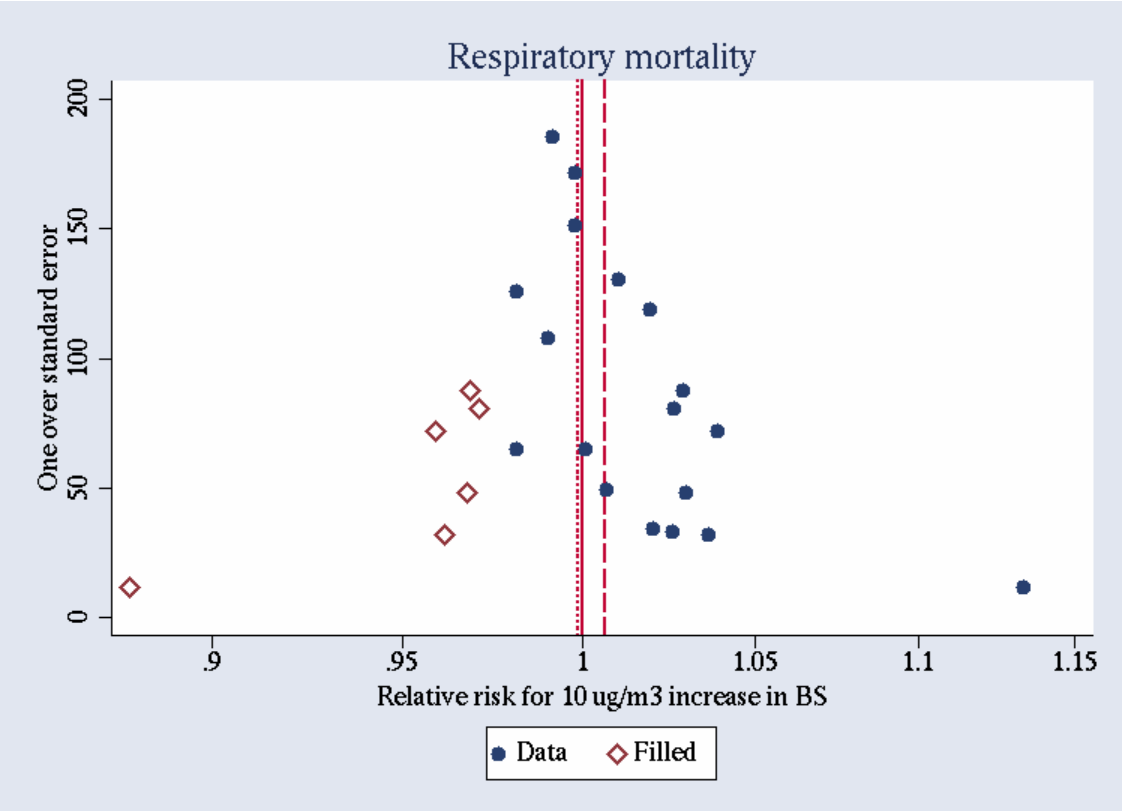
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 5. Funnel plot of estimates for respiratory mortality and PM_{10}



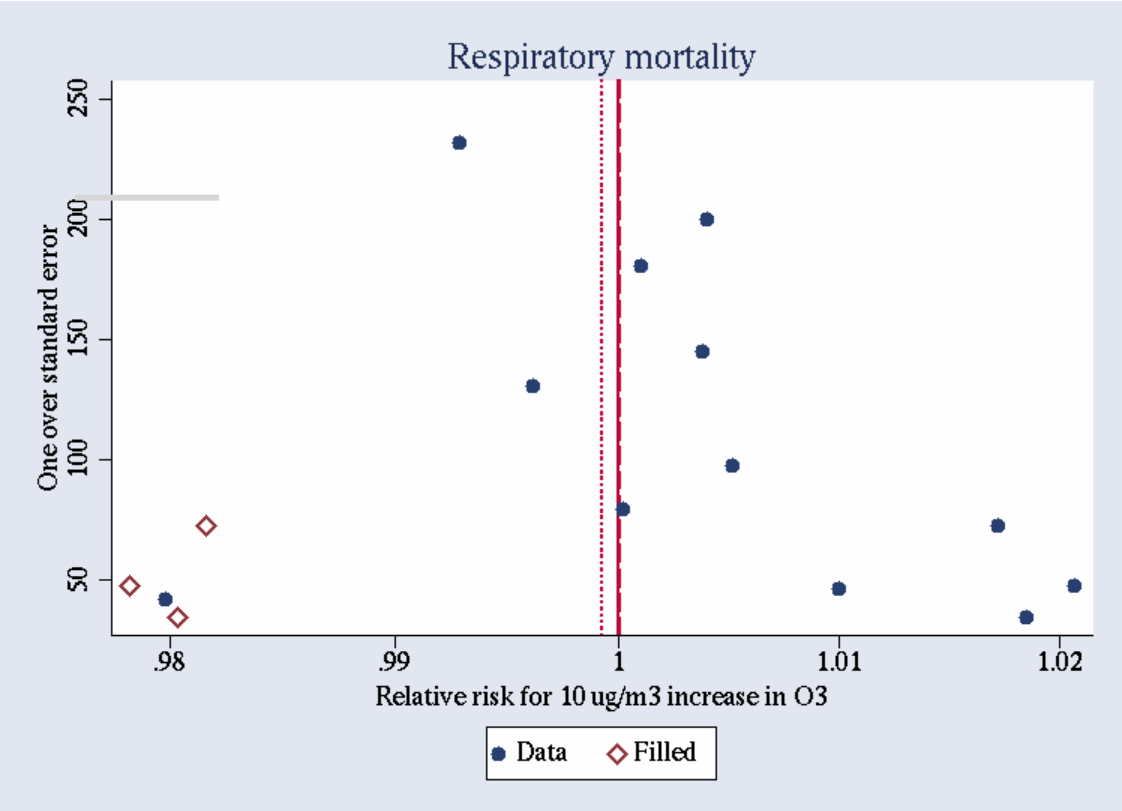
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 6. Funnel plot of estimates for respiratory mortality and black smoke



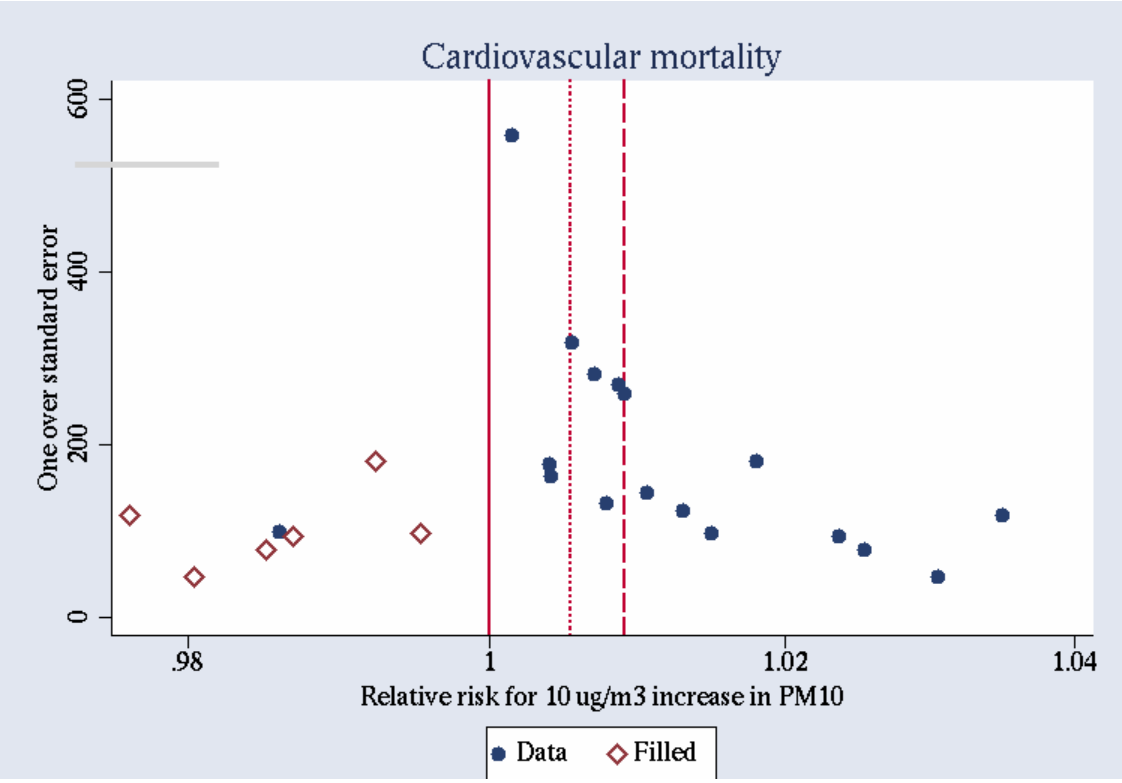
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 7. Funnel plot of estimates for respiratory mortality and ozone



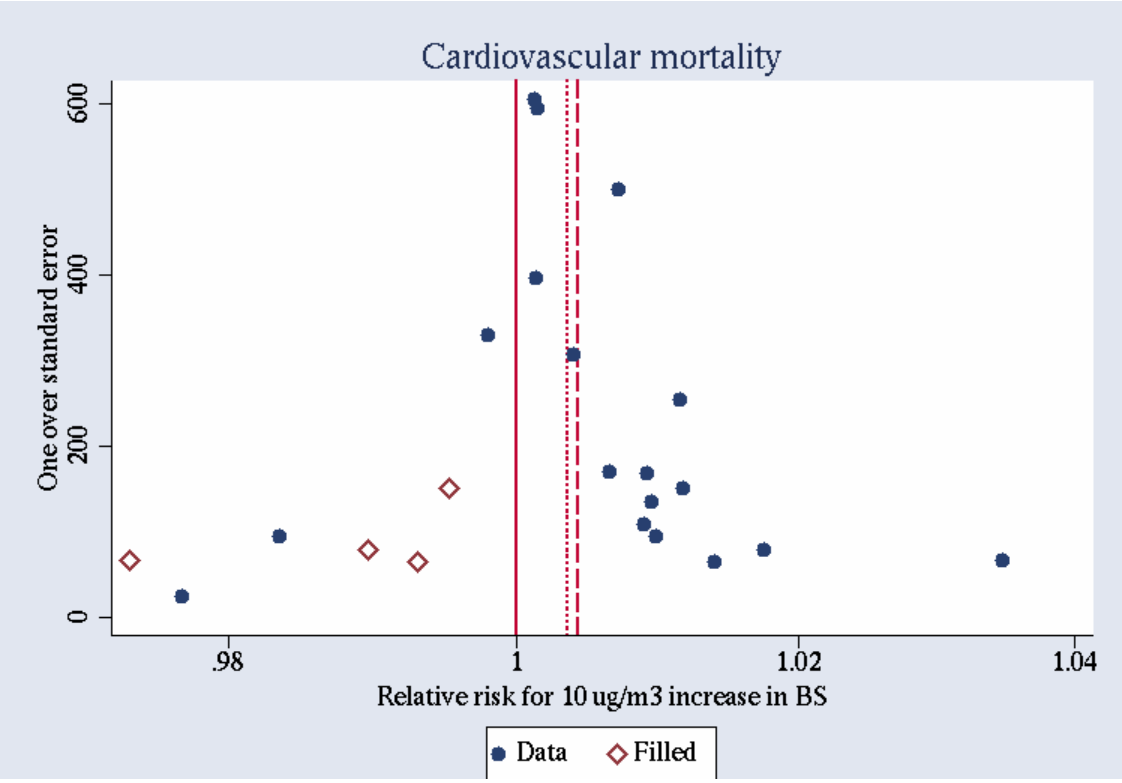
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 8. Funnel plot of estimates for cardiovascular mortality and PM_{10}



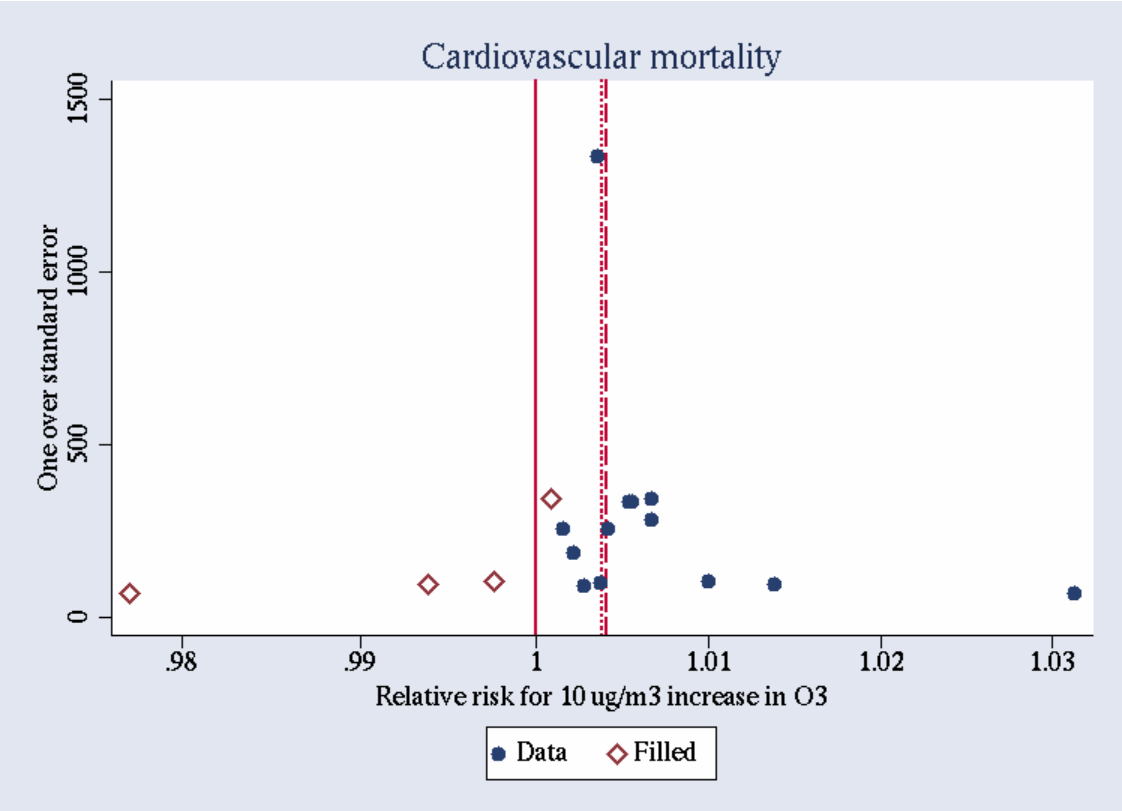
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 9. Funnel plot of estimates for cardiovascular mortality and black smoke



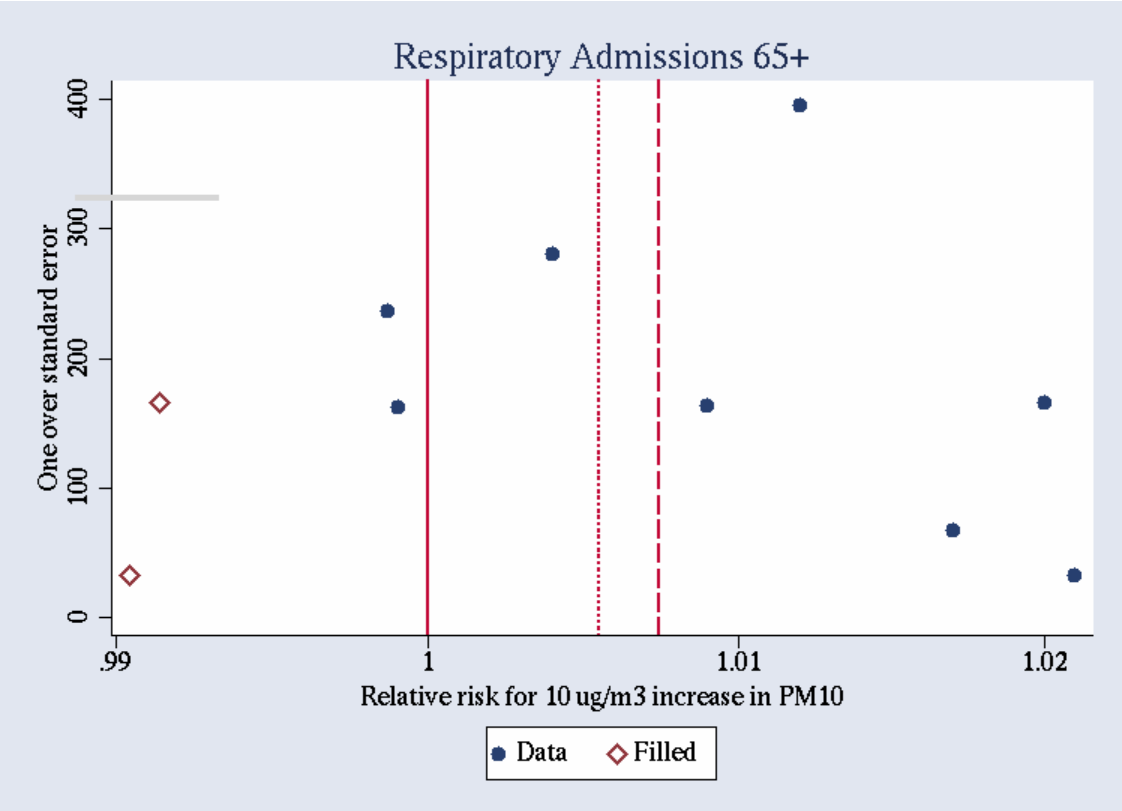
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 10. Funnel plot of estimates for cardiovascular mortality and ozone



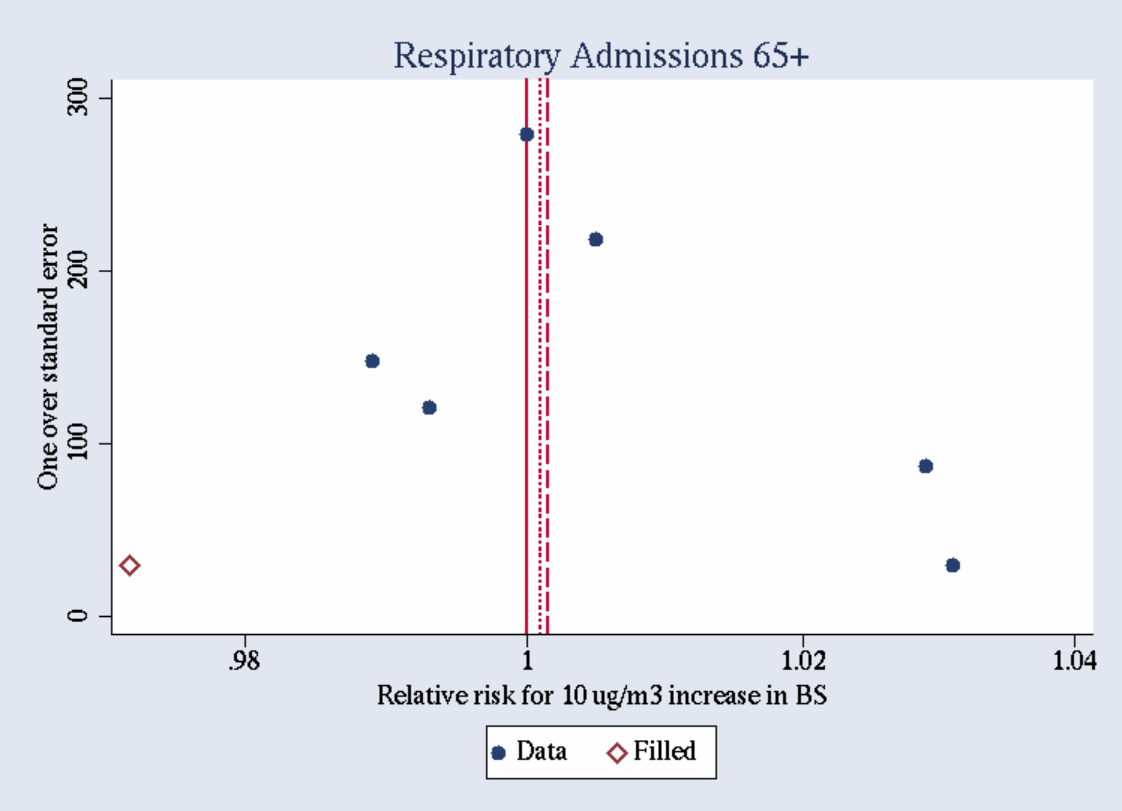
Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 11. Funnel plot of estimates for respiratory hospital admissions and PM_{10}



Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

Fig. 12. Funnel plot of estimates for respiratory hospital admissions and black smoke



Solid circles indicate original effect estimates plotted against the reciprocal of the standard error (precision of the estimates). Open diamonds are the study estimates generated by the trim and fill technique to make the funnel plot symmetrical. The long-dash line is the original summary estimate and the short-dash line the revised (including the generated estimates) summary estimate.

5.2.2 Panel studies

For the panel studies, there were seven pollutant-outcome pairs investigated, all of these relate to children. The original and revised estimates as a result of "trim and fill" are given in Table 7. There was no evidence of publication bias using either Begg's or Egger's test for any of the combinations. The only combination where there was asymmetry which resulted in the "trim and fill" technique "generating" new estimates was for black smoke and cough. This generated two estimates that changed the random effects estimate from 1.001 (95% confidence interval 0.982, 1.021) to 0.999 (95% confidence interval 0.980, 1.019). However, for this outcome the publication bias p-values for Begg's and Egger's tests are 0.975 and 0.650 respectively giving no evidence to suspect publication bias.

There are only three significant outcome-pollutant combinations, two indicating adverse effects of air pollution – lower respiratory symptoms and PM_{10} and peak expiratory flow rate (PEFR) and PM_{10}, the other being beneficial effects of air pollution, with upper respiratory symptoms and PM_{10}.

In conclusion there is no evidence of publication bias within the pollutant-outcome combinations studied within the panel studies.

Table 7. Original and revised summary Odds ratio (beta for PEFR) estimates for a 10 µg/m^3 increase for selected pollutants and child lung function and symptoms

Lung function/ symptom	***Summary Estimate***	***PM_{10}***	***BS***
Peak expiratory flow rate	Original (No. Estimates)	-0.085 (-0.136, -0.033) **41**	NA
	Revised (No. Estimates)	-0.085 (-0.136, -0.033) **41**	NA
Cough	Original (No. Estimates)	0.999 (0.987, 1.011) **34**	1.001 (0.982, 1.021) **33**
	Revised (No. Estimates)	0.999 (0.987, 1.011) **34**	0.999 (0.980, 1.019) **35**
Lower respiratory symptoms	Original (No. Estimates)	1.008 (1.000, 1.016) **39**	NA
	Revised (No. Estimates)	1.008 (1.000, 1.016) **39**	NA
Upper respiratory symptoms	Original (No. Estimates)	0.997 (0.994, 0.999) **39**	NA
	Revised (No. Estimates)	0.997 (0.994, 0.999) **39**	NA
Medication use	Original (No. Estimates)	1.005 (0.981, 1.029) **31**	1.008 (0.970, 1.049) **31**
	Revised (No. Estimates)	1.005 (0.981, 1.029) **31**	1.008 (0.970, 1.049) **31**

Revised estimates are calculated using the "trim and fill" technique. The total number of estimates used in the meta-analysis is indicated in bold.
NA – Not Applicable – publication bias not conducted due to small numbers of studies

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Annex 1

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Annex 2

MINUTES OF THE TASK GROUP MEETING IN LONDON

Background
The WHO project *"Systematic Review of Health Aspects of Air Quality in Europe"* aims to provide the Clean Air for Europe (CAFE) programme of the European Commission (DG Environment) with a systematic, periodic, scientifically independent review of the health aspects of air quality in Europe.

As part of this review process WHO convened a working group, which reviewed specific answers to a set of twelve questions in relation to the health effects of particulate matter, ozone and nitrogen dioxide. The report of this working group provides a comprehensive description of the hazards related to these pollutants, but no detailed guidance on risk assessment. Therefore, the working group also recommended conducting as a follow up of this work a quantitative meta-analysis of existing studies, which could subsequently *inter alia* be used for health impact assessments. The analysis will use the bibliographic database developed at the St George's Hospital Medical School as the main framework, and will be performed by a small task group of invited experts.

The meta-analysis will be used to update risk coefficients for selected health endpoints in relation to the exposure to ozone and particulate matter.

The experts from St. George's Hospital have prepared an interim report of their work. This report was distributed among the members of the task group at the end of March and highlighted a number of important questions to be answered by the task group in relation to the meta-analysis. Bert Brunekreef, Jordi Sunyer and Erich Wichmann, all members of the task group, provided written comments to the questions in advance, since they could not attend the meeting in London. The purpose of this meeting was therefore to review the progress of the meta-analysis, discuss any specific methodological issues identified by the task group members. The meeting was also supposed to discuss approaches to risk assessment. As a basis for this discussion, a proposal by IIASA on a methodology to perform an impact assessment of PM related mortality was also forwarded to the members of the working group.

Summary of discussion; its conclusions and recommendations

Discussion of the purpose of the meta-analysis
It was emphasized that the purpose of the meta-analysis was to provide updated concentration response (CR) functions for selected health outcomes for ozone and PM. These CR functions should be available for subsequent health impact assessments (calculation of attributable cases), but the process should also deepen the understanding of the relationship between exposure and the health outcomes, including aspects such as heterogeneity of effects, uncertainties and effect modifiers.

Discussion of meta-analysis of time-series and panel studies
Preliminary remark: The discussions of the task group were mainly focused on questions posed in a preliminary report by St. George's Hospital group. In answering the questions, the task group tried to take into account time and capacity constraints. Therefore, some of the

recommendations do not only reflect the scientific judgement of the group, but also reflects the priorities identified by the task group. (As a general approach, it was recommended to start with a rather inclusive approach, and to subsequently classify input and to perform sensitivity analyses.)

Is the number of estimates for a meta-analysis a relevant criterion in selecting studies for the purpose of the health impact assessment?
No, but there is a minimum number to justify the meta-analysis (as a rule of thumb: this number should be > 3).

Is the availability of base-rates relevant to the selection of the outcomes?
Yes, if the outcomes are to be used for subsequent health impact assessment. No, if the outcome will be used for other applications.

Which outcomes should be included?
Daily number of deaths from all causes (excluding accidents, murders, etc.), all respiratory disease and all cardiovascular disease. Calculations will be made for all ages; if a mortality study does not provides an estimate for all ages but does for an elderly group (defined as 65+ or other suitable age group) then they will be used instead.

Daily number of hospital admissions (incl. ED and ER admissions) for all respiratory diseases (All ages; 0–14; 15–65; 65+) and for all cardiovascular disease (All ages; 65+); Asthma (0–14, 15–64) and COPD (65+). Sensitivity analysis will be included to test the potential influence of ER and ED admissions compared to hospital emergency admissions (involving over night stay). The other sensitivity analysis involved an assessment of a study's ability to differentiate between emergency and elective hospital admissions – do you get different relative risks from studies of emergency hospital admissions compared to all hospital admissions (i.e. including elective admissions).

ER/ED/A&E visits for respiratory causes (All ages; 0–14; 15–65; 65+).

Symptom exacerbations in asthmatics: Analysis of cough in children and adults separately, medication use (both only to asthmatic subgroup applicable).

Sensitivity analyses would investigate effect of including estimates from what appeared to be post-hoc subgroup analyses within studies.

Which pollutants should be included?
PM measured as PM_{10}, $PM_{2.5}$, black smoke, and coarse particles.
Ozone.

Which lags should be chosen?
It was decided to use the "selected" lag for the analyses and to conduct a sensitivity analysis to assess the effect of using single-day lag versus a cumulative measure.

Which averaging time should be chosen?
For ozone, 8-hour average will be used at a first stage. The results from studies using 1 hour and 24 hours will be compared.

From which geographical areas should studies be selected?
It was decided to restrict the analysis to European studies. If not enough studies are available (e.g. for $PM_{2.5}$ or coarse fraction), these will be supplemented by studies from northern America.

If more than one study is available for a city/region, which one should be used?
Generally, the study that was published most recently should be used. However, exceptions to this rule might be warranted, but have to be justified case by case.

To what extent can differing definition of a disease category, in terms of ICD codes, be combined?
It was decided to allow all combinations, but to perform sensitivity analysis using more specific diagnosis.

To what extent should different seasons be analysed?
Analysis should be performed for the entire year and in addition, summer only and winter only (both ozone and PM).

Should results from multi-pollutant models be considered?
The group recommended to focus on single-pollutant models.

In addition, the Task Group added some more advice.

- It was recommended to investigate the potential publication bias in estimates derived from single-city studies. However, interpretation would have to be done very cautiously.
- The level of heterogeneity should be assessed, taking into account expected variations and calculating random-effect estimates. It was decided to dispense with the calculation of fixed-effect estimates and to go straight to the calculation of random-effects estimates.
- Unit risks should be used as intervals for summary estimates.
- Some studies have been re-analyzed recently using different statistical methods to derive effect estimates. Klea Katsouyanni was invited to prepare a proposal on how to handle these studies by 23 April.

Approaches to risk assessment
The group reiterated the usefulness of both long-term and short-term studies for risk assessments. There are currently no long-term studies on ozone showing convincing effects on mortality. In addition, short-term studies are needed to identify the health impacts on PM- and ozone-related morbidity. In contrast, PM-related mortality can be assessed more comprehensively based on results from cohort studies (for a more detailed discussions see: http://www.euro.who.int/document/e74256.pdf).

The outline of a methodology to estimate reduction of life expectation provided by IIASA was in general welcomed and regarded as appropriate. However, there are a number of points that would require a more deep discussion, including the following.

- The treatment of uncertainty described in the report was regarded as not sufficient.
- The motivation for the choice of the risk estimates should be discussed in more detail. Also the consequences of this choice have to be made transparent (for example, the finding that individuals with less than college education have an increased risk).

- The consequences of the use of a different method for the calculation life expectancy than the method described by Miller et al. should be investigated.
- Secondary organic aerosols should be included in the atmospheric modelling, since they can contribute significantly to the overall $PM_{2.5}$ mass and there are indications that this part is also critical from a health point of view.

WHO will get in contact with IIASA and propose a procedure for dealing with the issues mentioned above.

In addition, the need was identified to develop a comprehensive approach to the estimation of impacts using the concentration-response functions from time-series studies comparable to the one IIASA has developed for the estimation of impacts on survival.

Follow-up
The St. George's group is going to assess the work and prepare detailed plans for the work. The plan will be forwarded to WHO. Depending on the plan, it might be necessary to further prioritize the work. This will be done in close collaboration with WHO.

Annex 3

USE OF BIBLIOGRAPHIC DATABASE FOR SYSTEMATIC REVIEW

By Richard Atkinson, St. George's Hospital Medical School, London, United Kingdom

METHOD

1. Identification of time-series and panel studies

Three bibliographic databases were searched: Medline, Embase and Web of Science. Separate search strings for each study type, time-series and panel, were used. These were tested against known literature until we were satisfied that the search strings were sensitive enough to pick up all relevant studies. The full reference and abstract for each of the citations identified by the searches were downloaded from the source bibliographic databases into Reference Manager (RM) databases, one for potential time-series studies and one for potential panel studies. Within each of the RM databases the studies were assigned unique identification codes.

Papers already available to the academic department were checked for inclusion in the RM databases. Citations in reviews of the published literature (such as the recent consultation document on particles published by the United States Environmental Protection Agency) were also checked to ensure that no relevant papers were missed.

The process of identifying time-series or panel studies from those selected by the search strings comprised two stages. First, the abstracts of all studies were reviewed and obvious non-time series and non-panel studies (e.g. clinical, mechanistic, exposure assessment) were removed from the RM databases. In the second stage, copies of the remaining studies were obtained and the time-series and panel studies identified.

Once the time-series and panel studies had been identified they were assigned a code within RM indicating whether or not they provided *usable* numerical estimates of the effects of air pollution. If they did not provide usable estimates then the reason(s) was also recorded. Studies were classified as follows:

- studies providing *usable* numerical estimates of the effects of air pollution;
- studies providing numerical estimates that were *unusable* (e.g. because of inappropriate statistical methods or insufficient data provided in the paper);
- studies which did not provide numerical estimates for the effects of air pollution (e.g. where the association between air pollution and health is assessed using a correlation coefficient);
- those studies which reviewed published literature;
- those studies using existing data or simulated data to develop new analytical techniques;
- others (letters, editorials, errata, meeting abstracts, case crossover and case control study designs).

2. Studies providing usable numerical estimates

For all time-series and panel studies providing usable regression estimates a number of items of data were identified, recorded on a coding sheet and then entered into Access databases, one containing details of results for all time-series studies and the other containing similar information for all panel studies. These data described basic features of each study as well as recording the regression coefficients, standard errors and the information necessary to calculate standardized estimates of the health effects of each pollutant. Variables were also included that described relevant elements of the analysis such as the length of the study period, year of study, continent, average pollution levels, etc. General information about each study contained in the RM databases (title, authors, journal reference, etc.) was also downloaded into the Access databases. These study specific data were linked to the result specific data using the relational features of the Access software.

3. Studies providing unusable numerical estimates

A number of studies contained numerical estimates but were not included in the Access databases. The reason(s) for their exclusion were coded in the RM databases and fell largely into two categories, statistical method and data quality. The former included studies that did not control for seasonality and other confounders adequately and the latter included studies that were of a very limited period or a very small population (e.g. a single hospital).

4. Presentation of results

In time-series studies, relative risks, regression estimates and percentage changes in the mean number of events per day were all used to assess the association between the pollutants and health outcomes. In order to make results comparable estimates from Poisson and log-linear models (relative risks, regression estimates and percentage changes) were converted into a standard metric: percentage change in the mean number of daily events associated with a 10 $\mu g/m^3$ increase in the pollutant (100 mg/m^3 increase for CO). Access queries were written to calculate these adjusted estimates. Estimates from linear models were standardized to the change in the number of events associated with 10 $\mu g/m^3$ increases in the pollutant (100 mg/m^3 increases for CO). Where the logarithm of the pollutant was used in the model, the results were quoted for a unit change in the pollutant level on the logarithmic scale – in other words, the number of health events or percentage change in the number of health events associated with a doubling of the pollutant level.

A similar process was undertaken for panel study results. Most studies using binary outcomes used logistic regression and presented odds ratios. These have been converted to represent 10 $\mu g/m^3$ increases in the pollutant. The results for continuous outcomes were usually given as betas, sometimes as percentage change. These have been converted to betas for 10 $\mu g/m^3$ increases in the pollutant. Results recorded as percentage change have been converted to betas where this was possible (only a few cases). Units for lung function were standardized to litres (L) or L/min as appropriate.

Access forms provide a user interface to the databases. They allow the user to select a set of the results defined by outcome, disease, age group, pollutant etc. The standardized regression estimates are calculated and then displayed using a “forest” plot. The estimates are assumed to come from Poisson or log-linear models with linear terms for the pollutants. Results from other model specifications or where a non-linear term for the pollutant was used are highlighted on the plot.

5. Selection of lags

Many studies investigated and reported results for a number of pollutant lags or days prior to the health events. Some studies specified an *a priori* lag for investigation whilst others investigated a number of lags and reported only those that had the largest (or largest positive) effect or were statistically significant. It was desirable to be able to specify the lag for specific analyses but also it was essential that a result for each outcome/pollutant combination from each study could be easily selected for presentation without reference to a specified lag. For a given outcome defined by event type (mortality/admission, etc.), disease group and age group and a given pollutant, a single result was extracted and denoted as the "selected" result for that combination of outcome and pollutant. The selection was made in priority order as follows:

Only one lag measure presented (this may be because only one was examined or only one was presented in the paper).

Results for more than one lag presented. The lag selected was chosen as:

2.1 Lag focused on by author OR
2.2 Most statistically significant OR
2.3 Largest estimate.

In addition to this selected lag, results for lag 0 and lag 1 were recorded (if different to "selected" lag from above process). A result for a cumulative lag (mean of pollution measures over 2 or more days), chosen by criteria 2.1–2.3 above was also recorded when cumulative results were available.

Some studies only provided results by season, that is, if no all-year analyses were undertaken. In these cases the selection process described above applied to each season analysed. Where only results from multi-pollutant models (two, three, four pollutants in a single statistical model) were given then the results from the model with the most pollutants in it was selected for inclusion in the Access database.

For panel studies a similar approach was used.

6. Multicity studies

A number of recent studies have presented meta-analyses of results from several locations. As well as presenting results from each location, summary estimates have been calculated. Where such studies have used previously published data only the summary estimates have been recorded. Where previously unpublished city-specific results are presented they have been recorded separately.

7. Summary estimates

Regression estimates and standard errors for each group of studies were transferred into STATA where standard procedures within STATA were used to calculate fixed- and random-effects summary estimates.

Annex 4

TABLES OF INDIVIDUAL CITY RESULTS – TIME-SERIES

Table A1. All-cause mortality, PM_{10}

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Katsouyanni et al., 2001	Athens	Greece	1992–1996	<800	lag 0–1	1.55	0.98	2.11	0.01534	0.00284	1.01546	1.00982	1.02114	40
Katsouyanni et al., 2001	Barcelona	Spain	1991–1996	<800	lag 0–1	0.93	0.57	1.30	0.00928	0.00185	1.00932	1.00567	1.01299	60
Katsouyanni et al., 2001	Basel	Switzerland	1990–1995	<800	lag 0–1	0.41	–0.44	1.28	0.00412	0.00436	1.00413	0.99558	1.01275	28
Katsouyanni et al., 2001	Birmingham, West Midlands	United Kingdom	1992–1996	<800	lag 0–1	0.28	–0.23	0.80	0.00282	0.00262	1.00282	0.99768	1.00799	21
Katsouyanni et al., 2001	Budapest	Hungary	1992–1995	<800	lag 0–1	0.29	–0.61	1.20	0.00289	0.00462	1.00289	0.99385	1.01201	40
Katsouyanni et al., 2001	Cracow	Poland	1990–1996	<800	lag 0–1	0.13	–0.54	0.82	0.00135	0.00346	1.00135	0.99458	1.00816	54
Katsouyanni et al., 2001	Erfurt	Germany	1991–1995	<800	lag 0–1	–0.56	–1.33	0.21	–0.00564	0.00394	0.99438	0.98673	1.00208	48
Katsouyanni et al., 2001	Geneva	Switzerland	1990–1995	<800	lag 0–1	–0.10	–1.01	0.82	–0.00103	0.00468	0.99897	0.98986	1.00817	33
Katsouyanni et al., 2001	Helsinki	Finland	1993–1996	<800	lag 0–1	0.32	–0.51	1.17	0.00324	0.00427	1.00324	0.99488	1.01167	23
Katsouyanni et al., 2001	London	United Kingdom	1992–1996	<800	lag 0–1	0.69	0.35	1.04	0.00691	0.00175	1.00694	1.00349	1.01040	25
Katsouyanni et al., 2001	Lyon	France	1993–1997	<800	lag 0–1	1.36	0.31	2.42	0.01353	0.00531	1.01362	1.00313	1.02423	39
Katsouyanni et al., 2001	Madrid	Spain	1992–1995	<800	lag 0–1	0.53	0.07	1.00	0.00531	0.00238	1.00532	1.00065	1.01002	33
Katsouyanni et al., 2001	Milan	Italy	1990–1996	<800	lag 0–1	1.17	0.79	1.54	0.01160	0.00189	1.01167	1.00794	1.01542	47
Katsouyanni et al., 2001	Paris	France	1991–1996	<800	lag 0–1	0.43	–0.02	0.88	0.00427	0.00230	1.00428	0.99976	1.00881	22
Katsouyanni et al., 2001	Prague	Czech Republic	1992–1996	<800	lag 0–1	0.12	–0.24	0.48	0.00122	0.00183	1.00122	0.99763	1.00482	66
Katsouyanni et al., 2001	Rome	Italy	1992–1996	<800	lag 0–1	1.29	0.76	1.83	0.01283	0.00270	1.01292	1.00757	1.01829	57

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Katsouyanni et al., 2001	Stockholm	Sweden	1990–1996	<800	lag 0–1	0.39	–1.29	2.10	0.00389	0.00863	1.00390	0.98706	1.02102	14
Katsouyanni et al., 2001	Tel Aviv	Israel	1991–1996	<800	lag 0–1	0.64	0.13	1.15	0.00641	0.00259	1.00643	1.00134	1.01154	43
Katsouyanni et al., 2001	Teplice	Slovakia	1990–1997	<800	lag 0–1	0.64	–0.03	1.32	0.00641	0.00344	1.00643	0.99966	1.01325	42
Katsouyanni et al., 2001	Torino	Italy	1990–1996	<800	lag 0–1	1.05	0.72	1.39	0.01046	0.00169	1.01052	1.00717	1.01388	65
Katsouyanni et al., 2001	Zurich	Switzerland	1990–1995	<800	lag 0–1	0.43	–0.30	1.16	0.00424	0.00370	1.00425	0.99701	1.01155	28
Zeghnoun et al. 2001	Le Havre	France	1990–1995	<800	lag 1	0.79	–0.34	1.93	0.00788	0.00573	1.00791	0.99664	1.01929	30.8
Zeghnoun et al. 2001	Rouen	France	1990–1995	<800	lag 1	0.24	–0.54	1.03	0.00242	0.00397	1.00242	0.99464	1.01026	27.7
Zeghnoun et al. 2001	Strasbourg	France	1990–1995	<800	lag 2	0.60	–0.50	1.71	0.00596	0.00561	1.00598	0.99499	1.01710	29
Biggeri et al. 2001	Bologna	Italy	1996–1998	<800	lag 0–1	0.90	–0.10	1.91	0.00896	0.00508	1.00900	0.99900	1.01910	41.2
Biggeri et al. 2001	Florence	Italy	1996–1998	<800	lag 0–1	1.00	–0.30	2.32	0.00995	0.00661	1.01000	0.99700	1.02317	40.3
Biggeri et al. 2001	Palermo	Italy	1997–1999	<800	lag 0–1	3.30	2.20	4.41	0.03247	0.00546	1.03300	1.02200	1.04412	42.9
Roemer et al. 2001	Amsterdam	Netherlands	1987–1998		lag 1	0.27	–0.13	0.67	0.00266	0.00203	1.00267	0.99869	1.00666	34
Peters et al. 2000	Czech Republic	Czech Republic	1982–1994	<800	lag 1	0.94	0.07	1.82	0.00935	0.00441	1.00939	1.00070	1.01816	45
Daponte et al. 1999	Huelva	Spain	1993–1996	<800	lag 0	2.49	–0.21	5.26	0.02460	0.01362	1.02490	0.99790	1.05263	40
Spix et al., 1996	Koln	Germany	1975–1985		lag 1	0.36	–0.02	0.75	0.00361	0.00196	1.00362	0.99978	1.00747	34
Hoek et al., 2000	Netherlands	Netherlands	1986–1994	<800	lag 1	0.18	0.03	0.33	0.00178	0.00076	1.00179	1.00030	1.00327	34
Ocana–Riola et al. 1999	Seville	Spain	1992–1996	<800	lag 5	–1.99	–3.23	–0.74	–0.02013	0.00650	0.98007	0.96766	0.99264	42.68

Table A2. Cardiovascular mortality, PM_{10}

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Biggeri et al. 2001	Bologna	Italy	1996–1998	390–459	lag 0–1	1.30	–0.30	2.93	0.0129162	0.008123	1.013	0.997	1.0292568	41.2
Biggeri et al. 2001	Florence	Italy	1996–1998	390–459	lag 0–1	1.50	–0.50	3.54	0.0148886	0.010154	1.015	0.995	1.035402	40.3
Biggeri et al. 2001	Milan	Italy	1995–1997	390–459	lag 0–1	0.40	–0.70	1.51	0.003992	0.005621	1.004	0.993	1.0151219	45.2
Biggeri et al. 2001	Palermo	Italy	1997–1999	390–459	lag 0–1	3.50	1.80	5.23	0.0344014	0.00845	1.035	1.018	1.0522839	42.9
Biggeri et al. 2001	Rome	Italy	1995–1997	390–459	lag 0–1	1.80	0.70	2.91	0.0178399	0.005543	1.018	1.007	1.0291202	59
Biggeri et al. 2001	Turin	Italy	1995–1998	390–459	lag 0–1	0.70	0.00	1.40	0.0069756	0.003559	1.007	1	1.014049	63.8
Ocana–Riola et al. 1999	Seville	Spain	1992–1996	390–459	lag 5	–1.40	–3.31	0.55	–0.01409	0.01	0.98601	0.966871	1.0055252	42.68
Galan et al. 1999	Madrid	Spain	1992–1995	390–459	lag 0	0.91	0.15	1.68	0.0090588	0.003857	1.0091	1.0015	1.0167577	32.8
Daponte et al. 1999	Huelva	Spain	1993–1996	390–459	lag 5	3.05	–1.15	7.43	0.0300441	0.02123	1.0305	0.9885	1.0742845	40
Zeghnoun et al. 2001	Le Havre	France	1990–1995	390–459	lag 1	2.55	0.04	5.12	0.025169	0.012628	1.02549	1.000418	1.0511868	30.8
Zeghnoun et al. 2001	Paris	France	1990–1995	390–459	lag 2	0.86	0.13	1.60	0.0086108	0.003714	1.00865	1.001333	1.0160165	22
Zeghnoun et al. 2001	Rouen	France	1990–1995	390–459	lag 1	1.06	–0.29	2.43	0.0105638	0.00688	1.01062	0.997083	1.0243406	27.7
Zeghnoun et al. 2001	Strasbourg	France	1990–1995	390–459	lag 3	2.37	0.25	4.54	0.0234418	0.010688	1.02372	1.002497	1.0453898	29
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	0.41	–0.78	1.61	0.004078	0.006092	1.00409	0.992169	1.0161468	20
Bremner et al. 1999	London	United Kingdom	1992–1994	390–459	lag 1	0.55	–0.07	1.17	0.0054909	0.003134	1.00551	0.999348	1.0117019	24.8
Wichmann et al. 2000	Erfurt	Germany	1995–1998		lag 0	0.79	–0.69	2.29	0.0078561	0.007541	1.00789	0.993099	1.0228956	31
Hoek et al. 2001	Netherlands	Netherlands	1986–1994	390–448	lag 0–6	0.15	–0.20	0.50	0.0014911	0.001789	1.00149	0.997986	1.0050108	

Table A3. Respiratory mortality, PM_{10}

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/median
Biggeri et al. 2001	Bologna	Italy	1996–1998	460–519	lag 0–1	–4.30	–8.00	–0.45	–0.04395	0.02012	–0.05300	–0.09000	–0.01451	41.2
Biggeri et al. 2001	Florence	Italy	1996–1998	460–519	lag 0–1	–1.20	–6.00	3.85	–0.01207	0.02541	–0.02200	–0.07000	0.02845	40.3
Biggeri et al. 2001	Milan	Italy	1995–1997	460–519	lag 0–1	4.10	1.50	6.77	0.04018	0.01290	0.03100	0.00500	0.05767	45.2
Biggeri et al. 2001	Palermo	Italy	1997–1999	460–519	lag 0–1	8.70	5.00	12.53	0.08342	0.01767	0.07700	0.04000	0.11530	42.9
Biggeri et al. 2001	Rome	Italy	1995–1997	460–519	lag 0–1	3.10	0.10	6.19	0.03053	0.01507	0.02100	–0.00900	0.05190	59
Biggeri et al. 2001	Turin	Italy	1995–1998	460–519	lag 0–1	1.50	–0.20	3.23	0.01489	0.00862	0.00500	–0.01200	0.02229	63.8
Daponte et al. 1999	Huelva	Spain	1993–1996	460–519	lag 3	7.65	–0.64	16.63	0.07372	0.04089	0.06650	–0.01640	0.15632	40
Galan et al. 1999	Madrid	Spain	1992–1995	460–519	lag 1	0.80	–0.56	2.18	0.00797	0.00693	–0.00200	–0.01560	0.01179	32.8
Ocana–Riola et al. 1999	Seville	Spain	1992–1996	460–519	lag 2	–2.53	–6.37	1.46	–0.02565	0.02050	–0.03532	–0.07371	0.00464	42.68
Zeghnoun et al. 2001	Le Havre	France	1990–1995	460–519	lag 2	2.02	–1.82	6.02	0.02002	0.01959	0.01022	–0.02822	0.05016	30.8
Zeghnoun et al. 2001	Paris	France	1990–1995	460–519	lag 1	0.07	–1.40	1.56	0.00067	0.00756	–0.00933	–0.02405	0.00560	22
Zeghnoun et al. 2001	Strasbourg	France	1990–1995	460–519	lag 3	2.32	–1.87	6.69	0.02296	0.02133	0.01323	–0.02867	0.05692	29
Zeghnoun et al. 2001	Rouen	France	1990–1995	460–519	lag 0–1	1.78	–0.58	4.20	0.01764	0.01199	0.00779	–0.01584	0.03199	27.7
Wichmann et al. 2000	Erfurt	Germany	1995–1998		lag 0	2.92	0.61	5.28	0.02879	0.01158	0.01920	–0.00390	0.04283	31
Krzyzanowski et al. 1991	Krakow	Poland	1977–1989		lag 1–4	0.58	–0.10	1.26	0.00576	0.00346	–0.00422	–0.01102	0.00258	
Bremner et al. 1999	London	United Kingdom	1992–1994	460–519	lag 3	1.29	0.29	2.29	0.01278	0.00503	0.00286	–0.00708	0.01289	24.8
Zmirou et al., 1996	Lyon	France	1985–1990	460–519	lag 0	0.79	0.00	1.58	0.00784	0.00400	–0.00213	–0.01000	0.00581	38.1
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.58	–2.50	1.39	–0.00578	0.00999	–0.01576	–0.03504	0.00390	20

Table A4. Admissions, PM_{10}

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
All respiratory, ages 65+														
Atkinson et al. 2001	Barcelona	Spain	1994–1996	460–519	lag 0–1	2.00	0.80	3.21	0.01980	0.00604	1.02000	1.00800	1.03214	53.3
Atkinson et al. 2001	Birmingham, West Midlands	United Kingdom	1992–1994	460–519	lag 0–1	0.90	–0.30	2.11	0.00896	0.00610	1.00900	0.99700	1.02114	21.5
Atkinson et al. 2001	London	United Kingdom	1992–1994	460–519	lag 0–1	0.40	–0.30	1.10	0.00399	0.00357	1.00400	0.99700	1.01105	24.9
Atkinson et al. 2001	Netherlands	Netherlands	1992–1995	460–519	lag 0–1	1.20	0.70	1.70	0.01193	0.00253	1.01200	1.00700	1.01702	33.4
Atkinson et al. 2001	Paris	France	1992–1996	460–519	lag 0–1	−0.10	–1.30	1.11	−0.00100	0.00617	0.99900	0.98700	1.01115	20.1
Atkinson et al. 2001	Stockholm	Sweden	1994–1996	460–519	lag 0–1	1.70	–1.20	4.69	0.01686	0.01476	1.01700	0.98800	1.04685	13.6
Prescott et al. 1998	Edinburgh 1	United Kingdom	1981–1995	480–487, 490–496	lag 1–3	2.10	–3.80	8.36	0.02078	0.03037	1.02100	0.96200	1.08362	20.7
Michelozzi et al. 2000	Rome	Italy	1992–1997	460–519	lag 0	−0.13	–0.95	0.70	−0.00130	0.00423	0.99871	0.99046	1.00702	
All respiratory, ages 15–64														
Atkinson et al. 1999	London	United Kingdom	1992–1994	460–519	lag 2	1.36	0.41	2.32	0.01353	0.00482	1.01362	1.00409	1.02324	24.8
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	0.04	–1.66	1.77	0.00041	0.00874	1.00041	0.98341	1.01770	20
Michelozzi et al. 2000	Rome	Italy	1992–1997	460–519	lag 0	0.47	–0.56	1.52	0.00472	0.00528	1.00473	0.99438	1.01519	
All respiratory, ages 0–14														
Atkinson et al. 1999	London	United Kingdom	1992–1994	460–519	lag 1	1.55	0.67	2.45	0.01543	0.00447	1.01555	1.00670	1.02447	24.8
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	1.58	0.25	2.93	0.01568	0.00675	1.01580	1.00245	1.02933	20
Michelozzi et al. 2000	Rome	Italy	1992–1997	460–519	lag 0	−0.22	–1.39	0.97	−0.00216	0.00605	0.99784	0.98608	1.00974	
Cardiovascular, ages 65+														
Prescott et al. 1998	Edinburgh 1	United Kingdom	1981–1995	410–414, 426–429, 434–440	lag 1–3	4.80	0.90	8.85	0.04688	0.01935	1.04800	1.00900	1.08851	20.7
Atkinson et al. 1999	London	United Kingdom	1992–1994	390–459	lag 0	0.50	–0.04	1.04	0.00495	0.00274	1.00496	0.99958	1.01037	24.8

Table A5. All–cause mortality, black smoke

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Arribas et al. 1999	Saragossa	Spain	1991–1995	<800	lag 1	2.80	0.60	5.05	0.02762	0.01104	1.02800	1.00600	1.05048	44
Perez Boillos et al. 1999	Vitoria–Gasteiz	Spain	1990–1994	<800	lag 1	0.63	–0.32	1.59	0.00628	0.00484	1.00630	0.99680	1.01589	45
Taracido et al. 1999	Vigo	Spain	1991–1994	<800	lag 5	–0.40	–1.06	0.26	–0.00401	0.00339	0.99600	0.98940	1.00264	98.13
Aguinaga et al. 1999	Pamplona	Spain	1991–1995	<800	lag 0	2.98	–1.88	8.09	0.02941	0.02470	1.02985	0.98119	1.08092	21.67
Bellido Blasco et al. 1999	Castellon	Spain	1991–1995	<800	lag 2	1.51	–0.50	3.56	0.01499	0.01020	1.01510	0.99500	1.03561	20.3
Katsouyanni et al., 2001	Athens	Greece	1992–1996	<800	lag 0–1	0.66	0.43	0.89	0.00655	0.00117	1.00657	1.00426	1.00888	64
Katsouyanni et al., 2001	Barcelona	Spain	1991–1996	<800	lag 0–1	1.58	1.04	2.13	0.01570	0.00273	1.01583	1.01040	1.02129	39
Katsouyanni et al., 2001	Bilbao	Spain	1992–1996	<800	lag 0–1	0.82	–0.67	2.32	0.00813	0.00757	1.00817	0.99331	1.02324	23
Katsouyanni et al., 2001	Birmingham, West Midlands	United Kingdom	1992–1996	<800	lag 0–1	0.34	–0.59	1.28	0.00342	0.00475	1.00342	0.99413	1.01280	11
Katsouyanni et al., 2001	Cracow	Poland	1990–1996	<800	lag 0–1	–0.21	–0.62	0.21	–0.00207	0.00212	0.99793	0.99379	1.00209	36
Katsouyanni et al., 2001	Dublin	Ireland	1990–1996	<800	lag 0–1	1.04	0.09	2.00	0.01038	0.00483	1.01043	1.00092	1.02004	10
Katsouyanni et al., 2001	Ljubljana	Slovenia	1992–1996	<800	lag 0–1	–0.09	–1.27	1.11	–0.00087	0.00609	0.99913	0.98728	1.01113	13
Katsouyanni et al., 2001	Lodz	Poland	1990–1996	<800	lag 0–1	–0.06	–0.47	0.36	–0.00058	0.00211	0.99942	0.99530	1.00356	30
Katsouyanni et al., 2001	London	United Kingdom	1992–1996	<800	lag 0–1	0.93	0.34	1.53	0.00929	0.00300	1.00933	1.00341	1.01529	11
Katsouyanni et al., 2001	Marseille	France	1990–1995	<800	lag 0–1	1.08	0.37	1.80	0.01073	0.00361	1.01078	1.00365	1.01796	34
Katsouyanni et al., 2001	Paris	France	1991–1996	<800	lag 0–1	0.38	0.10	0.67	0.00383	0.00146	1.00383	1.00096	1.00672	21
Katsouyanni et al., 2001	Poznan	Poland	1990–1996	<800	lag 0–1	0.63	0.16	1.10	0.00624	0.00239	1.00626	1.00156	1.01098	23
Katsouyanni et al., 2001	Valencia	Spain	1994–1996	<800	lag 0–1	1.35	0.36	2.35	0.01342	0.00499	1.01351	1.00364	1.02348	40
Katsouyanni et al., 2001	Wroclaw	Poland	1990–1996	<800	lag 0–1	0.28	–0.16	0.73	0.00282	0.00228	1.00283	0.99835	1.00732	33
Roemer et al. 2001	Amsterdam	Netherlands	1987–1998		lag 1	3.30	1.43	5.19	0.03243	0.00928	1.03296	1.01434	1.05192	9

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Hoek et al. 2000	Netherlands	Netherlands	1986–1994	<800	lag 1	0.40	0.20	0.59	0.00396	0.00101	1.00397	1.00199	1.00595	10
Hoek et al. 1997	Rotterdam	Netherlands	1983–1991	all	lag 2	0.90	0.00	1.80	0.00891	0.00455	1.00895	1.00000	1.01799	13
Prescott et al. 1998	Edinburgh 1	United Kingdom	1981–1995	<900	lag 1–3	1.50	0.50	2.51	0.01489	0.00505	1.01500	1.00500	1.02510	8.7
Le Tertre et al. 2002	Bordeaux	France	1990–1995	<800	lag 0–1	1.53	0.00	3.09	0.01521	0.00776	1.01532	1.00000	1.03088	
Le Tertre et al. 2002	Le Havre	France	1990–1995	<800	lag 0–1	0.24	–1.46	1.97	0.00239	0.00873	1.00239	0.98538	1.01969	
Le Tertre et al. 2002	Rouen	France	1990–1995	<800	lag 0–1	0.14	–1.00	1.29	0.00140	0.00584	1.00140	0.99000	1.01292	

Table A6. Cardiovascular mortality, black smoke

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Le Tertre et al. 2002	Bordeaux	France	1990–1995	390–459	lag 0–1	1.76	–0.73	4.31	0.01742	0.01263	1.01757	0.99269	1.04307	
Le Tertre et al. 2002	Le Havre	France	1990–1995	390–459	lag 0–1	1.40	–1.61	4.50	0.01391	0.01538	1.01400	0.98389	1.04504	
Le Tertre et al. 2002	Marseille	France	1990–1995	390–459	lag 0–1	0.92	–0.24	2.10	0.00919	0.00592	1.00923	0.99759	1.02100	
Le Tertre et al. 2002	Paris	France	1990–1995	390–459	lag 0–1	0.40	–0.24	1.04	0.00396	0.00325	1.00397	0.99759	1.01039	
Le Tertre et al. 2002	Rouen	France	1990–1995	390–459	lag 0–1	0.98	–1.06	3.07	0.00976	0.01043	1.00981	0.98938	1.03066	
Wojtyniak et al. 1996	Krakow	Poland	1977–1989	390–459	lag 0	0.14	–0.19	0.47	0.00143	0.00168	1.00144	0.99814	1.00474	73.3
Wojtyniak et al. 1996	Lodz	Poland	1977–1990	390–459	lag 2	0.13	–0.20	0.45	0.00128	0.00165	1.00128	0.99804	1.00452	57.3
Wojtyniak et al. 1996	Poznan	Poland	1983–1990	390–459	lag 2	–0.20	–0.79	0.39	–0.00198	0.00302	0.99802	0.99212	1.00395	34
Wojtyniak et al. 1996	Wroclaw	Poland	1979–1989	390–459	lag 1	0.13	–0.36	0.63	0.00133	0.00252	1.00133	0.99641	1.00628	54.3
Bremner et al. 1999	London	United Kingdom	1992–1994	390–459	lag 1	1.18	–0.12	2.49	0.01169	0.00660	1.01176	0.99876	1.02493	10.8
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	0.90	–0.90	2.72	0.00892	0.00917	1.00896	0.99099	1.02725	10.9
Hoek et al. 2001	Netherlands	Netherlands	1986–1994	390–448	lag 0–6	0.72	0.32	1.11	0.00715	0.00200	1.00717	1.00323	1.01113	
Aguinaga et al. 1999	Pamplona	Spain	1991–1995	390–459	lag 5	–2.32	–9.94	5.93	–0.02351	0.04140	0.97676	0.90064	1.05931	21.67
Bellido Blasco et al. 1999	Castellon	Spain	1991–1995	390–459	lag 2	3.48	0.50	6.55	0.03421	0.01491	1.03480	1.00500	1.06548	20.3
Cambra et al. 1999	Bilbao	Spain	1992–1996	390–459	lag 4	–1.65	–3.64	0.38	–0.01664	0.01043	0.98350	0.96360	1.00381	23.09
Arribas–Monzon et al. 2001	Zaragoza	Spain	1991–1995	390–459	lag 1	0.66	–0.49	1.82	0.00658	0.00586	1.00660	0.99510	1.01823	
Garcia–Aymerich et al. 2000	Barcelona	Spain	1985–1989	390–459	lag 0–3	1.15	0.38	1.94	0.01147	0.00393	1.01153	1.00377	1.01935	42.4
Tenias Burillo et al. 1999	Valencia	Spain	1994–1996		lag 1	0.95	–0.51	2.43	0.00946	0.00743	1.00950	0.99490	1.02431	44.2

Table A7. Respiratory mortality, black smoke

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Le Tertre et al. 2002	Bordeaux	France	1990–1995	460–519	lag 0–1	2.00	–3.63	7.96	0.01979	0.02899	1.01999	0.96365	1.07961	
Le Tertre et al. 2002	Le Havre	France	1990–1995	460–519	lag 0–1	2.56	–3.31	8.80	0.02533	0.03011	1.02565	0.96688	1.08800	
Le Tertre et al. 2002	Marseille	France	1990–1995	460–519	lag 0–1	2.64	0.18	5.16	0.02603	0.01237	1.02637	1.00179	1.05155	
Le Tertre et al. 2002	Paris	France	1990–1995	460–519	lag 0–1	–0.22	–1.50	1.08	–0.00221	0.00661	0.99779	0.98495	1.01079	
Le Tertre et al. 2002	Rouen	France	1990–1995	460–519	lag 0–1	0.67	–3.24	4.74	0.00669	0.02024	1.00671	0.96756	1.04744	
Wojtyniak et al. 1996	Krakow	Poland	1977–1989	460–519	lag 1	–0.21	–1.34	0.94	–0.00209	0.00583	0.99791	0.98658	1.00938	73.3
Wojtyniak et al. 1996	Lodz	Poland	1977–1990	460–519	lag 1	–0.84	–1.89	0.21	–0.00849	0.00539	0.99155	0.98113	1.00208	57.3
Wojtyniak et al. 1996	Poznan	Poland	1983–1990	460–519	lag 0	–0.98	–2.76	0.83	–0.00984	0.00925	0.99021	0.97242	1.00833	34
Wojtyniak et al. 1996	Wroclaw	Poland	1979–1989	460–519	lag 1	–1.88	–3.39	–0.34	–0.01899	0.00793	0.98119	0.96605	0.99657	54.3
Garcia–Aymerich et al. 2000	Barcelona	Spain	1985–1989	460–519	lag 0–3	1.00	–0.51	2.53	0.00995	0.00766	1.01000	0.99495	1.02527	42.4
Bremner et al. 1999	London	United Kingdom	1992–1994	460–519	lag 3	1.91	0.25	3.61	0.01896	0.00841	1.01914	1.00248	1.03608	10.8
Tenias Burillo et al. 1999	Valencia	Spain	1994–1996		lag 3	–1.89	–4.81	1.12	–0.01908	0.01542	0.98110	0.95190	1.01120	44.2
Arribas–Monzon et al. 2001	Zaragoza	Spain	1991–1995	460–519	lag 1	2.89	0.62	5.21	0.02849	0.01138	1.02890	1.00620	1.05211	
Aguinaga et al. 1999	Pamplona	Spain	1991–1995	460–519	lag 1	13.36	–3.87	33.67	0.12540	0.08410	1.13360	0.96133	1.33674	21.67
Bellido Blasco et al. 1999	Castellon	Spain	1991–1995	460–519	lag 4	3.64	–2.57	10.25	0.03575	0.03153	1.03640	0.97430	1.10246	20.3
Cambra et al. 1999	Bilbao	Spain	1992–1996	460–519	lag 1	2.98	–1.11	7.24	0.02936	0.02068	1.02980	0.98890	1.07239	23.09
Prescott et al. 1998	Edinburgh 1	United Kingdom	1981–1995	480–487, 490–496	lag 1–3	3.90	1.10	6.78	0.03826	0.01394	1.03900	1.01100	1.06778	8.7
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	0.06	–2.90	3.11	0.00060	0.01533	1.00060	0.97097	1.03113	10.9

Table A8. Admissions, black smoke

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
All respiratory, ages 65+, hospital admissions														
Prescott et al. 1998	Edinburgh 2	United Kingdom	1992–1995	480–487, 490–496	lag 1–3	3.10	–3.50	10.15	0.03053	0.03375	1.03100	0.96500	1.10151	8.7
Atkinson et al. 2001	Barcelona	Spain	1994–1996	460–519	lag 0–1	–0.70	–2.30	0.93	–0.00702	0.00829	0.99300	0.97700	1.00926	36.2
Atkinson et al. 2001	Birmingham, West Midlands	United Kingdom	1992–1994	460–519	lag 0–1	2.90	0.60	5.25	0.02859	0.01153	1.02900	1.00600	1.05253	11.5
Atkinson et al. 2001	London	United Kingdom	1992–1994	460–519	lag 0–1	–1.10	–2.40	0.22	–0.01106	0.00675	0.98900	0.97600	1.00217	11.3
Atkinson et al. 2001	Netherlands	Netherlands	1989–1995	460–519	lag 0–1	0.00	–0.70	0.70	0.00000	0.00358	1.00000	0.99300	1.00705	9.1
Atkinson et al. 2001	Paris	France	1992–1996	460–519	lag 0–1	0.50	–0.40	1.41	0.00499	0.00459	1.00500	0.99600	1.01408	18.6
All respiratory, ages 15–64, hospital admissions														
Spix et al. 1998	Amsterdam, London, Paris, Rotterdam	Europe		460–519	single	0.55	0.12	0.99	0.00552	0.00221	1.00554	1.00120	1.00990	
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	0.72	–1.87	3.37	0.00714	0.01327	1.00717	0.98132	1.03370	10.9
All respiratory, ages 0–14, hospital admissions														
Atkinson, et al. 1999	London	United Kingdom	1992–1994	460–519	lag 0	1.08	–0.35	2.52	0.01071	0.00725	1.01077	0.99652	1.02523	10.8
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	2.32	0.42	4.25	0.02291	0.00956	1.02317	1.00419	1.04252	10.9
Cardiovascular, ages 65+, hospital admissions														
Prescott et al. 1998	Edinburgh 2	United Kingdom	1992–1995	410–414, 426–429, 434–440	lag 1–3	2.30	–1.90	6.68	0.02274	0.02139	1.02300	0.98100	1.06680	8.7
Atkinson, et al. 1999	London	United Kingdom	1992–1994	390–459	lag 0	1.67	0.76	2.60	0.01661	0.00463	1.01675	1.00756	1.02602	10.8

Table A9. Mortality and Admissions, $PM_{2.5}$

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
All cause, all ages, mortality														
Wichmann et al. 2000	Erfurt	Germany	1995–1998	<800	lag 3	–1.63	–3.234	–0.006	–0.01646	0.00837	0.98367	0.96766	0.99994	31
Peters et al. 2000	Czech Republic (coal basin)	Czech Republic	1982–1994	<800	lag 1	0.575	–0.202	1.358	0.00573	0.00396	1.00575	0.99798	1.01358	32
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	<800	lag 0–1	0.339	–0.85	1.542	0.00338	0.00608	1.00339	0.99150	1.01542	11.7
All respiratory, all ages, mortality														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.06	–3.088	3.069	–0.00057	0.01571	0.99943	0.96912	1.03069	11.7
Cardiovascular, all ages, mortality														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	0.507	–1.192	2.236	0.00506	0.00870	1.00507	0.98808	1.02236	11.7
All respiratory, ages 65+, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.74	–2.68	1.25	–0.00739	0.01010	0.99263	0.97317	1.01249	11.7
All respiratory, age 15 – 64, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–1.19	–3.67	1.35	–0.01199	0.01295	0.98808	0.96332	1.01348	11.7
All respiratory, ages 0–14, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	1.91	–0.06	3.91	0.01889	0.00993	1.01907	0.99943	1.03909	11.7
Cardiovascular, age 65+, hospital admissions														
No estimates														

Table A10. Admissions, Coarse Fraction

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
All cause, all ages mortality														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	<800	lag 0–1	–0.53	–3.73	2.77	–0.00533	0.01666	0.99469	0.96274	1.02770	8
All respiratory, all ages, mortality														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–6.76	–12.40	–0.74	–0.06995	0.03188	0.93244	0.87595	0.99257	8
Cardiovascular, all ages, mortality														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	–0.71	–4.26	2.97	–0.00711	0.01858	0.99292	0.95740	1.02975	8
Krzyzanowski et al. 1991	Krakow	Poland	1977–1989		lag 1–4	0.30	0.10	0.50	0.00300	0.00104	1.00301	1.00097	1.00505	
All respiratory, ages 65+, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–1.68	–5.33	2.10	–0.01698	0.01928	0.98317	0.94672	1.02102	8
All respiratory, age 15 – 64, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–4.35	–8.81	0.33	–0.04446	0.02439	0.95651	0.91187	1.00334	8
All respiratory, ages 0 – 14, hospital admissions														
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	3.88	–0.27	8.21	0.03811	0.02080	1.03884	0.99734	1.08206	8
Cardiovascular, ages 65+, hospital admissions														
No estimates														

Table A11. All–cause mortality, ozone

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Saez et al. 2002	Barcelona	Spain	1990–1996	<800	single	0.13	–0.17	0.43	0.00129	0.00155	1.00129	0.99826	1.00433	67.5
Saez et al. 2002	Madrid	Spain	1990–1996	<800	single	0.29	–0.06	0.64	0.00292	0.00179	1.00292	0.99941	1.00644	42.1
Saez et al. 2002	Valencia	Spain	1990–1996	<800	single	2.25	0.47	4.07	0.02228	0.00897	1.02253	1.00471	1.04067	45.5
Le Tertre et al. 2002	Le Havre	France	1990–1995	<800	lag 0–1	0.69	–0.46	1.86	0.00688	0.00588	1.00690	0.99536	1.01858	
Le Tertre et al. 2002	Lyon	France	1990–1995	<800	lag 0–1	0.73	–0.04	1.50	0.00727	0.00391	1.00729	0.99960	1.01505	
Le Tertre et al. 2002	Paris	France	1990–1995	<800	lag 0–1	0.42	0.04	0.79	0.00416	0.00192	1.00417	1.00040	1.00794	
Le Tertre et al. 2002	Rouen	France	1990–1995	<800	lag 0–1	1.04	–0.02	2.11	0.01033	0.00537	1.01038	0.99980	1.02108	
Le Tertre et al. 2002	Strasbourg	France	1990–1995	<800	lag 0–1	0.57	–0.08	1.23	0.00572	0.00333	1.00573	0.99920	1.01231	
Le Tertre et al. 2002	Toulouse	France	1990–1995	<800	lag 0–1	0.26	–0.83	1.36	0.00258	0.00559	1.00259	0.99166	1.01363	
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	<800	lag 0–1	0.50	–0.02	1.02	0.00500	0.00264	1.00501	0.99983	1.01022	48
Bremner et al. 1999	London	United Kingdom	1992–1994	<800	lag 2	–0.14	–0.45	0.18	–0.00137	0.00161	0.99863	0.99548	1.00180	32
Hoek et al. 2000	Netherlands	Netherlands	1986–1994	<800	lag 1	0.22	0.13	0.31	0.00223	0.00046	1.00223	1.00132	1.00314	47
Roemer et al. 2001	Amsterdam	Netherlands	1987–1998		lag 2	–0.17	–0.52	0.18	–0.00171	0.00180	0.99829	0.99478	1.00181	41
Michelozzi et al. 1998	Rome	Italy	1992–1995	<800	lag 1	0.38	–0.03	0.79	0.00379	0.00209	1.00380	0.99970	1.00792	21
Cadum et al. 1999	Turin	Italy	1991–1996	<800	lag 0	0.32	–0.12	0.76	0.00317	0.00223	1.00318	0.99880	1.00758	73.7

Table A12. Cardiovascular mortality, ozone

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/median
Le Tertre et al. 2002	Le Havre	France	1990–1995	390–459	lag 0–1	0.28	–1.80	2.40	0.00278	0.01071	1.00278	0.98196	1.02405	
Le Tertre et al. 2002	Lyon	France	1990–1995	390–459	lag 0–1	0.38	–1.59	2.38	0.00376	0.01010	1.00377	0.98410	1.02383	
Le Tertre et al. 2002	Paris	France	1990–1995	390–459	lag 0–1	0.42	–0.34	1.18	0.00416	0.00387	1.00417	0.99658	1.01181	
Le Tertre et al. 2002	Rouen	France	1990–1995	390–459	lag 0–1	1.38	–0.63	3.43	0.01372	0.01021	1.01381	0.99372	1.03431	
Le Tertre et al. 2002	Strasbourg	France	1990–1995	390–459	lag 0–1	0.22	–0.83	1.28	0.00219	0.00539	1.00219	0.99166	1.01283	
Le Tertre et al. 2002	Toulouse	France	1990–1995	390–459	lag 0–1	1.00	–0.85	2.89	0.00995	0.00945	1.01000	0.99146	1.02889	
Saez et al. 2002	Barcelona	Spain	1990–1996	390–459	single	0.55	–0.03	1.14	0.00552	0.00297	1.00554	0.99971	1.01140	67.5
Saez et al. 2002	Madrid	Spain	1990–1996	390–459	single	0.54	–0.04	1.13	0.00540	0.00298	1.00541	0.99955	1.01130	42.1
Saez et al. 2002	Valencia	Spain	1990–1996	390–459	single	3.14	0.35	6.00	0.03089	0.01397	1.03137	1.00352	1.05999	45.5
Cadum et al. 1999	Turin	Italy	1991–1996	390–459	lag 0	0.67	–0.02	1.37	0.00669	0.00351	1.00671	0.99980	1.01367	73.7
Bremner et al. 1999	London	United Kingdom	1992–1994	390–459	lag 2	0.67	0.10	1.25	0.00669	0.00292	1.00672	1.00097	1.01249	32
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	0.16	–0.60	0.92	0.00157	0.00388	1.00157	0.99397	1.00922	48
Hoek et al. 2001	Netherlands	Netherlands	1986–1994	390–448	lag 1	0.36	0.21	0.51	0.00357	0.00075	1.00358	1.00210	1.00505	
Peters et al. 2000	Germany (Rural)	Germany	1982–1994	390–459	lag 0	0.59	–0.38	1.57	0.00592	0.00494	1.00594	0.99624	1.01574	38
Wietlisbach et al. 1996	Zurich	Switzerland	1984–1989	390–459	lag 1	–0.03	–0.81	0.76	–0.00030	0.00400	0.99970	0.99189	1.00757	26.9
Wietlisbach et al. 1996	Basle	Switzerland	1984–1989	390–459	lag 1	–1.62	–3.83	0.65	–0.01630	0.01160	0.98383	0.96172	1.00646	23.9

Table A13. Respiratory mortality, ozone

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
Saez et al. 2002	Barcelona	Spain	1990–1996	460–519	single	0.40	–0.58	1.39	0.00398	0.00500	1.00399	0.99420	1.01388	67.5
Saez et al. 2002	Madrid	Spain	1990–1996	460–519	single	0.10	–0.98	1.20	0.00104	0.00554	1.00104	0.99022	1.01198	42.1
Saez et al. 2002	Valencia	Spain	1990–1996	460–519	single	1.85	–3.83	7.88	0.01836	0.02931	1.01853	0.96167	1.07875	45.5
Le Tertre et al. 2002	Le Havre	France	1990–1995	460–519	lag 0–1	–2.02	–6.54	2.72	–0.02041	0.02411	0.97980	0.93458	1.02721	
Le Tertre et al. 2002	Lyon	France	1990–1995	460–519	lag 0–1	1.72	–1.00	4.51	0.01705	0.01383	1.01720	0.99000	1.04514	
Le Tertre et al. 2002	Paris	France	1990–1995	460–519	lag 0–1	–0.38	–1.87	1.13	–0.00384	0.00767	0.99617	0.98131	1.01125	
Le Tertre et al. 2002	Rouen	France	1990–1995	460–519	lag 0–1	2.07	–2.06	6.38	0.02051	0.02110	1.02072	0.97937	1.06383	
Le Tertre et al. 2002	Strasbourg	France	1990–1995	460–519	lag 0–1	0.02	–2.41	2.51	0.00020	0.01257	1.00020	0.97586	1.02514	
Le Tertre et al. 2002	Toulouse	France	1990–1995	460–519	lag 0–1	1.00	–3.18	5.36	0.00995	0.02154	1.01000	0.96825	1.05355	
Bremner et al. 1999	London	United Kingdom	1992–1994	460–519	lag 2	–0.71	–1.55	0.13	–0.00713	0.00431	0.99289	0.98453	1.00132	32
Anderson, et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	0.38	–0.97	1.75	0.00380	0.00689	1.00381	0.99034	1.01746	48
Cadum et al. 1999	Turin	Italy	1991–1996	480–519	lag 0	0.51	–1.48	2.55	0.00513	0.01024	1.00515	0.98517	1.02553	73.7

Table A14. Admissions, ozone

Reference	City	Country	Study period	ICD group	Lag	% Δ	%LCL	%UCL	Beta	SE	RR Δ	RR LCL	RR UCL	mean/ median
All respiratory, ages 65+, hospital admissions														
Spix et al. 1998	Amsterdam, London, Paris, Rotterdam	Europe		460–519	single	0.75	0.36	1.14	0.00746	0.00199	1.00749	1.00357	1.01141	
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	0.03	–0.73	0.80	0.00035	0.00391	1.00035	0.99271	1.00805	48
All respiratory, ages 15–64, hospital admissions														
Spix et al. 1998	Amsterdam, London, Paris, Rotterdam	Europe		460–519	single	0.61	0.26	0.97	0.00611	0.00180	1.00612	1.00259	1.00967	
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.50	–1.39	0.41	–0.00496	0.00461	0.99505	0.98609	1.00409	48
All respiratory, ages 0–14, hospital admissions														
Atkinson et al. 1999	London	United Kingdom	1992–1994	460–519	lag 0	–0.32	–1.13	0.50	–0.00318	0.00416	0.99683	0.98873	1.00499	32
Fusco et al. 2001	Rome	Italy	1995–1997	460–519	lag 1	2.22	0.08	4.41	0.02201	0.01080	1.02225	1.00084	1.04412	27
Anderson et al. 2001	West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.93	–1.77	–0.08	–0.00934	0.00434	0.99071	0.98232	0.99917	48
Cardiovascular, ages 65+, hospital admissions														
Atkinson et al. 1999	London	United Kingdom	1992–1994	390–459	lag 2	0.65	0.22	1.08	0.00647	0.00219	1.00649	1.00217	1.01083	32

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Tables of individual city results – panel studies

Table A15. Cough in symptomatic children, PM_{10}

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Forsberg et al.1998	4 Northern Swedish villages	Sweden	03/01/1994–27/03/1994	cough	5–11	1	0.753	0.547	1.037
Nielsen et al. 1998	Almhult, Olofstrom	Sweden	1993–1994	cough	7–12	0	1.235	0.980	1.556
van der Zee et al. 1998	Amsterdam	Netherlands	20/11/1993–28/02/1994	cough	7–11	1	0.866	0.786	0.954
Kalandidi et al. 1998	Athens	Greece	10/01/1994–10/03/1994	cough	6–11	2	1.056	1.009	1.105
Vondra et et al. 1998	Benesov	Czech Republic	17/01/1994–12/04/1994	cough	6–13	2	1.013	0.957	1.072
Englert et al. 1998	Berlin	Germany	27/01/1994–25/03/1994	cough	7–11	1	0.937	0.842	1.043
Englert et al. 1998	Berlin suburb	Germany	27/01/1994–25/03/1994	cough	7–11	2	1.033	0.940	1.135
Rudnai et al. 1998	Budapest	Hungary	02/1994–04/1994	cough	6–12	1	1.016	0.966	1.069
Nielsen et al. 1998	Burlov, Malmo	Sweden	1993–1994	cough	7–12	2	1.077	0.936	1.239
van der Zee et al. 1998	Drenthe	Netherlands	20/11/1993–28/02/1994	cough	8–12	1	1.036	0.983	1.092
Beyer et al. 1998	Hettstedt	Germany	10/1993–03/1994	cough	6–11	2	1.047	0.959	1.143
Niepsuj et al. 1998	Katowice	Poland	17/01/1994–10/04/1994	cough	7–12	0	0.930	0.864	1.001
Haluszka et al. 1998	Krakow	Poland	10/01/1994–01/04/1994	cough	7–11	0	0.947	0.901	0.995
Timonen et al. 1998	Kuopio	Finland	08/02/1994–05/04/1994	cough	7–12	1	0.868	0.751	1.003
Tiittanen et al. 1999	Kuopio	Finland	13/03/1995–23/04/1995	cough	8–13	2	1.046	1.010	1.084
Timonen et al. 1998	Kuopio suburb	Finland	08/02/1994–05/04/1994	cough	7–12	2	0.927	0.728	1.180
van der Zee et al. 1999	Netherlands, rural	Netherlands	1992–1995	cough	7–11	1	1.009	0.998	1.019

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
van der Zee et al. 1999	Netherlands, urban	Netherlands	1992–1995	cough	7–11	2	1.005	0.991	1.019
Clench–Aas et al. 1998	Oslo	Norway	01/12/1993–14/02/1994	cough	6–12	1	0.965	0.811	1.148
Clench–Aas et al. 1998	Oslo suburb	Norway	01/12/1993–14/02/1994	cough	6–12	1	1.176	0.908	1.523
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	nocturnal cough	7–15	3	1.116	1.032	1.207
Just et al. 2002	Paris	France	01/04/1996 – 30/06/1996	nocturnal cough	7–15	0	1.100	0.880	1.375
Baldini et al. 1998	Pisa	Italy	1993–1994 (2 months)	cough	6–11	1	0.975	0.947	1.004
Kotesovec et al. 1998	Prachatice	Czech Republic	01/1994–03/1994	cough	7–11	0	1.025	0.938	1.120
Vondra et et al. 1998	Prague	Czech Republic	17/01/1994–12/04/1994	cough	6–13	1	1.029	0.958	1.105
Niepsuj et al. 1998	Pszczyna	Poland	17/01/1994–10/04/1994	cough	7–12	0	0.997	0.979	1.015
Haluszka et al. 1998	Rabka	Poland	10/01/1994–01/04/1994	cough	6–12	1	0.983	0.947	1.020
Peters et al. 1997	Sokolov	Czech Republic	01/09/1991–31/03/1992	cough	6–14	0	1.002	0.993	1.011
Kalandidi et al. 1998	Southern Greek villages	Greece	10/01/1994–10/03/1994	cough	5–12	0	0.891	0.815	0.974
Rudnai et al. 1998	Szentendre	Hungary	02/1994–04/1994	cough	6–12	0	0.935	0.868	1.007
Kotesovec et al. 1998	Teplice	Czech Republic	01/1994–03/1994	cough	7–13	1	1.021	0.977	1.067
Baldini et al. 1998	Torre del Lago Puccini	Italy	1993–1994 (2 months)	cough	6–11	2	0.977	0.957	0.997
Forsberg et al. 1998	Umea	Sweden	03/01/1994–27/03/1994	cough	5–11	2	0.766	0.577	1.017
Beyer et al. 1998	Zerbst	Germany	10/1993–03/1994	cough	6–11	0	0.952	0.847	1.070

Table A16. Cough in symptomatic adults, PM_{10}, black smoke and ozone

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Cough in symptomatic adults, PM_{10}									
Boezen et al. 1998	Amsterdam, Meppel	Netherlands	1993–1994	cough	16+	0	1.021	1.001	1.041
van der Zee et al. 20001	Amsterdam, Rotterdam	Netherlands	1992–1995	cough	50–70	1	1.000		
Hiltermann et al. 19982	Leiden	Netherlands	03/07/1995–06/10/1995	cough/phlegm	18–55	0	0.986	0.963	1.008
van der Zee et al. 20001	Meppel, Nunspeet	Netherlands	1992–1995	cough	50–70	1	1.000		
Neukirch et al. 1998	Paris	France	15/11/1992–09/05/1993	nocturnal cough	16–70	6	1.116	1.052	1.183
Dusseldorp et al. 1995	Vijk aan Zee	Netherlands	11/10/1993–22/12/1993	cough	16+	0	1.027	0.997	1.059
Cough in symptomatic adults, black smoke									
Boezen et al. 1998	Amsterdam, Meppel	Netherlands	1993–1994	cough	16+	0	1.031	0.969	1.098
van der Zee et al. 20001	Amsterdam, Rotterdam	Netherlands	1992–1995	cough	50–70	1	1.000		
Hiltermann et al. 19982	Leiden	Netherlands	03/07/1995–06/10/1995	cough/phlegm	18–55	0	0.980	0.900	1.067
van der Zee et al. 20001	Meppel, Nunspeet	Netherlands	1992–1995	cough	50–70	1	1.000		
Neukirch et al. 1998	Paris	France	15/11/1992–09/05/1993	nocturnal cough	16–70	6	1.077	1.016	1.143
Cough in symptomatic adults and ozone									
Hiltermann et al. 19982	Leiden	Netherlands	03/07/1995–06/10/1995	cough/phlegm	18–55	1	0.987	0.975	0.999
Higgins et al. 1995	Runcorn & Widnes	United Kingdom	28 days	cough	16+	0	1.050	0.910	1.212

Note:
[1] Estimate not given; results reported as “not significant” only.
[2] Estimate expressed as a relative risk and 95% confidence interval.

Table A17. Cough in symptomatic children, coarse fraction, $PM_{2.5}$ and ozone

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Cough in symptomatic children, coarse fraction									
Tiittanen et al. 1999	Kuopio	Finland	13/03/1995–23/04/1995	cough	8–13	2	1.086	1.023	1.152
Cough in symptomatic children, $PM_{2.5}$									
Tiittanen et al. 1999	Kuopio	Finland	13/03/1995–23/04/1995	cough	8–13	2	1.091	1.007	1.182
Cough in symptomatic children and ozone									
Just et al. 2002	Paris	France	01/04/1996 – 30/06/1996	nocturnal cough	7–15	0	1.040	0.920	1.176

Table A18. Cough in symptomatic children, black smoke

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Forsberg et al. 1998	4 northern Swedish villages	Sweden	03/01/1994–27/03/1994	cough	5–11	0	1.185	0.764	1.838
Nielsen et al. 1998	Almhult, Olofstrom	Sweden	1993–1994	cough	7–12	1	1.334	0.676	2.632
van der Zee et al. 1998	Amsterdam	Netherlands	20/11/1993–28/02/1994	cough	7–11	1	0.780	0.644	0.945
Kalandidi et al. 1998	Athens	Greece	10/01/1994–10/03/1994	cough	6–11	2	1.048	1.005	1.093
Vondra et al. 1998	Benesov	Czech Republic	17/01/1994–12/04/1994	cough	6–13	1	0.893	0.756	1.055
Englert et al. 1998	Berlin	Germany	27/01/1994–25/03/1994	cough	7–11	0	0.840	0.704	1.002
Englert et al. 1998	Berlin suburb	Germany	27/01/1994–25/03/1994	cough	7–11	0	1.113	0.942	1.315
Rudnai et al. 1998	Budapest	Hungary	02/1994–04/1994	cough	6–12	2	1.022	0.961	1.087
Nielsen et al. 1998	Burlov, Malmö	Sweden	1993–1994	cough	7–12	0	0.981	0.757	1.271
van der Zee et al. 1998	Drenthe	Netherlands	20/11/1993–28/02/1994	cough	8–12	1	1.128	0.954	1.334
Beyer et al. 1998	Hettstedt	Germany	10/1993–03/1994	cough	6–11	0	0.963	0.913	1.016
Niepsuj et al. 1998	Katowice	Poland	17/01/1994–10/04/1994	cough	7–12	2	0.982	0.956	1.009
Haluszka et al. 1998	Krakow	Poland	10/01/1994–01/04/1994	cough	7–11	1	0.961	0.893	1.034
Timonen et al. 1998	Kuopio	Finland	08/02/1994–05/04/1994	cough	7–12	1	0.845	0.711	1.004
Timonen et al. 1998	Kuopio suburb	Finland	08/02/1994–05/04/1994	cough	7–12	2	0.882	0.707	1.100
van der Zee et al. 1999	Netherlands, rural	Netherlands	1992–1995	cough	7–11	1	1.026	1.000	1.054
van der Zee et al. 1999	Netherlands, urban	Netherlands	1992–1995	cough	7–11	0	1.026	0.987	1.067
Clench–Aas et al. 1998	Oslo	Norway	01/12/1993–14/02/1994	cough	6–12	1	1.009	0.890	1.144

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Clench–Aas et al. 1998	Oslo suburb	Norway	01/12/1993–14/02/1994	cough	6–12	1	1.058	0.906	1.236
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	nocturnal cough	7–15	2	1.041	0.963	1.124
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	nocturnal cough	7–15	4	1.132	1.047	1.224
Just et al. 2002	Paris	France	01/04/1996–30/06/1996	nocturnal cough	7–15	0	1.220	0.990	1.503
Baldini et al. 1998	Pisa	Italy	1993–1994 (2 months)	cough	6–11	2	0.947	0.871	1.030
Kotesovec et al. 1998	Prachatice	Czech Republic	01/1994–03/1994	cough	7–11	0	1.131	0.976	1.311
Vondra et et al. 1998	Prague	Czech Republic	17/01/1994–12/04/1994	cough	6–13	1	1.047	0.927	1.183
Niepsuj et al. 1998	Pszczyna	Poland	17/01/1994–10/04/1994	cough	7–12	2	1.008	0.985	1.032
Haluszka et al. 1998	Rabka	Poland	10/01/1994–01/04/1994	cough	6–12	0	1.009	0.963	1.057
Kalandidi et al. 1998	Southern Greek villages	Greece	10/01/1994–10/03/1994	cough	5–12	0	0.896	0.800	1.004
Rudnai et al. 1998	Szentendre	Hungary	02/1994–04/1994	cough	6–12	0	0.880	0.802	0.966
Kotesovec et al. 1998	Teplice	Czech Republic	01/1994–03/1994	cough	7–13	1	1.013	0.968	1.060
Baldini et al. 1998	Torre del Lago Puccini	Italy	1993–1994 (2 months)	cough	6–11	1	0.980	0.942	1.020
Forsberg et al. 1998	Umea	Sweden	03/01/1994–27/03/1994	cough	5–11	0	1.145	0.877	1.495
Beyer et al. 1998	Zerbst	Germany	10/1993–03/1994	cough	6–11	2	0.968	0.875	1.071

Table A19. Medication use in symptomatic children, PM_{10}

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Forsberg et al. 1998	4 Northern Swedish villages	Sweden	03/01/1994–27/03/1994	bronchodilator use	5–11	0	1.275	0.702	2.316
Nielsen et al. 1998	Almhult, Olofstrom	Sweden	1993–1994	bronchodilator use	7–12	2	0.785	0.583	1.057
van der Zee et al. 1998	Amsterdam	Netherlands	20/11/1993–28/02/1994	bronchodilator use	7–11	0	1.154	0.953	1.397
Kalandidi et al. 1998	Athens	Greece	10/01/1994–10/03/1994	bronchodilator use	6–11	0	0.940	0.830	1.065
Vondra et et al. 1998	Benesov	Czech Republic	17/01/1994–12/04/1994	bronchodilator use	6–13	1	1.095	0.969	1.237
Englert et al. 1998	Berlin	Germany	27/01/1994–25/03/1994	bronchodilator use	7–11	0	0.872	0.692	1.099
Englert et al. 1998	Berlin suburb	Germany	27/01/1994–25/03/1994	bronchodilator use	7–11	1	1.092	0.872	1.368
Rudnai et al. 1998	Budapest	Hungary	02/1994–04/1994	bronchodilator use	6–12	2	0.832	0.703	0.985
Nielsen et al. 1998	Burlov, Malmo	Sweden	1993–1994	bronchodilator use	7–12	1	1.306	1.015	1.680
van der Zee et al. 1998	Drenthe	Netherlands	20/11/1993–28/02/1994	bronchodilator use	8–12	2	1.062	0.991	1.138
Beyer et al. 1998	Hettstedt	Germany	10/1993–03/1994	bronchodilator use	6–11	1	0.744	0.490	1.130
Haluszka et al. 1998	Krakow	Poland	10/01/1994–01/04/1994	bronchodilator use	7–11	1	0.890	0.707	1.120
Timonen et al. 1998	Kuopio	Finland	08/02/1994–05/04/1994	bronchodilator use	7–12	2	1.067	0.955	1.192
Timonen et al. 1998	Kuopio suburb	Finland	08/02/1994–05/04/1994	bronchodilator use	7–12	0	1.039	0.971	1.112
van der Zee et al. 1999	Netherlands, rural	Netherlands	1992–1995	bronchodilator use	7–11	0	0.980	0.952	1.010
van der Zee et al. 1999	Netherlands, urban	Netherlands	1992–1995	bronchodilator use	7–11	2	1.005	0.991	1.019
Clench–Aas et al. 1998	Oslo	Norway	01/12/1993–14/02/1994	bronchodilator use	6–12	1	0.910	0.784	1.056

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Clench–Aas et al. 1998	Oslo suburb	Norway	01/12/1993–14/02/1994	bronchodilator use	6–12	0	1.069	0.959	1.192
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	B2 agonist	7–15	0	1.145	0.852	1.539
Baldini et al. 1998	Pisa	Italy	1993–1994 (2 months)	bronchodilator use	6–11	0	0.866	0.700	1.071
Kotesovec et al. 1998	Prachatice	Czech Republic	01/1994–03/1994	bronchodilator use	7–11	2	1.520	1.064	2.171
Vondra et et al. 1998	Prague	Czech Republic	17/01/1994–12/04/1994	bronchodilator use	6–13	2	0.931	0.814	1.065
Niepsuj et al. 1998	Pszczyna	Poland	17/01/1994–10/04/1994	bronchodilator use	7–12	1	0.961	0.925	0.998
Haluszka et al. 1998	Rabka	Poland	10/01/1994–01/04/1994	bronchodilator use	6–12	1	1.016	0.913	1.131
Peters et al. 1997	Sokolov	Czech Republic	01/09/1991–31/03/1992	B agonist	6–14	0	1.011	0.974	1.049
Kalandidi et al. 1998	Southern Greek villages	Greece	10/01/1994–10/03/1994	bronchodilator use	5–12	2	0.882	0.650	1.197
Rudnai et al. 1998	Szentendre	Hungary	02/1994–04/1994	bronchodilator use	6–12	1	0.861	0.695	1.067
Kotesovec et al. 1998	Teplice	Czech Republic	01/1994–03/1994	bronchodilator use	7–13	0	1.035	0.998	1.073
Baldini et al. 1998	Torre del Lago Puccini	Italy	1993–1994 (2 months)	bronchodilator use	6–11	1	1.050	0.925	1.192
Forsberg et al. 1998	Umea	Sweden	03/01/1994–27/03/1994	bronchodilator use	5–11	0	1.498	0.899	2.496
Beyer et al. 1998	Zerbst	Germany	10/1993–03/1994	bronchodilator use	6–11	1	0.567	0.311	1.034

Table A20. Medication use in symptomatic children, black smoke

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Forsberg et al. 1998	4 northern Swedish villages	Sweden	03/01/1994–27/03/1994	bronchodilator use	5–11	1	0.480	0.155	1.486
Nielsen et al. 1998	Almhult, Olofstrom	Sweden	1993–1994	bronchodilator use	7–12	1	0.495	0.226	1.084
van der Zee et al. 1998	Amsterdam	Netherlands	20/11/1993–28/02/1994	bronchodilator use	7–11	2	1.618	1.104	2.371
Kalandidi et al. 1998	Athens	Greece	10/01/1994–10/03/1994	bronchodilator use	6–11	0	0.922	0.811	1.048
Vondra et et al. 1998	Benesov	Czech Republic	17/01/1994–12/04/1994	bronchodilator use	6–13	0	0.932	0.649	1.338
Englert et al. 1998	Berlin	Germany	27/01/1994–25/03/1994	bronchodilator use	7–11	1	0.736	0.486	1.115
Englert et al. 1998	Berlin suburb	Germany	27/01/1994–25/03/1994	bronchodilator use	7–11	1	1.163	0.830	1.630
Rudnai et al. 1998	Budapest	Hungary	02/1994–04/1994	bronchodilator use	6–12	1	0.847	0.700	1.025
Nielsen et al. 1998	Burlov, Malmo	Sweden	1993–1994	bronchodilator use	7–12	1	1.497	1.008	2.223
van der Zee et al. 1998	Drenthe	Netherlands	20/11/1993–28/02/1994	bronchodilator use	8–12	0	0.775	0.536	1.121
Beyer et al. 1998	Hettstedt	Germany	10/1993–03/1994	bronchodilator use	6–11	1	0.679	0.458	1.007
Haluszka et al. 1998	Krakow	Poland	10/01/1994–01/04/1994	bronchodilator use	7–11	0	1.223	1.048	1.427
Timonen et al. 1998	Kuopio	Finland	08/02/1994–05/04/1994	bronchodilator use	7–12	0	0.933	0.842	1.034
Timonen et al. 1998	Kuopio suburb	Finland	08/02/1994–05/04/1994	bronchodilator use	7–12	2	1.036	0.971	1.105
van der Zee et al. 1999	Netherlands, rural	Netherlands	1992–1995	bronchodilator use	7–11	2	0.952	0.880	1.029
van der Zee et al. 1999	Netherlands, urban	Netherlands	1992–1995	bronchodilator use	7–11	0	1.090	1.029	1.154
Clench–Aas et al. 1998	Oslo	Norway	01/12/1993–14/02/1994	bronchodilator use	6–12	1	0.941	0.848	1.044

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Clench–Aas et al. 1998	Oslo suburb	Norway	01/12/1993–14/02/1994	bronchodilator use	6–12	2	0.993	0.942	1.047
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	B2 agonist	7–15	0	1.105	0.856	1.427
Segala et al. 1998	Paris	France	15/11/1992–09/05/1993	B2 agonist	7–15	4	1.071	0.952	1.206
Baldini et al. 1998	Pisa	Italy	1993–1994 (2 months)	bronchodilator use	6–11	2	1.495	0.716	3.122
Kotesovec et al. 1998	Prachatice	Czech Republic	01/1994–03/1994	bronchodilator use	7–11	2	1.416	1.082	1.853
Vondra et et al. 1998	Prague	Czech Republic	17/01/1994–12/04/1994	bronchodilator use	6–13	2	0.852	0.679	1.069
Niepsuj et al. 1998	Pszczyna	Poland	17/01/1994–10/04/1994	bronchodilator use	7–12	1	0.975	0.938	1.013
Haluszka et al. 1998	Rabka	Poland	10/01/1994–01/04/1994	bronchodilator use	6–12	2	1.063	0.935	1.209
Kalandidi et al. 1998	Southern Greek villages	Greece	10/01/1994–10/03/1994	bronchodilator use	5–12	2	1.054	0.970	1.145
Rudnai et al. 1998	Szentendre	Hungary	02/1994–04/1994	bronchodilator use	6–12	1	0.763	0.568	1.025
Kotesovec et al. 1998	Teplice	Czech Republic	01/1994–03/1994	bronchodilator use	7–13	1	1.042	0.996	1.090
Baldini et al. 1998	Torre del Lago Puccini	Italy	1993–1994 (2 months)	bronchodilator use	6–11	0	0.923	0.730	1.167
Forsberg et al. 1998	Umea	Sweden	03/01/1994–27/03/1994	bronchodilator use	5–11	0	1.800	1.120	2.893
Beyer et al. 1998	Zerbst	Germany	10/1993–03/1994	bronchodilator use	6–11	1	0.947	0.668	1.343

Table A21. Medication use in symptomatic children and ozone

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Just et al. 2002	Paris	France	01/04/1996 – 30/06/1996	B2 agonist	7–15	0	1.410	1.052	1.890

Table A22. Medication use in symptomatic adults, black smoke, PM_{10}, coarse fraction and ozone

Reference	City	Country	Study period	Outcome	Ages	Lag	OR	OR LCL	OR UCL
Medication use in symptomatic adults, black smoke									
van der Zee et al. 2000	Amsterdam, Rotterdam	Netherlands	1992–1995	bronchodilator use	50–70	2	0.971	0.937	1.007
Hiltermann et al. 1998[1]	Leiden	Netherlands	03/07/1995–06/10/1995	bronchodilator use	18–55	0	0.970	0.910	1.034
van der Zee et al. 2000	Meppel, Nunspeet	Netherlands	1992–1995	bronchodilator use	50–70	1	1.010	0.987	1.033
Medication use in symptomatic adults, PM_{10}									
van der Zee et al. 2000[1]	Amsterdam, Rotterdam	Netherlands	1992–1995	bronchodilator use	50–70	2	0.993	0.977	1.009
Hiltermann et al. 1998[2]	Leiden	Netherlands	03/07/1995–06/10/1995	bronchodilator use	18–55	0	1.003	0.993	1.013
van der Zee et al. 2000[1]	Meppel, Nunspeet	Netherlands	1992–1995	bronchodilator use	50–70	1	1.005	0.997	1.013
Dusseldorp et al. 1995	Vijk aan Zee	Netherlands	11/10/1993–22/12/1993	bronchodilator use	16+	1	1.034	1.018	1.051
Medication use in symptomatic adults, coarse fraction									
von Klot et al. 2002	Erfurt	Germany	29/10/1996 – 30/03/1997	B2 agonist	16+	0	1.008	0.958	1.061
Medication use in symptomatic adults, ozone									
Hiltermann et al. 1998[2]	Leiden	Netherlands	03/07/1995–06/10/1995	bronchodilator use	18–55	1	1.009	0.997	1.020
Higgins et al. 1995	Runcorn & Widnes	United Kingdom	28 days	bronchodilator use	16+	1	1.440	1.140	1.819

Note:
[1] Estimate not given; results reported as “not significant” only
[2] Estimate expressed as a relative risk and 95% confidence interval

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Annex 5

META-ANALYSIS OF PM2.5 RESULTS FROM NON-EUROPEAN COUNTRIES

This Annex presents the results of an analysis of $PM_{2.5}$ and daily mortality estimates extracted from time-series studies in the Air Pollution Epidemiology Database held at St. George's Hospital Medical School. This was done because there were insufficient studies of $PM_{2.5}$ in Europe and consideration was given to taking studies from other countries, mainly North America into account.

Studies from North America, Canada, South America and other parts of the world have been identified in the database. Meta-analysis of North American and Canadian studies and all regions together (including European studies) were carried out for each mortality group. As in the original review, three main groups of mortality were investigated. These were all cause, cardiovascular and respiratory mortality. The details of the studies included are shown in Tables A, B and C for all-cause, respiratory and cardiovascular mortality respectively, together with those that were excluded on geographical or other grounds.

Table D provides fixed- and random-effects summary estimates for $PM_{2.5}$ and each of the causes of death, for American and Canadian studies and for all studies. The estimates are the relative risks associated with 10 $\mu g/m^3$ increases in $PM_{2.5}$. The European estimates have been added for comparison. Figures A5.1–A5.3 present these estimates graphically using forest plots.

The summary estimates for North America are larger than for any of the three European studies. This meta-analysis does not in itself answer the question of whether it is better to use a summary estimate based on the more numerous North American Studies or choose a single estimate from among the European studies. What is clear is that the estimates for the largest city studied in Europe (West Midlands Conurbation), are within the range of those from North America, and this indicates that although this estimate is not statistically significant (lower 95% confidence interval 0.992), it is likely that effects of $PM_{2.5}$ on mortality in Europe do exist. Whether or not these are smaller than in North America cannot be determined from the present analysis, and would require consideration of factors such as the source and composition of $PM_{2.5}$ in the respective regions and the differences in other potential effect modifiers. One reason for the larger estimate for North America may be positive publication bias, since a funnel plot of these estimates demonstrates some clear asymmetry (Figure A5.4). This bias was not significant however (P=0.08), so this is not likely to be a major reason for the regional differences. The plot does however emphasize the importance of not relying on small numbers of less statistically powerful individual studies.

Table A. All cause mortality and $PM_{2.5}$

City	Country	Study period	ICD	Lag	Beta	SE	RR	RR LCL	RR UCL
Montreal	Canada	1984–1993	<800	lag 1	0.0115	0.006	1.012	1.000	1.024
8 Canadian Cities	Canada	1986–1996	<800	lag 1	0.0119	0.0038	1.012	1.004	1.020
Toronto	Canada	1980–1994	<800	lag 0–1	0.0187	0.0029	1.019	1.013	1.025
Coachella Valley	United States	1989–1998	<800	lag 4	0.0436	0.0222	1.045	1.000	1.091
Georgia	United States	1998–1999	<800	lag 1	0.0251	0.0164	1.025	0.993	1.059
Pittsburgh	United States	1989–1991	<800	lag 0	0.0059	0.0094	1.006	0.988	1.025
Boston	United States	1979–1986	<800	lag 0–1	0.0218	0.0035	1.022	1.015	1.029
Knoxville	United States	1980–1987	<800	lag 0–1	0.0139	0.0061	1.014	1.002	1.026
Portage	United States	1979–1987	<800	lag 0–1	0.0119	0.0076	1.012	0.997	1.027
St Louis	United States	1979–1987	<800	lag 0–1	0.0109	0.0035	1.011	1.004	1.018
Steubenville	United States	1979–1987	<800	lag 0–1	0.01	0.0056	1.010	0.999	1.021
Topeka	United States	1979–1988	<800	lag 0–1	0.008	0.0144	1.008	0.980	1.037
Los Angeles	United States	1980–1986	<800	lag 0	0.0011	0.002	1.001	0.997	1.005
Eastern Tennessee	United States	1985–1986	<800	lag 1	0.0228	0.0186	1.023	0.986	1.061
Wayne County	United States	1992–1994	<800	lag 3	0.0122	0.0075	1.012	0.997	1.027
Santiago	Chile	1988–1996	<800	lag 1–2	0.0071	0.0011	1.007	1.005	1.009
Mexico City	Mexico	1993–1995	<800	lag 1–5	0.0147	0.0075	1.015	1.000	1.030
Chongqing	China	1995–1995	<800	lag 3	–0.004	0.0034	0.996	0.989	1.003
Melbourne	Australia	1991–1996	<800	lag 0	0.008	0.0087	1.008	0.991	1.025
Sydney	Australia	1989–1993	<800	lag 0	0.0153	0.006	1.015	1.004	1.027
West Midlands	United Kingdom	1994–1996	<800	lag 0–1	0.0034	0.0061	1.003	0.991	1.015
Czech Republic (coal basin)	Czech Republic	1982–1994	<800	lag 1	0.0057	0.004	1.006	0.998	1.014
Erfurt	Germany	1995–1998	<800	lag 3	–0.0165	0.0084	0.984	0.968	1.000
Excluded studies									
St Louis	USA	1985–1986	<800	lag 1	0.0171	0.0096	1.017	0.998	1.037
Mexico City	Mexico	1993–1995	<800	lag 4	0.0135	0.0059	1.014	1.002	1.025
Santiago	Chile	1988–1993	<800		0.004	0.0011	1.004	1.002	1.006
Mexico City	Mexico	1993–1995	<800	lag 3	0.0469	0.019	1.048	1.010	1.088

Table B. Cardiovascular mortality and $PM_{2.5}$

City	Country	Study period	ICD group	Lag	Beta	SE	RR D	RR LCL	RR UCL
Montreal	Canada	1984–1993	390–459	lag 1	0.0133	0.0092	1.013	0.995	1.032
Coachella Valley	United States	1989–1998	393–440	lag 4	0.0328	0.0282	1.033	0.978	1.092
Phoenix	United States	1995–1997	390–448	lag 1	0.0685	0.0236	1.071	1.022	1.122
Wayne County	United States	1992–1994	390–459	lag 1	0.0125	0.0111	1.013	0.991	1.035
Mexico City	Mexico	1993–1995		lag 1–5	0.0154	0.0143	1.016	0.988	1.044
Melbourne	Australia	1991–1996	390–459	lag 0	0.003	0.0123	1.003	0.979	1.027
Sydney	Australia	1989–1993	390–459	lag 0	0.0158	0.0083	1.016	1.000	1.033
West Midlands	United Kingdom	1994–1996	390–459	lag 0–1	0.0051	0.0087	1.005	0.988	1.022
Excluded studies									
Mexico City	Mexico	1993–1995	390–398, 401–417, 420, 430–438, 440–448	lag 4	0.0217	0.0111	1.022	1.000	1.044
Santa Clara County, California	United States	1989–1996	390–459	lag 0	0.0242		1.024		
Montreal	Canada	1984–1993	390–459	lag 0–2	0.0104		1.010		

Table C. Respiratory mortality and $PM_{2.5}$

City	Country	Study period	ICD group	Lag	Beta	SE	RR	RR LCL	RR UCL
Montreal	Canada	1984–1993	460–519	lag 1	0.0492	0.0212	1.050	1.008	1.095
Coachella Valley	United States	1989–1998	460–519	lag 4	–0.057	0.0834	0.945	0.802	1.112
Los Angeles	United States	1980–1986		lag 0	0.0082	0.0056	1.008	0.997	1.019
Wayne County	United States	1992–1994	460–519	lag 0	0.009	0.0268	1.009	0.957	1.063
Mexico City	Mexico	1993–1995		lag 1–5	0.0354	0.0235	1.036	0.989	1.085
Melbourne	Australia	1991–1996	460–519	lag 0	–0.007	0.0297	0.993	0.937	1.053
Sydney	Australia	1989–1993	460–519	lag 1	0.0231	0.0183	1.023	0.987	1.061
West Midlands	United Kingdom	1994–1996	460–519	lag 0–1	–0.0006	0.0157	0.999	0.969	1.031
Excluded studies									
Mexico City	Mexico	1993–1995	460–466, 480–487, 490–496, 500–508	lag 4	0.0247	0.0183	1.025	0.989	1.063
Montreal	Canada	1984–1993	460–519	lag 1	0.0451		1.046		
Philadelphia Pennsylvania Counties NJ counties	United States	1991–1995	460–519	lag 0–1	0.0058		1.006		
Santa Clara County, California	United States	1989–1996	11, 35, 472–519, 710.0, 710.2, 710.4	lag 0	0.0436		1.045		

Table D. Relative risk summary estimates (FE Fixed–Effects, RE Random–Effects) for $PM_{2.5}$ and daily mortality. Relative risks are for a 10 $\mu g/m^3$ increases in $PM_{2.5}$

	All Cause	Cardiovascular	Respiratory
United States and Canada	1.010 (1.008, 1.013) FE 1.013 (1.008, 1.018) RE	1.019 (1.005, 1.032) FE 1.023 (1.003, 1.044) RE	1.011 (1.000, 1.021) FE 1.016 (0.994, 1.038) RE
Global	1.008 (1.006, 1.009) FE 1.009 (1.006, 1.013) RE	1.013 (1.005, 1.021) FE 1.013 (1.005, 1.022) RE	1.011 (1.002, 1.020) FE 1.011 (1.002, 1.020) RE
Europe*	1.003 (0.992, 1.015) WM 1.006 (0.998, 1.014) CR 0.984 (0.968, 1.000) ER	1.005 (0.998, 1.022) WM	0.944 (0.969,1.031) WM

*:WM – West Midlands
CR – Czech Republic
ER – Erfurt

Fig. A5.1. All cause mortality. Percentage change in mean number of deaths associated with 10 $\mu g/m^3$ increase in daily $PM_{2.5}$

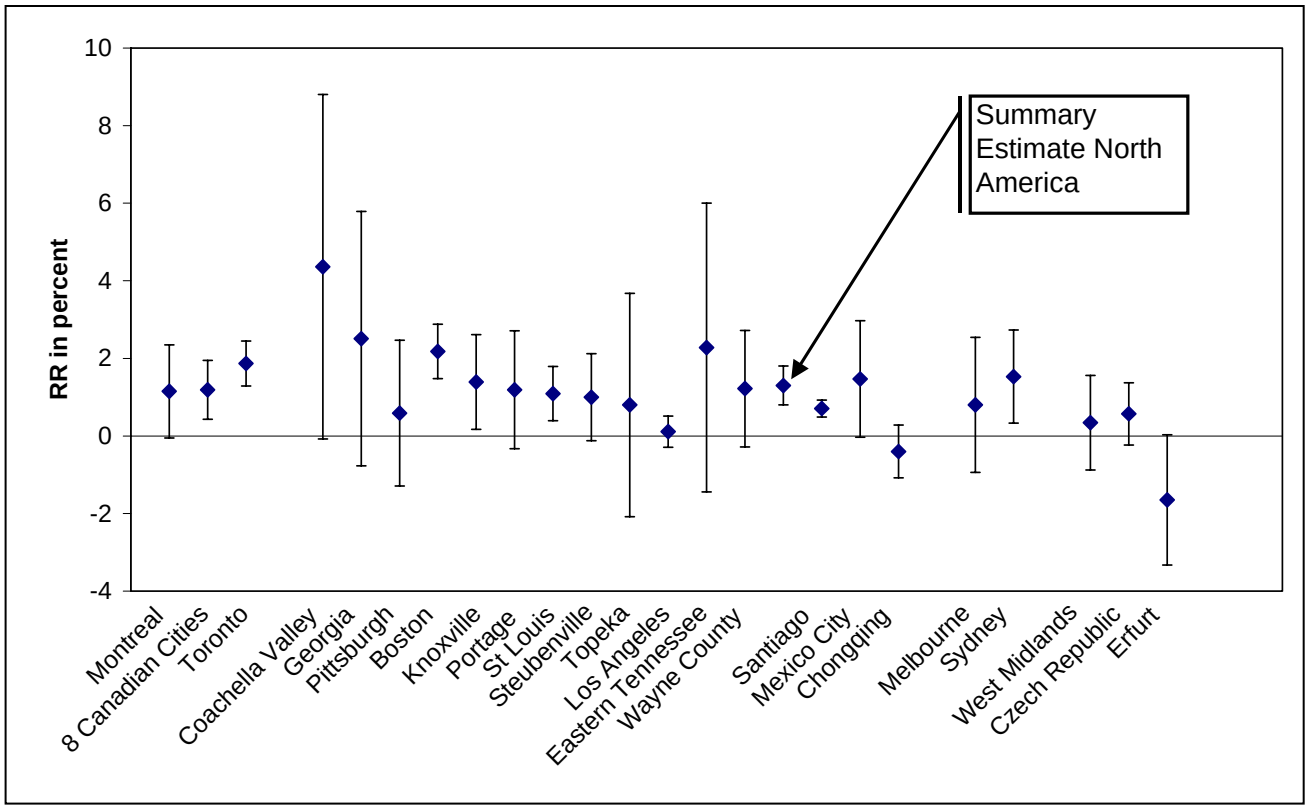


Fig. A5.2. Cardiovascular mortality. Percentage change in mean number of deaths associated with 10 μg/m^3 increase in daily PM2.5

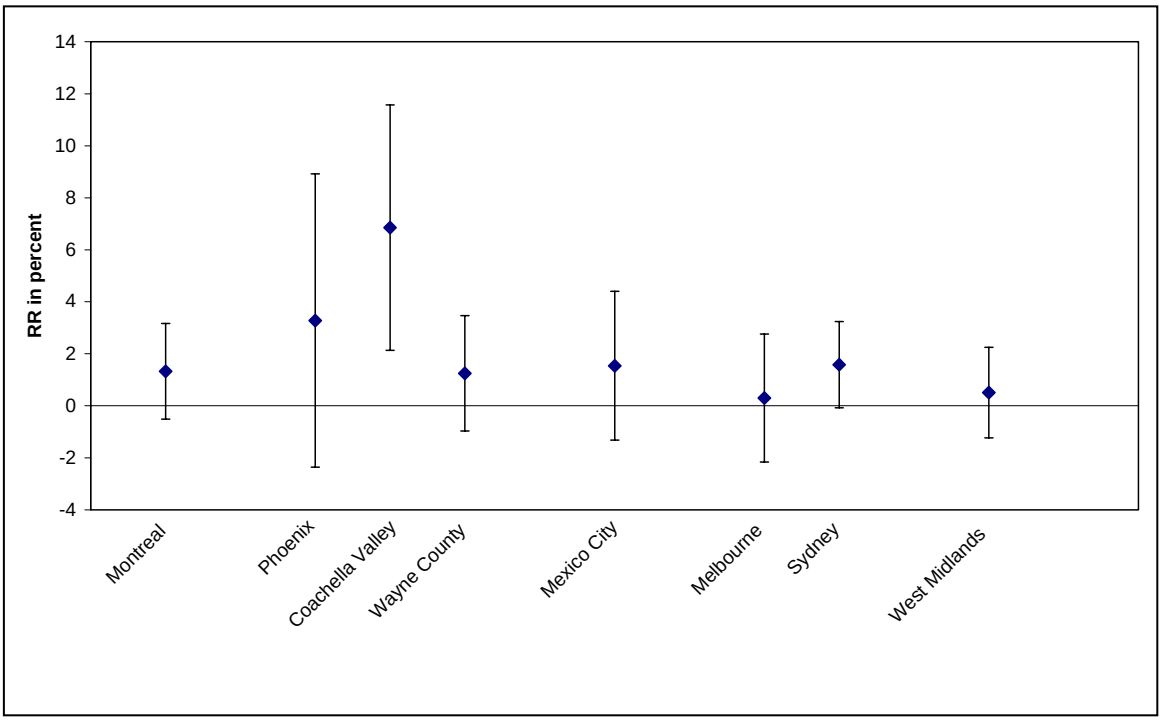
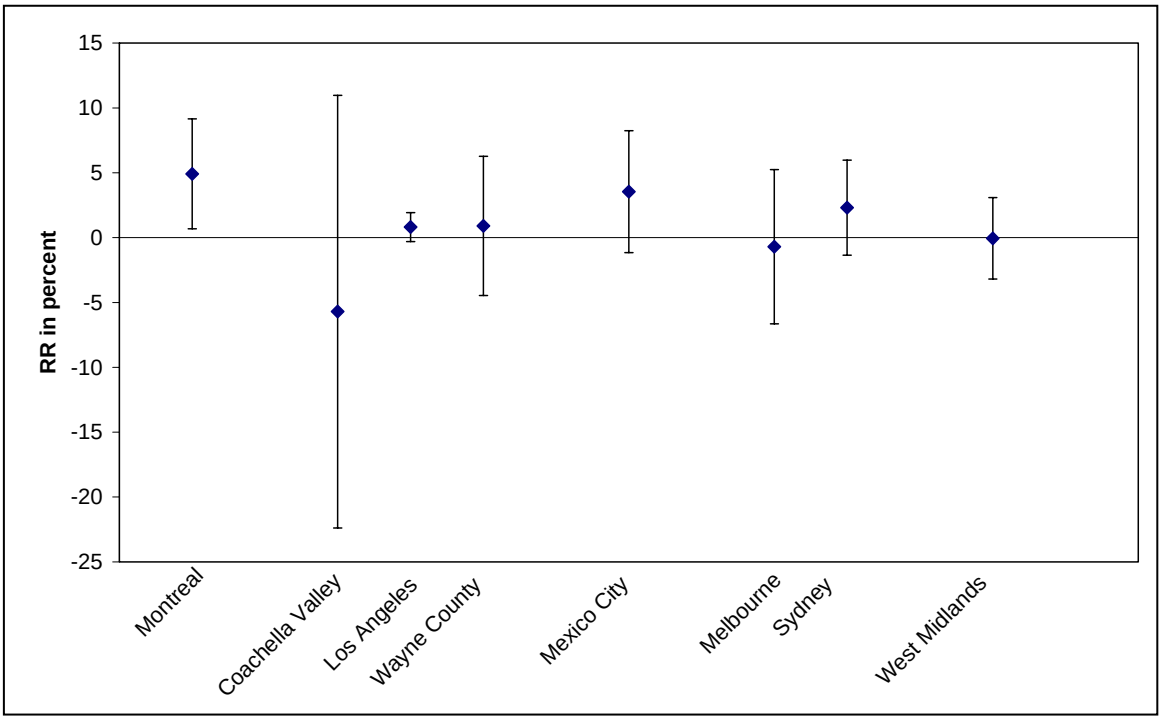


Fig. A5.3. Respiratory mortality. Percentage change in mean number of deaths associated with 10 μg/m^3 increase in daily $PM_{2.5}$



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