

Epidemiologic studies on the health effects of ambient particulate air pollution

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This review primarily considers studies published until 31 December 1997; it also focuses on studies of the last decade which have tended to investigate lower air pollution levels and use more developed methods. Mainly studies with actual measurements of particles that are subsequently used in the analyses are reviewed. We also consider a few important later publications (eg, updated reports from previously published large multicenter studies). In some cases, studies using similar methodology have already been analyzed together. In the case of such meta-analyses, we have focused on the pooled results and have discussed the results of the individual studies only when they provide contrasts of particular interest. To facilitate an overview of the abundant evidence, all relevant references with original data are included in an appropriate table. Occasional reference is made to recent comprehensive reviews [such as the 1996 report from the United States (US) Environmental Protection Agency (EPA) (1)], to which the reader can turn for more-detailed descriptions of individual studies. For older studies, previous EPA reports provide extensive reviews (2–5).

A problem in common with all epidemiologic studies on the health effects of ambient air pollution is that particles are only one component in a complex mixture of potentially noxious substances with which they may correlate. In addition, particulate air pollution is an extremely heterogeneous entity, composed of particles of various sizes and origins, which can vary in chemical composition and acidity. Particulate air pollution can also correlate with meteorological variables such as temperature or air humidity. It is thus difficult to elucidate etiologic relationships. Mainly studies that have made adequate attempts to control for other variables are reviewed, and they form the basis for the risk assessment.

Epidemiologic studies of the acute health effects of particulates fall into several different categories. Time-series analyses evaluate health effects of time-varying exposures. Individual-level time-series studies ("panel studies") use repeated measurements on the same person over a period of time, in effect using the person as his or her own control, to examine short-term effects. The outcomes evaluated are generally either continuous data (eg, lung function), or binary data (eg, presence or absence of symptoms, especially respiratory symptoms) (6). Binary outcomes are however sometimes aggregated for analysis into grouped daily prevalence or incidence data (7). Primarily aggregate-level time-series studies evaluate exposure and short-term temporal var-

iations in outcomes such as mortality, hospital admissions, or outpatient visits in a population as a whole, and the effect measure is generally the number of outcomes in the population in successive time periods (ie, count data). In any time-series study, different averaging times and lag times may be used for the exposure variable, and an attempt can even be made to evaluate the lag structure within a study (6). Most commonly, however, daily average particulate levels on the same day, or with 1 or possibly 2 days of lag time, have been correlated with the daily health effects under study. For some study purposes, more simple analytical methods are used (eg, comparing the proportion of persons with symptoms on days with high particle concentrations versus low concentrations). Chronic effects are best elucidated in longitudinal studies (ie, with a cohort design using survival-type data). Incident case-referent studies can also be used, but they have been less common in the epidemiology of particulate air pollution. Cross-sectional (prevalence) studies are also used to evaluate chronic effects, but it is difficult to separate clearly the effects of short- and long-term exposure in this type of study. In all of these study designs, other risk factors for the outcome under study which correlate with the studied exposure can potentially confound the exposure-outcome relationship and may need to be addressed in the analysis (8). In time-series studies of short-term effects, many traditional confounders are less problematic. Instead, potential confounding by factors which covary with air pollution on a daily basis (eg, temperature, infectious epidemics) has to be controlled in the analysis (9).

In epidemiologic research, the relative risk (RR) (ie, the ratio of disease or symptom incidence among the exposed to that among the unexposed) is often the effect parameter of fundamental interest, although it may also be the variation in other effect measures such as symptom severity or lung function due to exposure. Multiple regression techniques are commonly used to estimate the effect and simultaneously control for other exposure factors of relevance. In time-series studies, different types of regression models are used depending on the type of data collected. For continuous time-series data, models based on linear (Gaussian) regression are commonly used; for binary data logistic regression models are generally appropriate (6). Special techniques must be used to handle autocorrelation in the data due to the fact that successive observations on the same person over time are not independent of each other (6, 7). Interindividual heterogeneity in the response usually also needs to be

addressed by various modeling techniques, although it is sometimes ignored, for example, when binary outcomes are analyzed (eg, by logistic regression) with the use of aggregated daily prevalence or incidence data (7). For time-series count data, linear (Gaussian) regression is sometimes used, in particular in earlier studies. However, small counts such as daily deaths in a limited area may not be normally distributed, but tend to follow a Poisson distribution, and therefore log-linear Poisson regression is commonly used (6, 8, 9). From cohort data ("survival" data), the RR can be directly estimated using, for example, Cox proportional hazards regression. The term odds ratio (OR) is often used to denote the estimates obtained from logistic regression analyses, which are used for various types of binary or binomial data. It may be equivalent to the RR in studies of case-referent type, given that referents are adequately sampled. However, in other case-referent designs, in time-series analyses of binary data, and in cross-sectional studies of point prevalence, the OR should in fact be interpreted as the ratio of the odds of a positive outcome among the exposed as compared with the outcome of the unexposed, and it is similar to the RR or prevalence ratio only if the outcome is rare (8).

In epidemiologic studies, confidence intervals (CI) rather than P-values are usually computed for point estimates. In the text and tables, 95% CI values are used throughout. A P-value of <0.05 (2-sided test) thus corresponds to a 95% CI that does not include the null value (usually 0 for change in a continuous outcome, or 1.0 for an OR or RR). This review has not placed particular emphasis on P-values or tests of statistical significance, which are highly dependent on the size of the data set considered (10). With large enough numbers, almost any deviation from the null becomes statistically significant, and vice versa. Of public health importance and of concern here, however, is not the statistical significance per se but the magnitude of a possible effect as it is estimated in individual studies and pooling efforts, evaluated in relation to the total body of research. It is also generally more important to consider design and systematic errors carefully than it is to consider random variation in the evaluation of study results. For example, statistically significant but small deviations from the null may be wholly explained by bias, such as confounding or systematic measurement error.

In this review, a common effect measure relating to particulate matter <10 µm in diameter (PM₁₀) has been calculated where possible. One necessary assumption for such calculations is for a conversion factor to PM₁₀ from other particulate measures. Obviously, such fac-

tors are not constant, and therefore the original particle measure has also been given in the tables of this report. For example, a recent European study found ratios of daily average PM₁₀ to black smoke (BS) ranging from 0.67 to 3.67 and slopes from the univariate regression from 0.52 to 2.49 (11). For more exact comparisons (ie, formal meta-analyses) other conversion factors might be preferable, chosen individually for each study, but for simplicity we have used the following previously suggested conversion factors: PM₁₀ ≈ PM₁₅ ≈ BS ≈ SO₄ × 4 ≈ PM_{2.5}/0.60 ≈ CoH (in units of 10³ linear feet, used in most studies) × 55^a ≈ TSP × 0.55 (12, 13) and PM₁₀ ≈ light scattering (measured by nephelometry, in units of 10⁻⁵/m) × 10 (14, 15), with the remaining particle measures in micrograms per cubic meter. Even when the same measure has been used, one should be aware that there may be substantial variation between samplers and laboratories (17), and therefore any between-study comparison would be approximate. Knowing the conversion factors used, the interested reader can easily recalculate to another conversion factor. For more details on the calculation of the summary measure from various types of regression estimates, see the appendix.

Another implicit assumption is that estimates for different lag times of the exposure variable used in different studies can be combined. Most commonly, daily averages with lag times of 0 (same day) and 1 (previous day) have been related to the health effect, but lag times of 2, 3, 4, and rarely others have also been used. In other studies, averages over several days have been used (eg, lag time of 0–2 (3-day average) or 0–4 (5-day average)). Although multiday averages generally have a smaller range, there appears to be no consistent relation between the lag time or averaging time and effect estimates of per 10 µg/m³ PM₁₀ for the various health effects. It is also impossible to recalculate to a common lag time based on published data. Therefore, the effect estimates are taken as presented in the original studies and mostly the lag time is not explicitly stated in our text, although lag times are discussed in some places. As most studies use daily average particulate levels, the reader is thus advised to think generally of the particulate exposure in terms of 24-hour averages. In most cases the lag time for a particular study can be found in the corresponding table; otherwise the reader must turn to the original publication.

Time-series studies of variations in mortality

The studies on daily mortality and particulate air pollution are presented in table 1 (14, 16, 18–80).

^a PM₁₀ ≈ CoH/0.55 in reference 13 appears to be a printing error. In this equation, the CoH values referred to are 10 × CoH units, as given by Fairley (16), which apparently correspond to units of 10¹ linear feet, and in these units, CoH ≈ TSP rather than < PM₁₀ [ie, PM₁₀ ≈ CoH × 0.55 (12, 16)].

Table 1. Time series studies of daily mortality and particulate air pollution. (For any abbreviation not found in the footnotes, see page 4.)

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in mortality per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments ^d
			Cause	%	95% CI	
Schimmel & Murawski, 1976 (18); Schimmel, 1978 (19) - New York City 1963–1976	CoH, LT 0 days, M 1.96	M 108	All RD+CVD+ cancer	0.1 0.2	0.0–0.3 0.1–0.4	0.2 (95% CI 0.0–0.3) and 0.2 (95% CI 0.1–0.4) with SO ₂ in model. Stronger with LT 0–1 days: 0.3 (95% CI 0.1–0.5) and 0.4 (95% CI 0.2–0.6) with SO ₂ in model. No positive effect of SO ₂ .
Mazumdar & Sussman, 1983 (20) - Hazelwood/Bellevue/Logans Ferry, Pittsburgh (PA) 1972–1977	CoH, LT 0 days (?), M(R ₁) 1.0 (0–3.5)	M 54	All HD	0.1 0.3	-0.1–0.3 0.0–0.5	Very similar with SO ₂ in model. Estimates are here pooled over all 3 locations. Some inconsistency, however, with a clear effect seen mainly in Hazelwood.
Fairley, 1990 (16) - Santa Clara (CA) 1980–1982, 1984–1986 winters	CoH, LT 0 days, M 0.67	M 37	All All, ≥70years RD CVD	0.8 0.8 3.2 0.8	0.3–1.3 0.1–1.4 1.4–5.0 0.1–1.5	Linear regressions. With Poisson regression 0.7 (95% CI 0.3–1.1) for total mortality.
Schwartz, 1991 (21) - Detroit (MI) 1973–1982	TSP, LT 1 day, M(R ₂) 87 (46–137)	M 48	All	1.0	0.5–1.5	0.9 (95% CI 0.4–1.5) with SO ₂ in model. O ₃ in model did not alter estimates.
Schwartz & Dockery, 1992 (22) - Steubenville (OH) 1974–1984	TSP, LT 1 day, M(R ₃) 111 (36–209)	M 61	All	0.7	0.4–1.0	0.5 (95% CI 0.1–1.0) with SO ₂ in model.
Moolgavkar & Luebeck, 1995 (85) - Steubenville (OH) 1974–1984	TSP, LT 1 day, M(R ₃) 113 (38–212)	M 62	All	0.6	0.1–1.0	0.5 (95% CI 0.0–1.0) with SO ₂ in model.
Schwartz & Dockery, 1992 (23) - Philadelphia (PA) 1973–1980	TSP, LT 0–1 days, M(R ₂) 77 (37–132)	M 42	All All, >65 years COPD Pneumonia CVD	1.2 1.7 3.3 1.9 1.7	0.7–1.7 1.1–1.3 0.1–6.6 -0.6–4.4 1.0–2.4	0.9 (95% CI 0.3–1.6) with SO ₂ in model.
Moolgavkar et al, 1995 (24) - Philadelphia (PA) 1973–1988	TSP, LT 1 day, M(R ₁) 68 (14–338)	M 37	All, spring All, summer All, autumn All, winter	0.2 1.2 0.2 -0.2	-0.6–1.0 0.4–2.0 -0.6–1.0 -1.1–0.6	With SO ₂ in model. Analyses by season only. Slightly lower estimates with O ₃ also in model.
Li & Roth, 1995 (25) - Philadelphia (PA) 1973–1990	TSP, various LT, M(R ₂) 69 (32–120)	M 38	Results: estimates not available; most TSP results not significant			Article presents only t-values for various subgroup analyses, various models, etc.
Moolgavkar & Luebeck, 1996 (26) - Philadelphia (PA) 1973–1988	TSP, LT 1 day, M(R ₁) 68 (14–338)	M 37	All, summer All, winter	0.7 -0.2	-0.1–1.5 -1.0–0.6	With SO ₂ , O ₃ , and NO ₂ in model. Analyses by season only (data from figure).
Samet et al, 1997 (27); Kelsall et al, 1997 (28) - Philadelphia (PA) 1974–1988	TSP, LT 0–1 days, M(R ₁) 67 (14–222)	M 37	All All, 65–74 years All, ≥75 years RD ≥75 years CVD ≥75years	0.6 0.4 1.1 2.3 1.0	0.0–1.1 -0.4–1.2 0.4–1.8 -0.4–5.2 0.0–1.9	With SO ₂ , NO ₂ , O ₃ and lagged CO in model. As comparison – for total mortality: 0.6 (95% CI 0.2–1.0) with TSP singly in model and 0.4 (95% CI -0.1–0.9) for TSP with only SO ₂ added.
Pope et al, 1992 (29) - Utah County (UT) 1985–1989	PM ₁₀ , LT 0–4 days, M(R ₁) 47 (1–365)	M 47	All RD CVD	1.5 3.7 1.8	0.9–2.1 0.7–6.7 0.4–3.3	Very low levels of SO ₂ and low NO ₂ levels. Particles highest in winter
Pope & Kalkstein, 1996 (30) - Utah County (UT) 1985–1989	PM ₁₀ , LT 0–4 days, M(R ₁) 47 (1–365)	M 47	All RD CVD	1.3 3.1 1.9	0.4–2.2 0.4–5.9 0.6–3.2	With nonparametric smoothing and synoptic weather modeling. Results not sensitive to exact model specification.
Lyon et al, 1995 (31) - Utah County (UT) 1985–1992	PM ₁₀ , LT 0–4 days, M ~44	M ~44	All	1.2	0.4–2.0	For ≥50 versus <50 µg/m ³ : All + 4% (95% CI -2–+10) RD + 3% (95% CI -4–+25) CVD +13% (95% CI +4–+24)
Dockery et al, 1992 (32) - St Louis (MO) 1985–1986 - Kingston/Harriman (TN) 1985–1986	PM ₁₀ , LT 1 day, M(R ₁) 28 (1–97) PM ₁₀ , LT 1 day, M(R ₁) 30 (4–67)	M 28 M 30	All All	1.5 1.6	0.1–2.9 -1.3–4.6	For both locations, little change when SO ₂ was added to model. PM _{2.5} , SO ₄ and H ⁺ were not superior to PM ₁₀ as predictors.
Schwartz, 1991 (33) - Minneapolis-St Paul (MN) 1973–1982	TSP, LT 0 days (?), M 78	M 43	All	1.0	0.4–1.5	.

(continued)

Table 1. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in mortality per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments ^d
			Cause	%	95% CI	
Schwartz, 1993 (34) - Birmingham (AL) 1985–1988	PM ₁₀ , LT 0–2 days, M(R ₃) 48 (21–80)	M 48	All RD HD	1.0 1.5 1.6	0.2–1.9 -2.6–5.7 0.4–2.8	.
Samet et al, 1995 (35) (extensive reanalysis of the following) - Philadelphia (PA) 1973–1980 & 1973–1988 - St Louis (MO) 1985–1986 - Kingston/Harriman (TN) 1985–1986 - Utah County (Provo) (UT) 1985–1989 - Birmingham (AL) 1985–1988 - Santa Clara (CA) 1980–1982, 1984–1986 winters	See the respective original study		All Pneumonia CVD All All All All	1.5 3.7 1.9 1.5 1.6 1.6 1.0 0.8	1.1–2.0 1.1–6.3 1.2–2.5 0.1–2.9 -1.1–4.4 0.6–2.6 0.2–1.8 0.3–1.4	Results similar to those of the original analyses. All estimates are with no other co-pollutants in the model (not available in most cases). Philadelphia estimates for all causes and CVD but not pneumonia were somewhat attenuated by including SO ₂ in the model. [For multipollutant models in the Philadelphia dataset, see Kelsall et al, 1997 (28).]
Schwartz, 1994 (36) - Cincinnati (OH) 1977–1982	TSP, LT 0 days, M(R ₁) 76 (~15–155)	M 42	All All, ≥65 years Pneumonia CVD	1.1 1.6 2.7 1.4	0.5–1.7 1.2–2.0 -1.0–6.6 0.5–2.3	.
Schwartz et al, 1996 (37) - Six US cities, 1979–1988	PM ₁₀ , LT 0–1 days, Md (R ₂) 25 (8–68); PM _{2.5} , LT 0–1 days, Md(R ₂) 15 (4–43)	Md 25	All All, ≥65 years COPD Pneumonia IHD	0.8 1.0 2.0 2.4 1.3	0.5–1.1 0.7–1.3 0.6–3.4 1.1–3.7 0.8–1.7	Also associations with TSP, PM _{2.5} , H ⁺ , slightly stronger with PM _{2.5} . Tabulated estimate for total mortality is from PM ₁₀ model and estimates for ≥65 years and cause-specific mortality calculated from PM _{2.5} models.
Kinney & Özkaynak, 1991 (38); Shumway et al, 1988 (39) - Los Angeles County, Los Angeles (CA) 1970–1979	KM, LT 0 days, 25 units	.	Results: mortality associated with motor-vehicle pollutants (CO or KM or NO ₂)			Mortality also associated with temperature, and O ₃ . [In reference 39, weekly mortality counts were used.]
Kinney et al, 1995 (40) - Los Angeles County, Los Angeles (CA) 1985–1990	PM ₁₀ , LT 0 days, M(R ₁) 58 (15–177)	M 58	All	0.5	0.0–1.0	Changes little when O ₃ or CO included in model.
Ostro, 1995 (41) - San Bernardino + Riverside, Los Angeles (CA) 1980–1986	PM _{2.5} , LT 0 days, M(R ₁) 32.5 (9–190)	M 54	All All, ≥65 years All, summer RD	0.1 0.2 0.4 0.5	-0.1–0.3 -0.1–0.4 0.0–0.9 -0.1–1.1	Stronger effect during summer months (due mainly to RD). PM _{2.5} estimated based on visibility.
Styer et al, 1995 (42) - Cook County, Chicago (IL) 1985–1990 - Salt Lake County (UT) 1985–1990	PM ₁₀ , LT 0–2 days, Md(R ₁) 38 (3–365) PM ₁₀ , LT 0–2 days, Md(R ₁) 48 (9–194)	Md 38 Md 48	All, ≥65 years All, autumn RD, autumn All, ≥65 years	0.5 0.8 2.2 -0.2	0.1–0.9 0.0–1.6 -0.2–4.8 -1.1–0.6	In Cook County mostly spring and autumn effect, and effect particularly for RD. In Salt Lake County no effect of PM ₁₀ seen.
Ito et al, 1995 (43); Ito et al, 1996 (44) - Cook County, Chicago (IL) 1985–1990	PM ₁₀ , LT 0 days, M(R ₂) 41 (20–65)	M 41	All RD CVD	0.5 1.3 0.3	0.3–0.7 0.4–2.3 -0.1–0.7	0.4 (95% CI 0.1–0.7) with O ₃ in model. Higher for women than for men.
Mazumdar et al, 1982 (45) - London (United Kingdom) 1958–1972 winters	BS, LT 0 days (?), M 174	M 174	All	0.3	0.3–0.3	0.3 (95% CI 0.2–0.3) with SO ₂ in model. No association with SO ₂ . Possible synergism between BS and SO ₂ at high levels.
Ostro, 1984 (46) - London (United Kingdom) 1958–1972 winters	BS, LT 0 days (?), M(R ₁) 174 (11–1971)	M 174	Results: stronger effect on mortality below 150 µg/m ³ than above			Threshold search. No threshold could be found.
Schwartz & Marcus, 1990 (47) - London (United Kingdom) 1958–1972 winters	BS, LT 0 days, M 174	M 174	All	0.3	0.3–0.4	.
Ito et al, 1993 (48) - London (United Kingdom) 1965–1972 winters	BS, LT 0 days, M ~80	M ~80	All	0.4	0.2–0.5	BS, SO ₂ or acidity all with effect in separate models.

(continued)

Table 1. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (μg/m ³)	Increase in mortality per 10 μg/m ³ PM ₁₀ ^b or a short summary of the results			Comments ^d
			Cause	%	95% CI	
Derriennic et al, 1989 (49) - Lyon (France) 1974–1976 - Marseilles (France) 1974–1976	SP, LT varied, M 87 SP, LT varied, M 126	M 48 M 70	Results: SP not significant (various lag times). SO ₂ significant for different mortality at ages ≥65 years for RD in Lyon and Marseilles and for CVD in Marseilles.			SO ₂ and SP correlated 0.27–0.60 in different subareas.
Hatzakis et al, 1986 (50); Katsouyanni et al, 1990 (51) - Athens (Greece) 1975–1982	Smoke, GM 57	GM 57	Results: smoke not significant for mortality but SO ₂ was significant for mortality.			Effect contributed mainly by RD. SO ₂ and smoke highly correlated (r=0.73).
Katsouyanni et al, 1993 (52) - Athens (Greece), July 1987 compared with July 1981–1986	Smoke, M(R ₁) ?? (50–250)	.	Results: Interaction between temperature and air pollution significant for SO ₂ but not for smoke.			Analysis of pollution effects during a heat-wave episode.
Touloumi et al, 1994 (53) - Athens (Greece) 1984–1988	Smoke, M(R ₂) 83 (~35–175)	M 83	All	0.9	0.6–1.1	0.5 (95% CI 0.1–0.8) for smoke with SO ₂ in model. Similar effect for SO ₂ .
Spix et al, 1993 (54) - Erfurt (Germany) 1980–1989	SP, LT 0 days, Md(R ₁) 106 (10–650)	Md 58	All	1.1	0.1–2.1	0.9 (95% CI -0.4–2.3) with SO ₂ in model. Weaker effect for SO ₂ .
Rahlenbeck & Kahl, 1996 (55) - East Berlin (Germany) 1981–1989	SP, LT 2 days, M(R ₁) 66 (10–150) (truncated at 150) ^e	M 36	All	1.1	0.3–1.9	0.8 (95% CI -0.1–1.7) with SO ₂ in model. Slightly weaker effect for SO ₂ . Weaker effect when SP values >150 μg/m ³ were also included in model. ^e
Verhoeff et al, 1996 (56) - Amsterdam (The Netherlands) 1986–1992	PM ₁₀ , LT 0 days, M(R ₃) 38 (17–67)	M 38	All	0.6	-0.1–1.4	Somewhat attenuated with SO ₂ and O ₃ but not CO in model. BS had stronger effect than PM ₁₀ . Both were partly based on predicted values, PM ₁₀ more so.
Wietlisbach et al, 1996 (57) - Zurich (Switzerland) 1984–1989	TSP, LT 0–2 days, M(R ₁) 46 (?–182)	M 25	All All, ≥65 years RD CVD	0.7 1.0 2.5 0.5	0.0–1.4 0.2–1.8 0.8–4.3 -0.5–1.6	Mortality was similarly associated with TSP, NO ₂ , and SO ₂ . For SO ₂ , the effect was highly nonlinear with declining marginal effects at higher SO ₂ levels.
- Basle (Switzerland) 1984–1989	TSP, LT 0–2 days, M(R ₁) 45 (?–216)	M 25	All All, ≥65 years RD CVD	2.6 2.5 1.8 3.1	1.6–3.6 1.4–3.6 -0.3–3.9 1.6–4.7	
Wordley et al, 1997 (58) - Birmingham (United Kingdom) 1992–1994	PM ₁₀ , LT 1 day, M(R ₁) 26 (3–131)	M 26	All RD COPD IHD	1.1 1.8 4.8 1.7	0.1–2.1 -1.3–4.9 0.5–9.2 0.1–3.2	NO ₂ , SO ₂ or O ₃ in model did not change results appreciably. No clear effect for pneumonia deaths.
Ballester et al, 1996 (59) - Valencia (Spain) 1991–1993	BS, LT 3,0,1,4 days, M(R ₁) 68 (5–226)	M 68	All All, >70 years RD CVD	0.9 0.8 -0.7 1.2	0.3–1.5 0.1–1.6 -2.5–1.0 0.3–2.2	
Hoek et al, 1997 (60) - Rotterdam (Holland) 1983–1991	TSP, LT 1 day, Md(R ₂) 42 (21–112)	Md 23	All	1.0	0.2–1.8	0.8 with CO, SO ₂ or O ₃ + Fe in model. O ₃ was also consistently associated with mortality.
APHEA project - Katsouyanni et al, 1997 (61) - Katsouyanni et al, 1997 (62) (some center results & meta-analysis) - Zmirou et al, 1998 (63) (cause-specific mortality meta-analysis) - Anderson et al, 1996 (64) - London (United Kingdom), 1987–1991–1992 - Dab et al, 1996 (65) - Paris (France) 1987–1992	PM ₁₀ range over centers based on BS (8 cities)	Md 13–73, 90%ile 23–247	All, west & east All, west All, east RD, west RD, east CVD, west CVD, east	0.3 0.6 0.1 0.8 -0.4 0.4 0.0	0.2–0.3 0.4–0.7 0.0–0.2 0.3–1.3 -1.4–0.6 0.1–0.7 -0.3–0.3	Stronger effect in summer. No evidence of interaction between particulate measures and SO ₂ in interaction analyses, except for CVD in western cities (with effect mainly when both pollutants were high). O ₃ also has an effect on mortality in these data, as does NO ₂ , although it is somewhat inconsistent and may be as a proxy for other vehicle-derived pollutants (eg, particles) [Touloumi et al 1997 (74)]. Results for 2- to 4-day mean (also chosen by each center) were very similar in most of the analyses. For center-specific results, see the corresponding center-specific paper (references 64–73).
	PM ₁₀ range over centers based on PM ₁₃ (Paris, Lyon), on 90%ile PM ₇ (Köln), or on TSP (Milan, Barcelona, Bratislava)	Md 33–85, 90%ile 64–137	All, west & east All, west All, east (Bratislava)	0.4 0.4 0.8	0.3–0.6 0.2–0.6 0.1–1.6	

(continued)

Table 1. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in mortality per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments ^d
			Cause	%	95% CI	
- Spix & Wichmann, 1996 (66) (center results) - Köln (Germany) 1975–1985 - Sunyer et al, 1996 (67) - Barcelona (Spain) 1985–1991 - Touloumi et al, 1996 (68) - Athens (Greece) 1987–1991 - Vigotti et al, 1996 (69) - Milano (Italy) 1980–1989 - Wojtyniak & Piekarski, 1996 (70); Wojtyniak et al, 1997 (71) - Cracow, Lodz, Poznan, Wroclaw (Poland) 1977–1990 - Zmirou et al, 1996 (72) - Lyon (France) 1985–1990 - Bacharova et al, 1996 (73) - Bratislava (Slovak Republic) 1987–1991	LT 0, 1, 2 or 3 chosen by each center for each pollutant					
Borja-Aburto et al, 1997 (75) - Mexico City (Mexico) 1990–1992	TSP, LT 0 days, Md(R ₁) 204 (66–456)	M 118	All All, >65 years RD CVD	1.0 1.0 1.7 0.9	0.6–1.5 0.5–1.6 0.2–3.1 0.1–1.7	With SO ₂ and O ₃ in model. SO ₂ also associated with mortality (particularly CVD), O ₃ not consistently.
Saldiva et al, 1994 (76) - São Paulo (Brazil) 1990–1991 (children <5 years)	PM ₁₀ , LT 0–2 days, M 82	M 82	RD, <5 years	-2.0	-6.3–2.6	NO _x showed positive effect, but there was no PM ₁₀ effect.
Saldiva et al, 1995 (77) - São Paulo (Brazil) 1990–1991 (elderly)	PM ₁₀ , LT 0–1 days, M 82	M 82	All, ≥65 years	1.3	0.7–1.9	1.3 (95% CI 0.3–2.4) with SO ₂ , NO _x , O ₃ , and CO in model. Stronger in summer, but effect for all seasons.
Salinas & Vega, 1995 (78) - Santiago (Chile) 1988–1991	PM _{2.5} , LT 0 days (?), M(R ₁) ? (?–150) (truncated)	M ?	All	0.3	0.2–0.6	Weaker effect when PM _{2.5} values >150 µg/m ³ were also included in model. Also effect for CO.
Ostro et al, 1996 (79) - Santiago (Chile) 1989–1991	PM ₁₀ , LT 0 days, M(R ₁) 115 (30–367)	M 115	All All, ≥65 years RD CVD	0.7 0.8 1.1 0.7	0.4–0.9 0.5–1.1 0.6–1.7 0.3–1.0	Similar results for total mortality with other model specifications, including other LT. Suggested stronger effect for 3-day mean (LT 0–2).
Simpson et al, 1997 (14) - Brisbane (Australia) 1987–1993	Light scattering (nephelometry), LT 0 days, M(R ₁) 2.6 (0.3–15.2)	M 26	All All, ≥65 years RD HD	0.9 1.0 0.1 1.0	0.3–1.5 0.2–1.8 -2.0–2.3 -0.2–2.2	Similar effect with other pollutants in model. Effect also of O ₃ . No evidence of threshold for particle effect.
Xu et al, 1994 (80) - Beijing (China) 1989	TSP, LT 0 days, M(R ₂) 375 (155–760)	M 206	All All, summer COPD	0.3 0.7 2.3	-0.2–0.7 0.1–1.3 0.5–4.1	0.0 (95% CI -4.5–4.7) with SO ₂ in model. SO ₂ stronger effect. Effect for TSP in summer only, SO ₂ both seasons.

^a Given are the type of particle; lag time (LT); mean and range [M(R_n)] of daily air pollution readings, the range being as follows: R₁ = true range, R₂ = 5th to 95th percentile, R₃ = 10th to 90th percentile, R₄ = 20th to 80th percentile. The median (Md) or geometric mean (GM) is given when the mean was not available. Mostly daily means are used (eg, with LT 0 or LT 1); see page 49 for a discussion.

^b Conversion factors: PM₁₀ ≈ PM₁₅ ≈ BS ≈ SO₂ × 4 ≈ PM_{2.5}/0.60 ≈ CoH [in units of 10³ linear feet, used in most studies] × 55 ≈ TSP × 0.55 (12,13) and PM₁₀ ≈ light scattering (by nephelometry, in units of 10³/m) × 10 (14,15), with remaining particle measures in micrograms per cubic meter.

^c Values given are the mean (M), median (Md) or geometric mean (GM).

^d No co-pollutant in the main model unless indicated in this column.

^e In complete dataset – SP mean 97, range 10–566 — the estimate for total mortality was 0.4 (95% CI 0.1–0.7) per 10 µg/m³ PM₁₀.

Studies in the United States

A 1990 study in St Clara (16), a location with low levels of sulfur dioxide (SO₂), found a clear effect of same-day particulate levels measured as the coefficient of haze (CoH), equivalent to an 0.8% (95% CI 0.3–1.3) increase in daily mortality per a 10 µg/m³ increase in

daily PM₁₀, a finding which stimulated further research on this issue in the United States. Consequently, large contributions to our knowledge about the association between particulate air pollution and mortality have come from the United States in later years (21–23, 29, 30, 32–34, 36, 37). These studies have been carried

out using consistent methodology, with successive refinement. Initially the studies focused on total suspended particles (TSP), but, as the measurement of PM_{10} and smaller particle sizes has become more common in the United States, the focus has shifted accordingly. In a recent study of six US cities (37), $PM_{2.5}$ (particulate matter $<2.5 \mu m$ in diameter) was associated with a stronger effect than the coarse mass (the larger particles in PM_{10}) and overall with a slightly stronger effect than PM_{10} . A meta-analysis of eight locations in these US studies (21–23, 29, 32–34) estimated an increase of 1.06 (95% CI 1.04–1.06) per 100 $\mu g/m^3$ of TSP, corresponding to an increase in daily mortality of 1.1% (95% CI 0.9–1.2) per 10 $\mu g/m^3$ increase in PM_{10} (33). Two later studies also had similar results, with point estimates of 1.1% and 0.8% (36, 37).

Slightly smaller increases in mortality, around 0.5%, have been observed in Chicago (42–44), as well as Los Angeles (40, 41). An analysis of early Los Angeles data (1970–1979) (38) also showed associations with vehicle pollutants including KM (a particulate measure of optical reflectance), as well as ozone (O_3). A prior analysis of the same data (39) found that carbon monoxide (CO), hydrocarbons, and KM, all vehicle-derived pollutants, were the most highly correlated with low-frequency (ie, long-period) fluctuations in mortality, a result that may be of some relevance to health effects in relation to medium or long-term exposure.

Studies in Europe

The famous 1952 London air pollution episode with a very dramatic and acute peak of increased mortality provided a spectacular starting point for air pollution epidemiology. Subsequently, several analyses and reanalyses of mortality and air pollution data from London during more normal years have been performed; they confirmed an effect that appears to be associated with smoke levels more than with SO_2 , independently of episodic peaks (45–48). Early studies in France and in Athens, Greece, also observed increased mortality, although it appeared to be associated more with SO_2 than with smoke (49–52).

Since 1993, a large number of separate European studies has been performed in locations with varying pollution mixes (53–60), generally observing an increase of about 1% in daily mortality per a 10 $\mu g/m^3$ increase in PM_{10} , and often a similar or slightly weaker effect from SO_2 . Several of these studies have used the methodology developed within the APHEA study (short-term effects of Air Pollution and Health: a European Approach), a large multinational project aiming to quantify air pollution health effects in Europe using standardized methodology in multiple locations (9, 81, 82). In this collaborative effort, an effect of particles,

measured as TSP, PM_7 , PM_{10} , PM_{15} or BS was consistently observed, and an independent effect of SO_2 of similar magnitude appeared to be present in most study locations (61–73). The effect of an increase of 10 $\mu g/m^3$ in PM_{10} , based on conversion from gravimetric measures of particulates in six locations (see table 1), was a 0.4% (95% CI 0.2–0.6) increase in total mortality in five western European cities, but higher in Bratislava, the only eastern European city with such measurements [0.8% (95% CI 0.1–1.6)]. For BS, the west-east pattern was reversed, with 0.6% (95% CI 0.4–0.7) and 0.1% (95% CI 0.0–0.2) increases in mortality, respectively, based on results from four cities in each area (not including Bratislava). For SO_2 the pattern was similar to that for BS, and Bratislava did not differ from other eastern European sites. The reason for the heterogeneity of the observed effect is unclear. A positive correlation between average winter temperature and the size of the effect estimate exists for the cities participating in the APHEA study, although other factors, such as age-standardized mortality or proportion of older people, are similarly or even more strongly correlated (83, 84).

Other studies

From other parts of the world, high levels of TSP showed a strong relationship with mortality in Mexico City, whereas O_3 did not when analyzed together with particles, despite the high levels of photochemical pollution observed in this location (75). In Santiago, Chile, mortality was associated with $PM_{2.5}$ and PM_{10} (78, 79), and in Sao Paulo, Brazil, an effect on mortality among elderly people was shown, whereas child mortality was not affected by particles, but it was affected by nitrogen dioxide (NO_2) (76, 77). In Brisbane, effects were found for both particles and O_3 , but, whereas a threshold was suggested for the O_3 effect, no threshold was indicated for particles (14). In Beijing, where pollution levels were very high, SO_2 had a more consistent effect all year around, but there was an effect for TSP on total mortality during the summer (80).

Methodological issues

Research on the health effects of particles has become a field of great controversy, partly because of a revision of air pollution standards in the United States and Europe in the 1990s. A major discussion has focused on the appropriate statistical modeling for this type of data. One result has been multiple reanalyses of data — for example, in London (45, 47, 48), Steubenville, Ohio (85), Philadelphia, Pennsylvania (24–28, 35) (table 1), and, for hospital admissions, in Birmingham, Alabama, and Minneapolis-St Paul, Minnesota (86) (table 2),

Table 2. Time series studies of hospital admissions and particulate air pollution. (For any abbreviations not found in the footnotes, see page 4.)

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in admissions per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments
			Cause	%	95% CI	
Mazumdar & Sussman, 1983 (20) - Hazelwood/Bellevue/Logans Ferry, Pittsburgh (PA), 1972–1977	CoH, LT 0 days (?), M(R ₁) 1.0 (0–3.5)	M 54	All RD HD VD	0.3 0.3 0.5 0.4	0.2–0.3 0.1–0.5 0.4–0.7 0.2–0.6	Very similar with SO ₂ in model. Estimates are here pooled over all 3 locations, all of which gave relatively consistent results.
Thurston et al, 1992 (99) - Buffalo, Albany (NY) 1988–1989 - New York City (NY) 1988–1989	SO ₄ , LT 0 days, M(R ₁) 9 (?–37.4) SO ₄ , LT 0 days, M(R ₁) 9.3 (?–33.6)	M 36 M 37.2	RD Asthma RD Asthma	2.3 2.2 1.0 1.9	0.6–3.9 -0.7–5.1 0.2–1.8 0.4–3.4	Estimates from SO ₄ regressions using 1988 data. 1989 data gave similar results. O ₃ and H ⁺ showed as strong or stronger effects.
Schwartz, 1994 (95) - Philadelphia (PA) 1986–1989 (≥65 years)	TSP, LT 0 days (?), M ? ¹	M ?	Pneumonia	3.7	1.7–5.7	3.2 (95% CI 1.2–5.3) with O ₃ in model. Also associations with O ₃ and SO ₂ , although strongest with TSP.
Schwartz, 1994 (100) - Birmingham (AL) 1986–1989 (≥65 years)	PM ₁₀ , LT 0 days, M(R ₃) 45 (19–77)	M 45	COPD Pneumonia	2.4 1.8	0.8–4.1 0.7–2.8	O ₃ also associated, more weakly, with COPD and pneumonia.
Schwartz, 1994 (101) - Minneapolis-St Paul (MN) 1986–1989 (≥65 years)	PM ₁₀ , LT 0–1 days or 0 days, M(R ₃) 36 (18–58)	M 36	COPD Pneumonia	4.6 1.6	1.8–7.5 0.2–2.9	O ₃ also associated with pneumonia.
Moolgavkar et al, 1997 (86) - Birmingham (AL) 1986–1991 (≥65 years) - Minneapolis - St Paul (MN) 1986–1991 (≥65 years)	PM ₁₀ , LT 0 days, M(R ₃) 43 (18–74) PM ₁₀ , LT 0–1 days, M(R ₃) 34 (17–55)	M 43 M 34	COPD & Pneumonia COPD Pneumonia	0.3 0.9 0.5	-0.3–0.9 -0.6–2.4 -0.5–1.5	For both weaker effects than in 1986–1989 analyses by Schwartz. For Birmingham no clear O ₃ effect. For Minneapolis-St Paul the estimates given are with O ₃ , SO ₂ and NO ₂ in models; PM ₁₀ estimates stronger in single pollutant models; strongest and most consistent effect for O ₃ , however.
Schwartz, 1994 (102); Schwartz & Morris, 1995 (103) - Detroit (MI) 1986–1989 (≥65 years)	PM ₁₀ , LT 0–1 days, M(R ₃) 48 (22–82)	M 48	COPD Pneumonia IHD HF CDR	2.0 1.2 0.6 0.7 0.6	0.9–3.2 0.4–1.9 0.1–1.0 0.1–1.4 -0.1–1.3	No association seen for asthma admissions. O ₃ also associated with COPD and pneumonia. CO also associated with HF, but O ₃ and SO ₂ with neither IHD nor HF.
Schwartz, 1995 (104) - New Haven (CT) 1988–1990 (≥65 years) - Tacoma (WA) 1988–1990 (≥65 years)	PM ₁₀ , LT 0 days, M(R ₃) 41 (19–67) PM ₁₀ , LT 0 days, M(R ₃) 37 (14–67)	M 41 M 37	RD RD	1.2 1.9	0.0–2.5 0.6–3.2	Slightly higher estimates with O ₃ and SO ₂ in model. Independent effect also for O ₃ and more weakly for SO ₂ .
Schwartz, 1996 (105) - Spokane, WA 1988–1990 (≥65 years)	PM ₁₀ , LT 0 days, M(R ₃) 46 (16–83)	M 46	RD COPD Pneumonia	1.6 3.2 1.0	0.7–2.6 1.5–4.9 -0.3–2.4	Very low SO ₂ levels. O ₃ also associated with RD admissions.
Schwartz et al, 1996 (9) - Cleveland, OH 1988–1990 (≥65 years)	PM ₁₀ , LT 1–2 days, M(R ₃) 43 (19–72)	M 43	RD	1.1	0.1–2.2	O ₃ also significant, weaker evidence for SO ₂ .
Schwartz, 1997 (106) - Tucson, AZ 1988–1990 (≥65 years)	PM ₁₀ , LT 0 days, M(R ₃) 42 (21–63)	M 42	HD	1.2	0.2–2.2	1.0 (95% CI 0.0–2.0) with CO in model. Similar effect for CO. No effect for SO ₂ , O ₃ or NO ₂ . Low SO ₂ levels.
Bates & Sizto, 1983 (107), 1986 (108), 1987 (109), 1989 (110) - Ontario (Canada) 1974 and 1976–1978, –1982 or –1983, summer - Ontario (Canada) 1974 and 1976–1978, –1982 or –1983, winter	SO ₄ , LT 0,1,2 days, M 9.5 SO ₄ , LT 0,1,2 days, M 10.3	M 38 M 41	RD RD	Effect for SO ₄ No effect		Summer effect also for O ₃ for RD admissions. No effect for O ₃ or SO ₄ for a group of nonrespiratory admissions.

(continued)

Table 2. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in admissions per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments
			Cause	%	95% CI	
Lipfert & Hammerstrom, 1992 (111) - Ontario (Canada) 1979–1985, summer/winter	TSP, LT 0–2 days, M 62	M 34	RD	No significant effect for TSP in stepwise regression		Some effects for O ₃ , SO ₂ and SO ₄ were found, particularly in summer.
Burnett et al, 1994 (112) - Ontario (Canada) 1983–1988	SO ₄ , LT 1 day, M 5.3	M 21	RD	0.8	0.5–1.1	.
Burnett et al, 1995 (113) - Ontario (Canada) 1983–1988	SO ₄ , LT 1 day, M(R ₂) 4.4 (?–13)	M 17	RD, all ages RD, ≥65 years COPD Pneumonia Asthma HD, all ages HD, ≥65 years IHD CDR HF	0.7 0.7 0.9 0.6 0.6 0.5 0.7 0.4 0.2 0.6	0.5–0.9 0.3–1.1 0.5–1.4 0.3–0.9 0.2–1.0 0.3–0.7 0.4–1.0 0.1–0.7 -0.4–0.9 0.1–1.0	0.7 (95% CI 0.4–0.9) with O ₃ in model. No clear seasonal difference. Note: HD here is only IHD+CDR+HF (ICD-9 codes 410+413, 427, 428).
Delfino et al, 1994 (114) - Montreal (Canada) 1984–1988 May–October	PM ₁₀ , LT 3 days, M(R ₂) 30 (?–46)	M 30	Asthma	2.3	0.6–4.0	Effect of high versus low SO ₄ days on non-asthma admissions July–August also seen.
Thurston et al, 1994 (115) - Toronto (Ontario) 1986–1988 summer	PM ₁₀ , LT 0 days, M 33	M 33	RD	4.5	0.4–8.7	2.5 (95% CI -2.4–7.4) with O ₃ in model. Effect for H ⁺ >SO ₄ >PM _{2.5} >PM ₁₀ >TSP.
Burnett et al, 1997 (116) - Toronto (Ontario) 1992–1994 summer	PM ₁₀ , LT 0–3 days, M(R ₁) 28 (4–102)	M 28	RD CD	2.1 2.3	0.9–3.3 0.3–4.4	Effect sensitive to other pollutants (particularly NO ₂) in model. Associations with O ₃ , and also NO ₂ , SO ₂ and CoH, more consistent.
Burnett et al, 1997 (117) - 10 Canadian cities 1981–1991 (>65 years)	CoH, LT 0 days, M(R ₂) 0.3 (0–0.9)	M 17	HF	2.2	0.8–3.6	No effect with O ₃ , NO ₂ , SO ₂ and CO in model. CO strongest effect in multipollutant models.
Burnett et al, 1997 (118) - 16 Canadian cities 1981–1991	CoH, LT 0 days, M(R ₂) 0.64 (?–1.5)	M 35	RD	1.1	0.6–1.6	With O ₃ and CO in model. Similar effects of these 2 pollutants.
Díaz-Caneja & Gutiérrez, 1991 (119) - Santander (Spain) 1979–1982	SPM, LT 0 days, M 66	M 36	COPD HF	8.7 6.3		Stepwise linear regression. Association with square and quadratic root of SPM.
Pantazopoulou et al, 1995 (120) - Athens (Greece) 1988 (winter & summer separately)	BS, LT 0 days (?), M(R ₂) 135 (46–281)	M 135	RD, winter HD, winter	0.9 0.7	0.2–1.7 0.3–1.1	Less effect in summer for both RD and HD.
Walters et al, 1994 (121) - Birmingham (United Kingdom) 1988–1990	BS, LT 2 days, M(R ₃) 13 (4–29)	M 13	RD, winter Asthma, winter	13.1 9.7	6.0–20.6 1.0–19.2	Less effect in summer, little observed in spring and autumn. SO ₂ similar but weaker effects.
Wordley et al, 1997 (58) - Birmingham (United Kingdom) 1992–1994	PM ₁₀ , LT 1 day, M(R ₁) 26 (3–131)	M 26	RD Asthma Bronchitis Pneumonia COPD IHD CerebroVD	2.9 4.0 5.8 6.2 1.8 0.3 2.1	1.2–4.5 0.8–7.6 1.7–11.9 2.5–10.1 -1.7–5.4 -0.9–1.5 0.0–4.2	.
Poloniecki et al, 1997 (122) - London (United Kingdom) 1987–1994	BS, LT 1 day, Md(R ₁) 12 (1–62)	Md 12	CVD AMI AP CDR HF	0.5 2.0 2.0 1.7 0.5	-1.0–2.1 0.6–3.5 0.2–3.9 -0.3–3.7 -1.0–2.1	No effect on cerebroVD. For AMI mainly effect in cool season, and similar effects for NO ₂ , SO ₂ , CO (SO ₂ most consistent) but not O ₃ .

(continued)

Table 2. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,e} (µg/m ³)	Increase in admissions per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments
			Cause	%	95% CI	
APHEA project						
- Katsouyanni et al, 1997 (61) [center results for RD (≥65 years) and COPD (all ages) admissions]	BS (5 cities), range over centers Md 6–41	Md 6–41	RD, 15–64 years	0.6	0.1–1.0	<i>RD admissions:</i> Most consistent effect for O ₃ . No consistent effect for SO ₂ . Particle effect somewhat unstable. Effect of BS significantly stronger at high NO ₂ levels, but no clear overall NO ₂ effect.
- Amsterdam, Rotterdam, London, Paris, Milan			RD, ≥65 years	0.4	-0.1–0.9	
- Spix et al, 1998 (123) (meta-analysis for RD admissions)			COPD	0.7	0.2–1.2	
- Amsterdam, Rotterdam, London 1987–1991, Paris, Milan			COPD, cool season	0.6	0.0–1.2	
- Anderson et al, 1997 (124) (some center results & meta-analysis for COPD admissions)	TSP (4 cities), range over centers Md 41–155	Md 23–85	COPD, warm season	1.0	-0.4–2.3	<i>COPD admissions:</i> Most consistent effect for O ₃ . Some effect also observed for NO ₂ and SO ₂ . Seasonal variation inconsistent between BS and TSP.
- Amsterdam, Rotterdam, London Paris, Milan, Barcelona 1986–1992			Asthma, ≤14 years	0.6	-0.4–1.6	
- Sunyer et al, 1997 (125) (some center results & meta-analysis for asthma admissions)			Asthma, 15–64 years	0.4	-0.3–1.2	
- London, Paris, Barcelona, Helsinki ^d						
- Dab et al, 1996 (65)	LT 0, 1, or 3 chosen by each center for each pollutant		RD, 15–64 years	0.4	-0.4–1.1	<i>Asthma admissions:</i> Significant effects of NO ₂ in adults and SO ₂ in children were also seen, independent of particle effects. While the particle effect was weakened in 2-pollutant models, NO ₂ and SO ₂ , respectively, were strengthened. For O ₃ , no effect was seen in children and inconsistent results in adults. Seasonally, the particle effect was stronger in winter.
- Paris 1987–1992 (all ages)			RD, ≥65 years	0.6	-0.2–1.4	
- Schouten et al, 1996 (127)			COPD	0.8	-0.1–1.7	
- Amsterdam/Rotterdam 1977–1989			COPD, cool season	1.4	-0.3–3.2	
- Ponce de Leon et al, 1996 (126)			COPD, warm season	0.4	-0.9–1.6	
- London 1987–1988, 1991–1992;						
- Vigotti et al, 1996 (69)						
- Milano 1980–1989						
- Sunyer et al, 1991 (128);						
- Sunyer et al, 1993 (129)						
- Barcelona 1985–1989						
- Pönkä & Virtanen, 1996 (130)						
- Helsinki 1987–1989 ^d						

^a Given are the type of particle; lag time (LT); the mean and range [M(R_n)], the range being as follows: R₁ = true range, R₂ = 5th to 95th percentile, R₃ = 10th to 90th percentile. The median (Md) is given when the mean was not available. Mostly daily means are used (eg, with LT 0 or LT 1); see page 49 for a discussion.

^b Conversion factors: PM₁₀ ≈ PM₁₅ ≈ BS ≈ SO₄ × 4 ≈ PM_{2.5}/0.60 ≈ CoH [in units of 10³ linear feet, used in most studies] × 55 ≈ TSP × 0.55 (12,13) and PM₁₀ ≈ light scattering (by nephelometry, in units of 10⁻⁵/m) × 10 (14,15), with remaining particle measures in micrograms per cubic meter.

^c Values given are the mean (M) or median (Md).

^d No particle data for Helsinki.

in some cases with different conclusions. The US Health Effects Institute sponsored an extensive project to re-analyze six previous studies of mortality and particulate air pollution (35). With partly new methods, the original analyses were generally confirmed. In the case of Philadelphia, separate effects of SO₂ and TSP were found, and earlier observations of stronger relative increases associated with TSP in summer and autumn, but with SO₂ in winter and spring (24), were initially replicated, but not confirmed in detailed analyses by the new analysts (27, 28). Others have also investigated the sensitivity to modeling assumptions. For example, assumptions regarding the distribution of residual variability in mortality were investigated in a Los Angeles 1985–1990 dataset (average 153 deaths per day), and small differences were found between linear (Gaussian) and log-linear Poisson regressions (40). However, it is now generally recognized that some type of Poisson regression is the method of choice for data of this kind be-

cause it accommodates nonnormally distributed, small daily outcome counts and generally because the variance of the outcome may not be constant over the range of exposure, as assumed in a linear regression.

Seasonal differences have been observed in several studies, in some locations with higher effects of particles in the summer (24, 40, 41, 77) or spring or autumn (42), while others have found little variation (27, 28). The divergent findings are difficult to interpret, but could be due to, for example, a varying influence of photochemical or other pollutants, differing weather conditions, or industrial or other human activity that could lead to a variation in the composition of particles and hence to a variation in their biological effect by season. Uncontrolled confounding by unidentified or known risk factors (eg, temperature) could also vary by season. Other possible explanations include varying exposure misclassification (eg, due to indoor-outdoor activity patterns) or a true season or temperature

interaction with air pollution. This question deserves further study.

Several aspects of the mortality observed to be related to daily air pollution levels are important. First, the pattern of increased deaths on days with high versus low particulate pollution was shown in Philadelphia, Pennsylvania, to be similar to the pattern observed in the London air pollution episode in 1952. A disproportionate increase in chronic obstructive pulmonary disease (COPD) and pneumonia deaths was observed, as were increases in heart disease and stroke deaths, particularly with respiratory factors as contributing causes and a disproportionate increase in dead-on-arrival deaths and deaths outside of hospitals and clinics (87). Second, an important question to consider is how much the life of those dying from air pollution is shortened. According to one hypothesis, the effect seen in the daily time-series studies is largely a "harvesting effect", whereby death occurs for sensitive persons who would have died in the immediate future from preexisting disease. This hypothesis is biologically plausible and has some epidemiologic support (54). There is however also evidence of more long-term effects (88, 89). A third, related question, is whether the increased mortality is limited to sensitive subgroups or whether it affects even the previously "healthy" population. No data directly answering this question currently exist. The biological mechanisms underlying an effect on mortality are not clear. According to one hypothesis (90), low-grade inflammation caused by alveolar deposition of ultrafine particles may lead to increased blood coagulability. Indeed, a cross-sectional study observed an increased OR of approximately 3 for plasma viscosity above a 95th percentile cut point ($1.38 \text{ mPa} \times \text{s}$) for subjects of either gender sampled during an air pollution episode when they were compared with those sampled at other times (91). However, since ultrafine particles are not routinely measured, no time-series studies have yet investigated this pollutant measure in relation to mortality or hospital admissions, although initial contradictory results are available in relation to pulmonary function and symptoms of asthmatics (92, 93).

Exposure measurement is mainly of an ecological (aggregated) nature — generally one fixed air pollution monitor or an average from several monitors is used to estimate daily exposure for all persons in a study. Such exposure assignment has been shown to have a reasonably high correlation with personal exposure measurements (eg, for PM_{10}) (94). Some measurement error is inevitable but can generally be expected to be nonsystematic, and therefore there would generally be some attenuation of estimates for continuous exposure variables (8).

The analytical methods used attempt to control for confounding by season and long-term trends and there-

by eliminate the need to consider other traditional confounders that lack day-to-day variation. Weather variables, including temperature, are important potential confounders with short-term variation to consider, as well as day of week, holidays, and epidemics (eg, influenza). Several different methods may be appropriate to model such covariates in the regression analysis, ranging from dummy variables over parametric approaches to nonparametric smoothing, which may be incorporated into a generalized additive model (9, 95). In most instances, there is no general answer as to which approach is the most correct, and reanalyses of existing datasets have illustrated that alternative model specifications often make surprisingly little difference. Consequently, each study is best judged individually on the subject of confounding control.

Obviously, another set of vital potential confounders is other air pollutants. Most studies have not performed analyses including co-pollutants or including only one co-pollutant, often because of lacking data. It is also difficult to model meaningfully many co-pollutants when they are highly correlated, especially in small datasets. This problem is important in respect to future analyses, as particle measures can be sensitive to the inclusion of other pollutants in the statistical model (27, 28). In many instances, however, the estimated effects of particles have not been very sensitive to the inclusion of co-pollutants (96). Studies have also found significant associations with O_3 (38, 74, 97), generally a daily 1-hour or 8-hour maximum with 0, 1 or 2 days of lag time, although for O_3 , the evidence is stronger for other types of health effects than for mortality (98). In several locations, significant associations have also been observed for SO_2 and NO_2 (38, 47, 62, 74). Meta-analyses from the APHEA study indicate that all of the mentioned air pollutants show significant associations with mortality (62, 74). On the other hand, some studies were designed to take advantage of low levels of other air pollutants in specific locations, and effects of particles have been observed also in such locations (16, 29, 30).

Previous studies have examined various lag times and averaging times for the exposure variable. These are almost always less than 5 days, and generally particulate levels on the same or previous day are associated with increased daily mortality, even when another lag time or averaging time has been chosen in the final model. It is not clear whether the datasets have been extensive enough and the methods rigorous enough to draw any conclusions from the various lag times and averaging times used, as day-to-day particulate levels are highly correlated and these variable constructs may be measuring essentially the same thing with different amounts of measurement error, which may vary between studies. Recently, new methods have appeared to evaluate appropriate lag times more formally using the Akaike

information criterion within the framework of analyses employing generalized additive models (27, 28).

Evaluation

A large number of studies has consistently observed increased mortality in association with levels of particulate air pollution on the previous day or days. Different gravimetric measures such as TSP and PM_{10} and reflectance or visibility measures such as BS or CoH have been used with similar results. It has lately been suggested that the smaller particulate fractions (eg, $PM_{2.5}$ or even smaller) are primarily responsible for the health effects observed (37). The possibility that particles are a surrogate for other pollutants cannot be completely dismissed. However, the association has been consistently observed even in locations with low levels of other pollutants — for example, SO_2 in Utah Valley or St Clara — or high levels — for example, O_3 in Mexico City. The size of the effect is around a 0.5–1% increase in daily mortality for a $10 \mu g/m^3$ increase in PM_{10} , and it appears generally to be stronger for respiratory deaths and cardiovascular deaths than for total death counts. The effect appears to follow within one to a few days after high particle levels; depending on the study, the health effects have been related to daily mean particulate levels with a lag time of 0 to 4 (same day or closest preceding days) or an average over 2–5 days previously. Associations have been observed at particulate levels well below $100 \mu g/m^3$, and some studies indicate weaker relationships at higher levels. Similarly, several studies have reported stronger effects in the summer (when PM_{10} levels are usually lower), and a positive correlation between the average winter temperature and the size of the effect estimate exists for the cities that participated in the APHEA study.

Time-series studies of hospital admissions and outpatient visits

Hospital admissions

A large number of studies has also appeared relating particulate air pollution for one or a few days to morbidity, measured as daily hospital admissions for all causes, all or specified respiratory causes, or cardiovascular causes (9, 20, 58, 61, 65, 69, 86, 95, 99–130). For ease of reference, the studies are listed in table 2 with brief relevant information.

Studies in the United States. After a few early studies reporting an effect of particles on admissions for respiratory disease, including asthma, as well as cardiovascular disease (20, 99, 131–133), some of which used longer averaging times (see table 5 under “Miscellaneous

Health Effects in Relation to Medium-term Exposure”) (131–133), a large number of studies of this type has been conducted in the United States (9, 95, 100–106). These studies used a relatively consistent methodology, employing variants of Poisson regression and all focusing on PM_{10} as the exposure measure, and therefore the intercomparison is relatively straightforward. They all investigated admissions among elderly people and have reported consistent associations for all respiratory, COPD and pneumonia hospital admissions, as well as for heart disease admissions, with PM_{10} levels. Most of the studies have considered O_3 , and in some cases SO_2 , but otherwise multipollutant models were not investigated in the original reports. A reanalysis of data from two of the sites, which considered several pollutants, reported weaker effects than originally found and further weakening of the PM_{10} effect in multipollutant models (86). In some of the other studies, however, the study site was selected to have low levels of another pollutant or low correlations between pollutants.

Studies in Canada. A well-organized hospital system has provided substantial amounts of data for these kinds of analyses in Canada. Bates & Sizto (107–110) were the first to relate Ontario hospital admissions to air pollution data; they found consistent relationships during the summer with sulfates and O_3 , but not with CoH. They hypothesized that oxidant air pollution and irritating gases or acid aerosols, which tend to appear in summer, were responsible for the effects. Subsequent studies in Canada also tended to see O_3 effects, and thus analyses were focused on oxidants, acid aerosols, and sulfate ions (SO_4), as well as on seasonal differences or the summer season exclusively (115, 116). The study of effects of particulates was also hampered by the fact that, apart from SO_4 , the CoH was the only measure of particulate air pollution available on a large scale. Since it is a measure of sample filter staining, it is not particularly well characterized and is not ideally suited for studying particles. Until very recently, these studies used techniques based on linear regressions, and this approach may have been a reasonable analytic strategy considering the large number of daily admissions in most studies, even in subgroup analyses. As a group, the studies suggest that there may be an effect of particles on hospital admissions for respiratory disease, asthma, and some cardiac disease, but more extensive monitoring by gravimetric measuring methods would be helpful to determine which particulate components may be responsible.

Studies in Europe. The studies in Europe have used BS, a similar measure of sample filter staining, and only lately have gravimetric methods become more common. Similarly, before the coordinated APHEA study, which

employed Poisson regression methods, linear regression was generally used. In general, an effect of BS or other particulate measures has been observed for total respiratory admissions, bronchitis, and asthma, as well as for some cardiovascular conditions. The particulate effect has often been stronger in the cool season (58, 120–122), in contrast to the findings of mortality studies. In the large APHEA study a seasonal difference was consistently found for asthma admissions but not for total respiratory admissions or COPD (123–125). One explanation for finding a weaker effect for asthma in summer could be that the strong effect of elevated pollen levels makes it difficult to discern a particle effect when pollen data are lacking. The European results are generally consistent with other data in suggesting effects of air pollution including particles on respiratory and possibly cardiovascular admissions. The increased risks observed, especially in the APHEA study, are however generally somewhat lower than in studies from the American continent (in the range of a 0.4–0.9% increase per 10 $\mu\text{g}/\text{m}^3$ of PM_{10} for different end points in different subgroups of the APHEA study), and there is also clear heterogeneity between locations. Possible reasons for this heterogeneity include differences in population composition, baseline morbidity, meteorological conditions (including temperature), and a particulate air pollution mix due to different emission sources (heating, traffic, industry).

Outpatient visits

Fewer studies have investigated outpatient visits, partly because such data are more rarely routinely available. The studies are listed in table 3 (15, 120, 134–149).

In the United States, an overall increase in daily asthma visits by $\geq 2.0\%$ has been related to a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{10} (135, 137–140). One of these studies reported a higher effect of PM_{10} at temperatures above 0°C than below 0°C (138), whereas in another the increase in asthma visits was 1.8% at the study mean temperature (5°C) but 6.1% at low temperatures (140). In addition, visits for respiratory disease in general (134), bronchitis (136, 139), and upper respiratory infections (139) have shown increases, although of a smaller magnitude. Another US study, as well as two Canadian studies, found relationships between asthma visits and other pollutants to be stronger (141–143), and a Canadian study of visits for respiratory disease found an effect of particles only in the age group of >64 years, although this effect was marked, 7.3% (95% CI 2.0–12.6) (144).

In Europe, a pronounced increase in croup cases in relation to TSP exposure was reported from Germany, corresponding to approximately 8% per 10 $\mu\text{g}/\text{m}^3$ (145).

Other studies have observed a possible limited effect of particles on all-cause visits (120), as well as a stronger effect on asthma visits specifically (146, 147), although NO_2 and sometimes also other pollutants (147) have been as strongly implicated. One study of asthma visits noted a seasonal interaction indicating a stronger effect on asthma at higher temperatures (146), whereas no seasonal variation in effect was seen for all-cause visits (120). A particularly strong effect on asthma in children was seen in a study on physician house calls in Paris, where an effect of O_3 only at 10°C or higher was also noted (147). No clear effect on cardiovascular visits could be observed. In Beijing, with very high pollution levels, only weak effects of particles and SO_2 on total all-cause emergency visits were found (148, 149). The effect size was similar to that of the European study of all visits (120) and may at least partly reflect that the outcome measure was nonspecific. In Australia, high particulate levels after extensive bush fires could not be related to asthma visits (15).

Evaluation

Several methodological aspects of relevance have already been discussed in the section on mortality. One difference is that, in relation to the underlying outcome of interest, in this case health deterioration, hospital admissions or outpatient visits are potentially more affected by the behavior of study subjects (eg, decision on whether to seek care or not at equivalent disease states) or societal factors (variations in access to care, etc). This difference may paradoxically result in greater misclassification for these morbidity outcomes than for mortality outcomes, although the morbidity outcomes are in a sense more specific. The possible impact of “harvesting” (ie, short-term advancement of the outcome) may also have a different implication than for mortality, as a proportion of admissions or visits due to air pollution is likely to represent cases which would not otherwise have occurred at all. Overall the studies on hospital admissions and emergency room visits provide additional evidence for adverse health effects due to short-term exposure to particles. Increases in daily admissions range from 0.5% to 3% per 10 $\mu\text{g}/\text{m}^3$ PM_{10} in most studies. The lag time between exposure and effect appears to be similar to that found for mortality end points — from one to a few days. An effect on many respiratory end points has been found, and in some studies there has also been an effect on certain cardiovascular conditions. Generally the estimated effect is stronger on respiratory disease such as COPD and pneumonia (ranging up to over 6% per 10 $\mu\text{g}/\text{m}^3$ of PM_{10}) and lower for cardiovascular disease or specific cardiac disease end points (up to 2.3% per 10 $\mu\text{g}/\text{m}^3$ of PM_{10} reported). The results regarding daily asthma admissions

Table 3. Time series studies of emergency visits and particulate air pollution. (For any abbreviations not found in the footnotes, see page 4.)

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in visits per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments
			Cause	%	95% CI	
Samet et al, 1981 (134) - Steubenville (OH) 1974–1977	TSP, LT 0 days, M(R ₁) 156 (14–696)	M 86	All visits RD	0.2 0.5	0.0–0.4 0.0–1.0	RD: effect also of SO ₂ .
Schwartz et al, 1993 (135) - Seattle (WA) 1989–1990, <65 years	PM ₁₀ , LT 0–3 days, M(R ₁) 30 (6–103)	M 30	Asthma, <65 years	3.7	1.2–6.3	No association was seen for persons ≥65 years of age.
Hefflin et al, 1994 (136) - Washington State (US) 1991	PM ₁₀ , LT 0 days, M(R ₁) 40 (3–1689)	M 40	Bronchitis Sinusitis	0.4 0.5 ^d	0.3–0.4 0.3–0.6	URI or asthma: no significant association. Two days of dust storms during study.
White et al, 1994 (137) - Atlanta (GA) summer 1990	PM ₁₀ , LT 1 day, M(R ₁) 39 (19–87)	M 39	Asthma	2.0	-6.0–10.7	With O ₃ in model. High O ₃ days were also associated with asthma visits.
Choudhury et al, 1997 (138) - Anchorage (AK) 1990–1992	PM ₁₀ , LT 0 days, M(R ₁) 41 (1–565)	M 41	Asthma	4.2	2.4–6.2	Simple linear regression. Suggested lower PM ₁₀ effect at low temperature.
Gordian et al, 1996 (139) - Anchorage (AK) 1992–1994	PM ₁₀ , LT 0 days, M(R ₁) 46 (5–565)	M 46	Asthma Bronchitis UR illness	2.5 0.9 1.2	0.0–5.1 NS 0.0–2.4	Effects similar by season. UR illness: effect especially for ages <11 years and >45 years.
Lipsett et al, 1997 (140) - Santa Clara County (CA) 1988–1992, winter	PM ₁₀ , LT 0–2 or 2 days, M(R ₁) 61 (9–165)	M 61	Asthma	9.6 (overall estimate for LT 0–2)	0.1–20.0	Temperature interaction model, lag 2: 6.1 (95% CI 2.8–9.1) at -7°C (minimum temperature), 1.8 (95% CI 0.5–2.9) at 5°C (mean temperature).
Yang et al, 1997 (141) - Reno (NV) 1992–1994	PM ₁₀ , LT 0 day(?), M(R ₁) 34 (2–157)	M 34	Asthma	No significant PM ₁₀ effect		Effect of O ₃ , but not significant for PM ₁₀ or CO.
Bates et al, 1990 (142) - Vancouver (Canada) 1984–1986 (0–14, 15–60 & >60 years)	SO ₄ , LT 0, 1 & 2 days, M(R ₁) 3.4 ?–14.5	M 13	RD & asthma	Some correlations noted for SO ₂ , SO ₄ and NO ₂		Correlation analysis. Unclear, season-specific results.
Stieb et al, 1996 (143) - Saint John (Canada) 1984–1992	TSP, LT 3 days, M(R ₁) 37 (5–108)	M 20	Asthma	2.0	-11.4–17.3	With O ₃ and SO ₄ (!) in model. Primarily O ₃ effect (>95th versus <95th percentile). Limited sample size for TSP however.
Delfino et al, 1997 (144) - Montreal (Canada) 1993 summer	PM ₁₀ , LT 1 day, M(R ₁) 22 (?–51)	M 22	RD, all ages RD, ≥65 years RD, <2 years	3.5 7.6 4.8 ^e	0.7–6.4 2.0–13.5 0.1–9.8	RD: no effect among 2- to 64-year-olds. For ≥65 years also effects for PM _{2.5} , SO ₄ and O ₃ .
Schwartz et al, 1991 (145) - Five German cities, 1983–1987	TSP, LT 0 days, Md 17–56 across cities	Md 9–31 across cities	Croup	~4.1	..	Based on a 27 % increase in croup cases for TSP increase from 10 to 70 µg/m ³ (log TSP model). No seasonal difference. No evidence of effect for obstructive bronchitis visits.
Pantazopoulou et al, 1995 (120) - Athens (Greece) 1988, winter	BS, LT 0 days (?), M(R ₂) 135 (46–281)	M 135	All visits	0.3	-0.1–0.6	Only NO ₂ had significant effect. CO similar to BS. No multipollutant analyses.
- Athens (Greece) 1988, summer	BS, LT 0 days (?), M(R ₂) 106 (50–184)	M 106	All visits	0.2	-0.1–0.6	
Castellsague et al, 1995 (146) - Barcelona (Spain) 1985–1989, winter	BS, LT 0 days, M 68	M 68	Asthma	0.9	-0.8–2.6	Similar association with NO ₂ , but not with SO ₂ and O ₃ .
- Barcelona (Spain) 1985–1989, summer	BS, LT 0 days, M 48	M 48	Asthma	3.2	0.5–6.0	

(continued)

Table 3. Continued.

Study	Measurement data (particle measure, lag time and levels) ^a	Measured or calculated PM ₁₀ ^{b,c} (µg/m ³)	Increase in visits per 10 µg/m ³ PM ₁₀ ^b or a short summary of the results			Comments
			Cause	%	95% CI	
Medina et al, 1997 (147) - Paris (France) 1991–1995	PM ₁₀ , LT 0,1,2 & 0–3 days in different models, M(R ₁) 25 (6–96)	M 25	Asthma, all ages	2.4	1.0–3.8	Asthma: very similar risks for BS, NO ₂ and SO ₂ , as well as O ₃ at 10°C or higher and only BS and O ₃ were stable in multipollutant models for 0–14 years. AP/AMI: BS effect was +3.8% (95% CI 0.3–7.5), however, but the strongest effects for CVD visits overall and AP/AMI visits were for O ₃ , followed by SO ₂ and NO ₂ .
			Asthma, 0–14 years	7.2	3.7–10.8	
			Asthma, 15–64 years	1.2	-0.6–3.0	
			CVD visits	0.7	0.0–1.5	
			AP/AMI visits	-2.1	-7.3–3.5	
			Headache	3.1	2.3–3.9	
Xu et al, 1995 (148); Xu et al, 1995 (149) - Beijing (China) 1990	TSP, LT 0 days (?), M(R ₁) 387 (106–1255)	M 213	All visits	0.2	0.1–0.4	Similar effect for SO ₂ . Little seasonal difference for TSP.
			Internal medicine	0.2	0.0–0.4	
			Pediatrics	0.4	0.1–0.6	
Smith et al, 1996 (15) - Sydney (Australia) January 1994	Light scattering (nephelometry), Md 0.19	Md 18 (some PM ₁₀ data also)	Asthma, obstructive respiratory disease, not associated with maximum nephelometry readings			Visits were not significantly more frequent during a bushfire period.

^a Given are the type of particle; lag time (LT); mean and range [M(R_n)], the range being as follows: R₁ = true range, R₂ = 5th to 95th percentile. The median (Md) is given when the mean was not available. Mostly daily means are used (eg, with LT 0 or LT 1); see page 49 for a discussion.

^b Conversion factors: PM₁₀ ≈ PM₁₅ ≈ BS ≈ SO₄ × 4 ≈ PM_{2.5}/0.60 ≈ CoH [in units of 10³ linear feet, used in most studies] × 55 ≈ TSP × 0.55 (12,13) and PM₁₀ ≈ light scattering (by nephelometry, in units of 10⁻⁵/m) × 10 (14,15), with remaining particle measures in micrograms per cubic meter.

^c Values given are the mean (M) or median (Md).

^d Analysis only including high particle days (>150 µg/m³), with LT 2 days.

^e Estimate based on SO₄ measurement data.

show a larger variability that may be partly due to a smaller sample size, but asthma visits, particularly of children, appear to be rather consistently associated with particulate air pollution levels, with increases of roughly 1% to 4% reported per 10 µg/m³ of PM₁₀. The effects estimated in recent European studies of hospital admissions (0.4–0.9% increase per 10 µg/m³ of PM₁₀ for different end points in different subgroups) appear to be weaker than previous findings from the United States and elsewhere.

Lung function changes and respiratory symptoms

Temporal variations in symptoms such as cough, phlegm, chest discomfort and the like are examined in this section, as well as symptom exacerbation among asthmatics (wheeze, medication use) and patients with other respiratory conditions. Many studies measure both symptoms and lung function and are listed for ease of reference with their principal characteristics and results in table 4 (92, 93, 150–187). Because these studies show greater variation in design, they have been described in more detail than the studies in the previous sections.

Lung function changes and symptoms in healthy children

Lung function. In the ambitiously designed Harvard study of air pollution and health effects in six US cit-

ies, 330 children in Steubenville performed repeated pulmonary function tests. Only a small effect of TSP on forced vital capacity (FVC) and forced expiratory volume in 0.75 seconds (FEV_{0.75}) was observed, corresponding to less than 1% of the mean outcome level over the range of pollutant exposure studied (150). A sensitivity reanalysis confirmed this finding (151). In another of the six cities, 154 children in normal daily activity performed spirometry weekly during February to April (152). Significant negative regression coefficients for lung function parameters were obtained for 1-hour maximal O₃ concentrations (range 7–156 µg/m³), whereas no negative effect was seen for PM_{2.5}.

For 144 Pennsylvanian schoolchildren who daily measured peak expiratory flow rate (PEFR), neither SO₂ nor particle pollution measured as CoH nor O₃ were associated with a substantially decreased morning PEFR (153). Another study in an Ontario summer camp focused on acid aerosols and showed substantial variations in O₃, acid aerosols, and SO₄ levels. Among the 112 nonasthmatic girls studied, a methacholine test was positive (MCh⁺) for 40.6% and therefore indicated increased lung reactivity (154). Comparisons were made between afternoon lung function on days of a major pollution episode and the mean lung function on several preceding reference days. Maximum decrements of 3.5% for forced expiratory volume in 1 second (FEV_{1.0}) and 7% for PEFR were observed in the positive methacholine test group (corresponding to -0.63 ml per µg/m³ and -3.0 ml/s per µg/m³), whereas the results of the pulmonary function tests in the negative methacholine

Table 4. Studies of lung function changes and symptoms in relation to particulate air pollution. (For any abbreviations not found in the footnotes, see page 4.)

Study	Size of study data set for the analyses ^a			Measurement data (particle measure and levels) ^{d,e}	Outcome estimates or short summary of results						Comments
	Study subjects	Data points per subject ^a			Symptoms studied and effect per 50 µg/m ³ PM ₁₀			Lung function change in ml (PEFR: ml/s) per 50 µg/m ³ PM ₁₀			
		Diary days ^b	Pulmonary test days ^c		Symp- tom	OR ^f	95% CI ^f	Test	Change ^g & 95% CI		
Dockery et al, 1982 (150); Brunekreef et al, 1991 (151) (sensitivity reanalysis) - Steubenville (OH) 1978-1980	330 children, ~8-10 years (3rd-5th grade)	-	3-20 (mean 11)	TSP, R 11-292	-	-	-	FVC FEV _{0.75} FVC FEV _{0.75}	-7.4* (Md slope) -1.6* (Md slope) -9.0 (M slope) -7.8 (M slope)	Mean slope estimates from reanalysis of 165 children (74% of data) (Brunekreef et al)	
Kinney et al, 1989 (152) - Kingston (TN) 1981	154 schoolchildren, 10-12 years, 61% male	-	6	PM _{2.5} , R 15-35	-	-	-	FVC FEV _{1.0} MMEF	+47 +126 +357*	Significant negative effects of O ₃ .	
Vedal et al, 1987 (153) - Chestnut Ridge (PA) 1980-1981	128 (diary)& 144 (PEFR) elementary school children, mean age10 years, 62% male	240	45	CoH, M(R) 0.4 (0.1-1.3)	LRI URI, wheeze	1.6 No effect	0.9-3.0	PEFR	No substantial effect of any pollutant or lag time.	-	
Raizenne et al, 1989 (154) - Ontario (Canada), summer 1986	112 girl guide camp (Lake Eire) participants, 8-14 years	-	5	SO ₄ , R 7-83	-	-	-	FEV _{1.0} PEFR	Decrease Decrease	FEV _{1.0} -3.5% and PEFR -7% on episode versus control days.	
Pope & Dockery, 1992 (155) - Utah Valley (UT), winter 1990/1991	40 healthy school-children, 10-12 years, 32% male	~82	~82	PM ₁₀ , M(R)76 (7-251)	URS LRS Cough	1 1.2 1.4	0.8-1.4 0.9-1.6 1.1-1.7	PEFR	-21 (-37--6)	Results are for 5-day mean PM ₁₀ . Relationships to same-day PM ₁₀ were slightly weaker for both symptoms and PEFR	
	39 children with "asthma symptoms", 10-12 years, 54% male	~82	~82	PM ₁₀ , M(R)76 (7-251)	URS LRS Cough	1.3 1.4 1.4	1.1-1.6 1.1-1.7 1.2-1.7	PEFR	-30 (-49--11)		
Koenig et al, 1993 (156) - Seattle (WA), winters 1988-1990	298 schoolchildren, ~8-11 years (3rd-6th grade), ~50% male	-	~2	PM _{2.5} , M~15 ? (in 1991)	-	-	-	FVC FEV _{1.0}	+10 (-1--22) +5 (-7--16)	PM _{2.5} was estimated indirectly from light scattering data (nephelometry).	
	30 asthmatics, ~8-11 years (3rd-6th grade), ~50% male	-	~6	-	-	-	-	FVC FEV _{1.0}	-55 (-83--28) -51 (-83--19)	Mean PM _{2.5} level estimated from figure	
Schwartz et al, 1994 (157) - Six US cities, 1985-1988	1844 schoolchildren, ~7-10 years (2nd-5th grade)	153	-	PM ₁₀ , Md(R) 30 (?-117)	URS LRS Cough	1.4 2.0 1.4	1.0-2.0 1.4-3.0 1.1-1.9	-	-	-	
Neas et al, 1995 (158) - Uniontown (PA), summer 1990	83 schoolchildren, ~9-10 years (4th-5th grade), 57% male, (no asthma)	-	43	PM _{2.5} , M(R) 24 (?-88)	Cough Wheeze, cold	1.6 Similar effects	1.1-2.3	PEFR	-28 (-55--0.3)	Effect possibly attributable to particle strong acidity.	
Linn et al, 1996 (159) - Los Angeles area (CA), autumn-spring 1993-1994	269 schoolchildren, ~9-10 years (4th-5th grade), 51% male	~16	~16	PM ₅ , M(R)24 (1-145)	Respiratory symptom score not related to pollutants	-	-	FVC FEV _{1.0}	-13 (-22--4) -6 (-15--4)	-	

(continued)

Table 4. Continued.

Study	Size of study data set for the analyses ^a		Measurement data (particle measure and levels) ^{d,e}	Outcome estimates or short summary of results					Comments	
	Study subjects	Data points per subject ^a		Symptoms studied and effect per 50 µg/m ³ PM ₁₀			Lung function change in ml (PEFR: ml/s) per 50 µg/m ³ PM ₁₀			
		Diary days ^b		Pulmonary test days ^c	Symptom	OR ^f	95% CI ^f	Test		Change ^g & 95% CI
Dassen et al, 1986 (160) - IJmond area (The Netherlands), winter 1984–1985	163 schoolchildren, 7–11 years	2	TSP, R ?– ~220					FVC FEV _{1.0} PEFR	Significantly lower Significantly lower Significantly lower	Episode-post-episode test compared with baseline test. Other lung parameters also negatively affected.
Braun-Fahrländer et al, 1992 (161) - Basel & Zurich (Switzerland), 1985–1986	Random sample of 625 Swiss children, 0–5 years, 48% male	42	TSP Md(R) 43 (33–117)	URI Cough, dyspnea (daily incidence): no significant effect	1.5	1.1–2.1				6-week mean TSP also associated with incidence and duration of URI and cough.
Hoek & Brunekreef, 1994 (162) - 4 towns (The Netherlands), winters 1987–1990	695 (diary) & 782 (lung function) children, 7–11 years, ~50% male	~90	PM ₁₀ , M(R) 45 (14–126)	URS, LRS, cough (both, prevalence and incidence): no clear effect of air pollutants				FVC FEV _{1.0} MMEF PEFR	+1 (-5–+6) -5 (-11–+1) -26 (-43–-9) -41 (-69–-13)	Four nonindustrial towns.
Hoek & Brunnekreef, 1993 (163) - Wageningen (Holland) winter 1990/1991	59 (diary) & 90 (lung function) children, 7–12 years, 57% male	98	PM ₁₀ , R 30–144	URS, LRS, cough: no clear effect on prevalence for air pollutants despite air pollution episode				FVC FEV _{1.0} MMEF PEFR	-30 (-41–-19) -28 (-37–-18) -32 (-55–-9) -41 (-90–+8)	Lung function parameters similarly associated also with BS and SO ₂ .
Hoek et al, 1993 (164) - Deurne (The Netherlands), spring/summer 1989	314 children, 7–11 years, ~50% male	8	PM ₁₀ , only 1 day >100					PEFR	-109 (-180–-37)	Clear O ₃ effects also.
Hoek & Brunekreef, 1995 (165) - Deurne (The Netherlands), spring/summer 1989	241 children, 7–11 years, 49% male	~94	PM ₁₀ , M(R) 48 (13–124)	URS, LRS, cough, any. respiratory symptom: no association to PM ₁₀						Also no association with O ₃ , SO ₂ , NO ₂ , SO ₄ , or NO ₃ .
von Mutius et al, 1995 (166) - Leipzig (Germany), 1991–1992	1492 schoolchildren 9–11 years, 47% male	1 physician's examination per child (Md 15 subjects/day)	PM/TSP, Md(R) ~105 (~30–270)	URS (daily prevalence): OR significantly increased for daily mean NO _x , SO ₂ , and daily maximum PM						Confounders assessed by parent questionnaire.
Studnicka et al, 1995 (167) - Summer camp (Austria), 1991	133 children in rural summer camps, ≥7 (mean 10) years, 51% male	Up to 19	PM ₁₀ , M(R) 9 (5–58)	URS (daily prevalence): OR significantly increased for daily mean NO _x , SO ₂ , and daily maximum PM				FVC FEV _{1.0} PEFR	-18 (-99– +64) -67 (-143–+10) -99 (-294–+96)	Similar effects for H ⁺ (mean level ~20 nmol/m ³).
Scarlett et al, 1996 (168) - Surrey (England), summer 1994	154 schoolchildren, 7–11 years, 41% male	~27	PM ₁₀ , M(R) 71 (20–150)					FVC, FEV _{0.75}	-9 (-14–-3) -3 (-8–+1)	No relation to O ₃ or NO ₂ .
Awasthi et al, 1996 (169) - Lucknow (India), 1993–1994	664 slum children, 1 month-4.5 years, 56% male	~13	SPM, M(R) 370 (187–547)	"Respiratory symptom complex"	1.1	1.0–1.2				Very high SPM levels. Six months of interview data (biweekly) per child.

(continued)

Table 4. Continued.

Study	Size of study data set for the analyses ^a			Measure- ment data (particle measure and levels) ^{d,e}	Outcome estimates or short summary of results						Comments
	Study subjects	Data points per subject ^a			Symptoms studied and effect per 50 µg/m ³ PM ₁₀			Lung function change in ml (PEFR: ml/s) per 50 µg/m ³ PM ₁₀			
		Diary days ^b	Pulmo- nary test days ^c		Symp- tom	OR ^f	95% CI ^f	Test	Change ^g & 95% CI		
Krzyzanowski et al, 1992 (170); Lebowitz et al, 1992 (171) - Tucson (AZ), 1986–1988	287 children 6–15 years, 53% male, 13% asthmatic 523 adults, ≥16 years, 54% male 9% asthmatic, all non-smokers	~17	~10	.	.	Allergic or irritant symptoms related to the interaction between high PM and high O ₃ for both groups	.	PEFR	Negative PM effect overall for both groups	.	
Ostro et al, 1993 (172) -South California, 1978–1979	321 nonsmoking adults, ≥18 years, 48% male	181	.	CoH, M(R) 1.2 (0.4–2.6)	LRS, URS: no effect of CoH for either symptom, but LRS affected by SO ₄	.	.	.	.	SO ₄ was 2–37 (mean 8) µg/m ³ . LRS related also to O ₃ .	
Whittemore & Korn, 1980 (173) - Los Angeles area (CA) 1972–1975	259 child & 184 adult asthmatics in several different communities, ≤16 years, 64% male; >16 years, 35% male	.	.	TSP, R of daily Md 51–121 across com- munities	Asthma attacks	1.07 1.02– 1.13	.	.	.	Effect similar for adults and children.	
Ostro et al, 1991 (174) - Denver (CO), winter 1987–1988	207 asthmatics, 18–70 years, 34% male	90	.	PM _{2.5} , M(R) 22 (1–73)	Asthma rating: associ- ated with PM _{2.5} and H ⁺ Cough, dyspnea: More effect with H ⁺ (mean 10, range 2–41 neq/m ³)	.	.	.	.	Some symptom associations with SO ₄ , but not with NO _x or nitric acid.	
Quackenboss et al, 1991 (175) - Tucson (AZ) 1986–1988	30 asthmatic children, 6–15 years, 58% male	.	Up to 12	Indoor PM _{2.5} (& others)	Increased allergic symptoms: related to PM ₁₀	.	.	PEFR (morn- ing)	-450 (-58–842)	PEFR change per 50 µg/m ³ PM ₁₀ estimated based on measured indoor PM _{2.5} .	
Pope et al, 1991 (176) - Utah Valley (UT), winter 1990–1991	34 schoolchildren with “asthma symptoms”, 9–11 years, 62% male 21 asthma patients, 8–72 years, 48% male	~90	~90	PM ₁₀ , M(R) 46 (11–195) PM ₁₀ , M(R) 46 (11–195)	URS LRS RM use XM use URS LRS RM use XM use	1.2 1.3 1.6 1.7 1.0 1.0 1.2 1.8	1.0–1.4 1.1–1.6 1.1–2.2 1.1–2.6 0.8–1.2 0.8–1.3 0.9–1.6 1.3–2.5	PEFR PEFR	-53 (-84–22) -13 (-60–+35)	Stronger total effects on PEFR in both groups with multiple-day polynomial- distributed lag models.	
Pope & Kanner, 1993 (177) - Salt Lake City (UT) 1987–1989	251 current smokers with mild COPD, 35–60 years, 69% male	.	2	ΔPM ₁₀ M(R) 30 (0–133)	.	.	.	ΔFVC ΔFEV _{1.0}	-15 (-44–+14) -29 (-51–+7)	Effect of ΔPM ₁₀ between 2 test sessions on ΔFVC or ΔFEV _{1.0} .	
Silverman et al, 1992 (178) -Toronto (Canada) summer & winter	17+19 asthmatics, mean age 48 years, 25% male	.	PM ₂₅ & PM ₁₀ (personal)	Up to 20	.	.	.	FVC & FEV _{1.0}	Negative effect in summer, overall positive in winter	Interaction between negative PM effect & positive effect of medication use in winter. Personal exposure sampling used.	

(continued)

Table 4. Continued.

Study	Size of study data set for the analyses ^a			Measurement data (particle measure and levels) ^{d,e}	Outcome estimates or short summary of results						Comments
	Study subjects	Data points per subject ^a			Symptoms studied and effect per 50 µg/m ³ PM ₁₀			Lung function change in ml (PEFR: ml/s) per 50 µg/m ³ PM ₁₀			
		Diary days ^b	Pulmonary test days ^c		Symp- tom	OR ^f	95% CI ^f	Test	Change ^g & 95% CI		
Forsberg et al, 1993 (179) - Piteå (Sweden), March–April	31 asthmatics, 9–71 years, 42% male	49		BS, M(R) 7.1 (1–21)	Dyspnea Cough, phlegm	2.3 No effect	0.1–52 per 10 µg/m ³ BS ^h				Very low BS levels. However, nearby 12-hour TSP was a mean of 35 and a maximum of 101.
Roemer et al, 1993 (180) - Wageningen & Bennekorn (The Netherlands), winter 1990–1991	69 (diary) & 67 (PEFR) children with chronic respiratory symptoms, 6–12 years, ~55% male	50–83	~71	PM ₁₀ , R 10–174	Wheeze, BD use: prevalence related to daily PM ₁₀ , BS and SO ₂ Asthma attacks, dyspnea, cough, phlegm, runny nose: less clear relation between prevalence and daily PM ₁₀ , BS and SO ₂			PEFR (evening) PEFR (morning)	-23 (-49–+3) -34 (-59–10)		Prevalence effects generally stronger for weekly means of air pollutants. Symptom <i>incidence</i> showed few clear associations.
Dusseldorp et al, 1995 (181) - Wijk aan Zee (The Netherlands) 11 October–22 December 1993	32 patients with obstructive airway disease, 26–79 years, 34% male	17–67	66	PM ₁₀ , M(R) 54 (4–137)	Cough Wheeze Phlegm Dyspnea BD use RM use	1.1 1.2 1.1 1.2 1.1 1.1	1.0–1.3 1.0–1.5 0.9–1.3 1.1–1.4 1.0–1.2 1.0–1.2	PEFR (evening) PEFR (morning)	-45 (-81–9) -77 (-119–34)		Results given for a lag time of 0, except wheeze, dyspnea and RM use (lag time 2 days).
Romieu et al, 1996 (182) - Mexico City (Mexico) 1991–1992	71 children with light asthma, 5–13 years, 70% male	Up to 60	50	PM ₁₀ , M(R) 167 (29–363)	LRI Cough Wheeze Phlegm Dyspnea BD use	1.2 1.3 1.1 1.2 1.2 1.0	1.1–1.4 1.2–1.4 0.9–1.3 1.0–1.5 1.0–1.3 0.9–1.0	PEFR (evening) PEFR (morning)	-80 (-133–28) -78 (-128–28)		
Peters et al, 1996 (183) - Erfurt & Weimar (Germany) & Sokolov (Czech Republic) 1990–1992	102 (for PM ₁₀ only 72) asthmatic adults, 32–80 years, ~46% male 155 (for PM ₁₀ only 110) children, 7–15 years, ~63% male	~179 (~145)	~179 (~145)	PM ₁₀ , M(R) ~60 (?–247) PM ₁₀ , M(R) ~60 (?–247)	Symptom score: increase with PM ₁₀ , stronger for 5-day mean for both groups and also increase with SO ₂ , SO ₄ , and particle strong acidity			PEFR PEFR	-19 (-42–+4) -19 (-35–2)		SO ₂ and SO ₄ best predictors overall, especially for 5-day mean. PM ₁₀ only available for Erfurt & Sokolov 1991–1992 (most data; number of subjects, diary days and test days in parentheses)
Peters et al, 1997 (184) - Sokolov (Czech Republic), winter 1 September 1991 – 31 March 1992	89 asthmatic children, 6–14 years, 63% male	~151	~151	PM ₁₀ , M(R) 55 (3–171)	Cough Phlegm Dyspnea Runny nose Fever BD use	1.1 1.1 1.2 1.1 1.2 1.3	1.0–1.2 1.0–1.2 1.1–1.3 1.0–1.1 0.9–1.5 1.1–1.6	PEFR (evening) PEFR (morning)	-29 (-61–16) -15 (-46–+15)		Estimates are for 5-day mean. Largest effect was for SO ₄ .
Peters et al, 1997 (185) - Sokolov (Czech Republic) 15 November 1991–4 February 1992	82 asthmatic children, 6–14 years, 61% male, both medicated and nonmedicated	77	77	SO ₄ , M(R) 8.8 (?–24)	Nonmedicated: similar to above. Medicated: effect for cough and BD use, little else.			PEFR	Little effect among nonmedicated, strong among medicated		Analysis stratified for asthma medication and based on SO ₄ as particulate air pollution indicator.
Thurston et al, 1997 (186) - “Asthma camp” (CT) 1 week in June 1991–1993	52+58+56 children with asthma, 7–13 years	5	5	SO ₄ , M(R) 7 (1–27), also H ⁺	BD use: effect for SO ₄ and H ⁺ . LRS: mainly effect for O ₃			PEFR	Suggested effect for SO ₄		O ₃ most consistently associated with health effects.
Gielen et al, 1997 (187) - Amsterdam (The Netherlands), summer 1995	61 chronically ill schoolchildren, 77% on asthma medication, 7–13 years	35–46	35–46	PM ₁₀ , M(R) 30 (16–60), also BS	Cough, LRS, URS, BD use: positive effect of BS and PM ₁₀ but not of O ₃ .			PEFR (evening) PEFR (morning)	Most strongly associated with BS Most strongly associated with BS		Strongest associations with 5-day mean.

(continued)

Table 4. Continued.

Study	Size of study data set for the analyses ^a			Measure- ment data (particle measure and levels) ^{d,e}	Outcome estimates or short summary of results					Comments
	Study subjects	Data points per subject ^a			Symptoms studied and effect per 50 µg/m ³ PM ₁₀			Lung function change in ml (PEFR: ml/s) per 50 µg/m ³ PM ₁₀		
		Diary days ^b	Pulmo- nary test		Symp- tom	OR ^f	95% CI ^f	Test	Change ^g & 95% CI	
Peters et al, 1997 (93) - Erfurt (Germany) 1 October 1991– 31 March 1992	27 nonsmoking asthmatic adults, 44–80 years, 37% male	~100	~100	PM ₁₀ , Md(R) 59 (12–247)	Cough Phlegm, dyspnea, asthma attacks: no effect	1.3	1.2–1.5	PEFR (even- ing) PEFR (morn- ing)	-6 (-30–+18) -21 (-39–+4)	Stronger association with number of ultrafine particles.
Pekkanen et al, 1997 (92) - Kuopio (Finland) February–April 1994	39 asthmatic children, · 7–12 years, 54% male		34– 57	PM ₁₀ , M(R) 18 ?–60				PEFR (even- ing) PEFR (morn- ing)	-18 (-77–+40) -72 (-132–+12)	Estimates for daily mean PM ₁₀ , lag time 2 days. Stronger effect for 4-day mean. Not stronger effect for number of ultrafine particles.

^a Note that the number of days *do not* represent the entire study period. The approximate number of subjects and days of data or days of tests per subject for the analyses included in the table were extracted as possible from the publications to suggest the amount of data providing the results cited. Approximate person-days for the corresponding analyses are thus obtained by multiplying subjects x days or subjects x tests.

^b Number of days of diary data per subject.

^c Number of days with PEFR or full pulmonary test data per subject.

^d Conversion factors: PM₁₀ ≈ PM₁₅ ≈ BS ≈ SO₄ × 4 ≈ PM_{2.5}/0.60 ≈ CoH [in units of 10³ linear feet, used in most studies] × 55 ≈ TSP × 0.55 (12,13) and PM₁₀ ≈ light scattering (by nephelometry, in units of 10⁻⁵/m) × 10 (14,15), with remaining particle measures in milligrams per cubic meter.

^e Median (Md) is used when the mean (M) was not available (R=range). Mostly daily mean levels are used.

^f OR and 95% CI (in parentheses) per 50 µg/m³ PM₁₀ (measured or calculated), unless otherwise indicated.

^g Milliliters (PEFR: ml/s) per 50 µg/m³ PM₁₀ (measured or calculated), unless otherwise indicated. 95% CI values in parentheses. (* = significant, Md = median, M = mean).

^h Ratio of PM₁₀ to BS may be as high as 3 (value for Umeå, also in northern Sweden) (11).

group were less consistent across episodes. Effects of the acid haze and O₃ were difficult to separate.

In two studies comparing healthy children with asthmatics, slightly stronger effects of particulate pollution on PEFR among the children with asthma symptoms were found in Utah (155). Similarly, in Seattle, with heavy particulate pollution from wood burning in winter, decrements in the lung function parameters FVC and FEV_{1.0} in association with particle levels were seen in asthmatics, but this time not at all in healthy children (156). However, two subsequent US studies again found discrete but observable effects in healthy children. In Uniontown, Pennsylvania, 83 nonasthmatic children who recorded PEFR values in summer exhibited moderate decrements associated mainly with PM_{2.5} and particle strong acidity (158), and in another study on healthy schoolchildren in Los Angeles, FVC and FEV_{1.0} were weakly associated with particulate air pollution (159).

For Dutch children, significant decrements in several lung function parameters were observed up to 16 but not 25 days after an air pollution episode with TSP in the range of 200–250 µg/m³ when the figures were compared with pre-episode baseline data (160). Later, more ambitious Dutch studies on large numbers of children repeated the observation of decrements in lung

function parameters most consistently related to PM₁₀, especially for PEFR and MMEF, both for healthy children (162, 163) and children with chronic respiratory symptoms (180) (summarized in reference 188). In the largest study, slightly stronger effects were again observed in a subgroup of children with physician-diagnosed asthma, but the numbers were small (N=27) (162). In a spring-summer study in The Netherlands that focused on photochemical air pollution, independent effects of both O₃ and PM₁₀ on PEFR were also noted (164). Similarly, lung function decrements related to particulate air pollution have been reported in Austria (167) and southern England (168).

Symptoms. For Pennsylvania elementary-school children who recorded symptoms daily during 8 months, only low temperature was significantly related to lower respiratory symptoms (eg, wheeze, dyspnea, chest tightness, phlegm) and upper respiratory symptoms (eg, cough, sore throat, runny or stuffy nose, sneezing) in multivariate analyses (153). An increased OR for lower respiratory symptoms was, however, suggested in relation to the CoH. In the Utah study already mentioned, which compared healthy children with asthmatics, 5-day PM₁₀ averages were related to cough and lower respiratory symptoms among both healthy and asthmatic

children, but to upper respiratory symptoms only among asthmatics (155). In children from the Harvard Six Cities Study, cough was associated with both the O_3 and PM_{10} levels. For lower respiratory symptoms, the OR was higher, with a monotonic concentration-response relationship, and a similar effect was suggested for upper respiratory symptoms (157). For schoolchildren in Uniontown, Pennsylvania, studied in the summer with PEFR and symptom diaries, cough was associated with particulate measures, including $PM_{2.5}$ and particle strong acidity but also with O_3 and SO_2 (158). Similar associations were seen for wheeze and cold, and the associations were stronger when weighted by the proportion of hours spent outdoors during the previous 12 hours. Another study on schoolchildren in Los Angeles found no association between air pollution and a respiratory symptom score (159).

In a Swiss study, the incidence and duration of symptoms were reported daily in diaries from May to October. TSP was related to daily incidence rates of fever with earache and sore throat (upper respiratory infection). Another set of analyses examined 6-week averages of air pollutant levels and found that the TSP averages were related to both the incidence and duration of coughing and upper respiratory infection, but not to episodes of breathing difficulty. Some relationships were also found for NO_2 , but not for O_3 (161). Two later large Dutch studies on healthy children in winter found no consistent relationships between air pollutants and the daily prevalence or incidence of respiratory symptoms as reported in diaries (162, 163), nor did yet another spring-summer study in The Netherlands, which focused on photochemical air pollution (165). Among Dutch children with chronic respiratory symptoms, however, the daily prevalence but not the incidence of various symptoms, in particular wheeze, was related to PM_{10} , SO_2 , and BS but not to NO_2 , and the relationships appeared to be stronger for the weekly average air pollution variables than for the same-day or lagged variables (180).

In Leipzig, former East Germany, a large number of children was examined by a physician for upper respiratory symptoms. In a logistic regression analysis, statistically elevated OR values for such symptoms were observed in relation to the daily mean nitrogen oxides (NO_x), SO_2 , and daily maximum particulate matter (PM) levels (166). A study in India with even higher levels of suspended particulate matter (SPM) observed a statistically significantly elevated OR for a respiratory symptom complex ascertained in home interviews (169).

Lung function changes and symptoms in healthy adults

The only study available on PM and lung function in healthy adults focused on indoor-outdoor exposures and

respiratory effects in Tucson, Arizona, with basic screening data on 2322 persons (189). A subsample of primarily families with children was studied with detailed health questionnaires, skin prick tests, blood analyses, and pulmonary function tests. The exposure evaluation included household inventory questionnaires, personal or household samplers for NO_2 , particulates, and formaldehyde and ambient air monitoring data. Both outdoor PM and O_3 were associated with a decrease in PEFR in the whole study population (adults and children, mostly nonasthmatics) (171). Further analysis specifically addressed O_3 and found evening PEFR to be decreased by O_3 exposure, especially among asthmatics who spent much time outdoors (170). The effects of both O_3 and PM_{10} were stronger when the level of the other pollutant was high and at high temperatures. An increase in allergic or irritant symptoms related to the interaction between outdoor PM_{10} and the 8-hour maximum O_3 concentration was also suggested (170, 171). In another study of symptoms in nonsmoking adults during winter in greater Los Angeles, an increased OR of lower respiratory symptoms but not upper respiratory symptoms was related to both SO_4 and O_3 , but not significantly to CoH as a measure of particulate air pollution (172). Further data on healthy adults are not available.

Lung function changes, symptoms and symptom exacerbation in subjects with a respiratory disease

Lung function. For 30 asthmatic children in the Tucson study already described, the indoor $PM_{2.5}$ levels were associated with a decreased morning PEFR, and a similar effect was found in relation to PM_{10} measured by personal monitoring (175). A study in Utah found stronger effects on the PEFR (and symptoms) of children with light "asthma symptoms" than in a group of clinic-recruited asthmatics of all ages (176). Extra medication use among the diagnosed asthmatics was, however, strongly related to PM_{10} . The authors concluded that symptoms and pulmonary function among these asthmatics were possibly being managed by medication and life-style changes. Evidence for cumulative effects over several days was found using cumulative lag-time models. Another, previously mentioned, Utah study observed a similar effect on PEFR among children with "asthma symptoms" (155). A third Utah study on adults who were current smokers with moderate COPD measured $FEV_{1.0}$ and FVC on two occasions and found an association with the difference in the PM_{10} levels between the test sessions (177). For more severely ill asthmatics in a Canadian study, negative effects on the same parameters were observed in summer but not in winter. In winter, however, an interaction between medication use and particulate levels was noted, the finding suggesting again that a main negative effect may be modified by

medication use (178). Among children, too, effects on these parameters in asthmatics have been noted (156). A large number of recent studies has found moderate negative effects on PEFr with the use of various particulate measures, both for children (180, 182–187) and adults (181, 183). In some studies, especially focusing on more severely ill asthmatics, bronchodilator use may have modified the effect observed (186, 187). Most studies, except one from Mexico City (182), found bronchodilator use to be associated with particles. In a study from the Czech Republic, medication was mainly with theophylline, and the effect of particulate air pollution measured as SO_4 was stronger among the medicated subjects (185). Several studies noted stronger effects for multiple-day average particulate concentrations (92, 180, 184, 187) or multiple lag times (155) or particulate levels more than 1 day previously (181). These findings may reflect the true time course and cumulative effects of particulate exposure on PEFr. It is also possible that extra medication use may modify the effect observed for recent exposure more than for exposure several days ago.

Recently it has been hypothesized that the large number of ultrafine particles in urban air may be the explanation for the observed health effects related to low levels of PM_{10} or other particulate measures (90). A study in Erfurt, in eastern Germany, with particulate emissions from the burning of brown coal included 27 adult asthmatic nonsmokers and focused on fine and ultrafine particles (93). Morning and evening PEFr values were related to daily PM_{10} , but the relationship appeared to be stronger for longer averaging times and for smaller particle fractions. Most of the particles (73%) were in the ultrafine fraction (<0.1 per μm), whereas most of the mass (82%) was attributable to particles in the size range 0.1 to 0.5 per μm . The two fractions were only moderately correlated, and the effect was stronger for the number of ultrafine particles than for measures of particle mass. A Finnish study attempting to replicate these results in children with asthmatic symptoms did not, however, find that the number of ultrafine particles was more strongly associated with PEFr than PM_{10} and BS concentrations were (92). The main emission source in this study was road traffic.

Symptoms. An early large study on asthmatics, both adults and children, in the United States found a small but significant increase in asthma attacks in relation to TSP exposure (173), and in another study of only adult asthmatics, asthma ratings were associated with $\text{PM}_{2.5}$ and acid particles (H^+), cough mainly with H^+ (174). For 30 asthmatic children in the Tucson study already described, increased allergic symptoms were related to PM_{10} exposure (175). As noted previously, the study in Utah found generally stronger effects of PM_{10} on vari-

ous symptoms in children with light “asthma symptoms” than in a group of clinic-recruited asthmatics of all ages, whereas the opposite was true for extra medication use (176). A Swedish study with very low levels of BS found no effect of air pollution levels on cough or phlegm in asthmatics of all ages, but dyspnea appeared to be related to BS levels (179). Other later studies have often observed associations between particulate air pollution and shortness of breath and dyspnea, wheeze and bronchodilator use, as well as cough and phlegm, for both children (180, 182–187) and adults (181, 183). Modification of the effect observed by medication use is a clear possibility in this case too, especially among adults who are better able to modulate their medication. The longer optimal lag time for dyspnea and wheeze than for cough and phlegm in one study (181) and the association only for cough in another (93) suggest that medication may modify primarily the immediate effect on asthma-type symptoms.

In the Erfurt study focused on ultrafine particles, PM_{10} and various number and mass particle fractions were related to feeling ill during the day and to cough among 27 asthmatic nonsmokers (93). The OR values were similar across an interquartile range for different particulate measures. Asthma attacks, dyspnea, and phlegm showed no association.

Evaluation

Particulate air pollution has been related to both the respiratory symptoms and lung function of healthy persons. Mostly children have been studied, often in the age span 5–15 years. The lung function decrements are of a relatively limited magnitude (ie, only about 0.5–1.5% per 50 $\mu\text{g}/\text{m}^3$ increase in PM_{10} levels). The largest database and most consistent effects concern PEFr, for which an effect was usually found and the absolute decrements centered around 30–60 ml/s. The decrements were often more strongly related to longer averaging or lag times than to previous-day levels, and therefore they raise the possibility of persistent, chronic effects. A comparison with O_3 suggests that different etiologic mechanisms may be operating. Short-term peaks of O_3 show a clear association to lung function decrements and some association to symptoms, but chiefly at high concentrations or high exposure levels due to increased physical activity (98). In contrast, the particle effect appears to be related to longer averaging or lag times, and the effect on symptoms is clearer and seems to exist even at relatively low exposure levels. The results for symptoms are, however, not fully consistent. Several studies observed no significant relationships for various end points. Many others reported increased OR values. Results appeared more consistent for lower respiratory

symptoms and cough than for upper respiratory symptoms, with generally a 10–40% excess RR associated with a 50 $\mu\text{g}/\text{m}^3$ increase in the PM_{10} level when an effect was observed. Among asthmatics, a somewhat stronger effect on pulmonary function has often been observed, while no stronger effect on symptoms has been found. Extra asthma medication, generally bronchodilator use, has mostly been associated with particulate exposure and may modify the observed effect on symptoms and lung function.

Miscellaneous health effects in relation to medium-term exposure

Table 5 lists studies of some additional health outcomes in relation to particulate pollution levels during the last weeks to months (131–133, 190–204).

Ostro & Rothschild (190–192) studied adults from the US National Health Interview Survey from 1976 to 1981, in which over 100 000 persons responded nationwide to questions on acute illnesses during the previous fortnight. $\text{PM}_{2.5}$ and O_3 were studied as air pollutant exposures. The number of “restricted activity days” (particularly respiratory-related) for each person was related to the particulate levels but not to the O_3 concentrations. For minor restrictions in activity (minor restricted activity days, excluding more serious work loss or bed disability conditions), O_3 showed a weak association. In a subset analysis controlling for active and passive smoking exposure, a 1–3% increase in respiratory-related restricted activity days among adults, as well as a 1% increase in bed disability days among children, was estimated per microgram-per-cubic-meter increase in the 2-week average $\text{PM}_{2.5}$ levels (193). When alternative particulate measures were investigated in the whole adult sample in 1979–1981, it was suggested that SO_4 was more strongly related to health effects than TSP, PM_{10} , or $\text{PM}_{2.5}$ (194). School absenteeism as a marker of illness was investigated in Utah Valley and found in two separate analyses to increase from approximately 4% to 6% with an increase of 100 $\mu\text{g}/\text{m}^3$ in the average PM_{10} level during the previous month (195). Hospital admissions for respiratory disease adjusted for temporal trend and meteorological variables (131–133), as well as pulmonary function decrements in children (196), have also been found to be associated with 4-week average PM_{10} levels, with a magnitude similar to that reported for the association with shorter averaging times (see tables 2 and 4). In a study from Hong Kong, quarter-yearly hospital discharge rates in the age group 1–4 years were also related to TSP levels (197), but long-term temporal trend and meteorological variables were not adjusted for. Because of the few data

points this analysis was inconclusive, and the result may largely reflect coincidentally correlated secular trends for TSP and asthma discharges among 1- to 4-year-olds over the 27 quarters. A similar relationship was not found in other age groups.

In Beijing, with high levels of TSP and SO_2 , pregnancy outcomes were studied. Preterm delivery was associated with the average TSP level during the week before delivery (198) and low birthweight (<2500 g) was associated with the average TSP levels during the third trimester of pregnancy (199). This relation held also on average, with an estimated average reduction in birthweight of 6.9 grams for each 100 $\mu\text{g}/\text{m}^3$ increase. For all outcomes, similar results were obtained with SO_2 as the air pollution indicator.

Sudden infant death syndrome is defined as the sudden death of an infant who was previously well, without any explanation found after examination and autopsy. It has been shown to be associated with passive smoking (205) and a prone sleeping position (206). Air pollution has also been implicated in its causation. The available studies are described in this section as the designs vary and the hypotheses tested include effects from both shorter and longer exposures. Three early studies that did not include particulate measures as such are mentioned briefly. A study in Chicago found no association between SO_2 exposure and sudden infant death syndrome, the only consistent finding being an inverse relationship between the syndrome and temperature (207). Pursuing a possible link, Hoppenbrouwers et al (208) found that deaths from sudden infant death syndrome peaked in Los Angeles a few weeks after air pollution peaked in midwinter, the finding suggesting an effect of air pollution. However, confounding by winter infections, which also peaked at that time, could not be excluded. Finally, a cross-sectional study in Germany found an increased incidence of sudden infant death syndrome in districts with a poor air quality index (209). Particulate air pollution in a subtropical climate (Brisbane, Australia) tended, on the average, to decrease from a slightly elevated level on the days prior to a death from the syndrome, and visibility increased during the days around the death (table 5) (200). The analyses were not multivariate, and the authors hypothesized an effect by light or increasing outdoor exposure on successively clearer days. More recently an association between sudden infant death syndrome and low visibility was reported from Taiwan (201). A longer averaging time gave a stronger result than daily visibility, the OR being 5.1 (95% CI 3.2–8.1) for the lowest category of average visibility 1 to 9 days before death when compared with the highest, in a multivariate analysis controlling for socioeconomic, weather, and disease confounders. Another study with more individual-level data and PM_{10} measurements from the United States found an OR of 1.26

Table 5. Studies of miscellaneous health effects in relation to short-to-medium-term exposure to particulate air pollution. (For abbreviations, see page 4.)

Study	Characteristics of study population	Exposure measure and levels ^a	Outcome	Results
Ostro, 1983 (190); Ostro, 1987 (191); Ostro & Rothschild, 1989 (192); Ostro, 1989 (193); Ostro, 1990 (194) - US (Health Interview Survey) 1976–1981, 1979–1981	~70 000 adults, 18–65 years, in total; ~5300 adults, 18–65 years, with smoking data; 1575 children, ≤6 years with parental smoking data; during 2 weeks	2-week means, SO ₄ ~8, PM _{2.5} ~23, TSP ~69	Restricted activity days (ie, work loss, bed confinement or minor restrictions); minor restricted activity days; work loss days; respiratory-related restricted activity days; bed disability days (children)	Restricted activity days: ~+0.5% per µg/m ³ PM _{2.5} . Work loss days: less consistent, up to +1.5%. Minor restricted activity days: +0–+1%, but more consistent association with O ₃ . Respiratory-related restricted activity days: +1–+3% per µg/m ³ PM _{2.5} . Bed disability days (children): +1%. Stronger results with 2-week lag time.
Ransom & Pope, 1992 (195) - Utah Valley (UT) 1985–1990	~1000 children, kindergarten–6th grade, during 1065 days; ~6800 children, 1st–6th grade, during 169 weeks	4-week mean PM ₁₀ 50	Daily or weekly school absence rates	Approximately 40% increase in absences per 100 µg/m ³ of PM ₁₀ (4-week mean). Similar results for kindergarten children.
Pope, 1989 (131); Pope, 1991 (132) - Utah Valley (UT) 1985–1988 Utah, Salt Lake & Cache Valleys (UT) 1985–1989	4742 pneumonia, 1635 bronchitis, 1914 asthma admissions; 48 months of data	Monthly mean PM ₁₀ 22–120	Monthly admissions for pneumonia, chronic bronchitis and asthma; all ages and preschool children	Approximately 3–7% increase in respiratory admissions (all ages) for 10 µg/m ³ increase in PM ₁₀ over a month or more (133). Slightly stronger among preschool children.
Spektor et al, 1991 (196) - Cubatao (Brazil) 1988	456 children, 55% male; 6–8 monthly lung function tests per subject	4-week mean PM ₁₀ (levels not given)	Lung function (annual mean PM ₁₀ was 59–110 in different school locations)	FVC -6 ml per 50 µg/m ³ PM ₁₀ . FEV _{0.1} -22 ml per 50 µg/m ³ (significant), PEFR -99 ml/s per 50 µg/m ³ (significant), MMEF -92 ml/s per 50 µg/m ³ (significant) (mean regression slopes, weighted by number of children in each school)
Tseng et al, 1992 (197) - Hong Kong, 1983–1989	Mean quarterly asthmatic hospital discharge rates: 15.4/10 ⁵ (0–1 years), 122.1/10 ⁵ (1–4 years), 106.1/10 ⁵ (4–15 years), 24.6/10 ⁵ (>15 years)	TSP quarter-yearly mean 54–136	Age-category-specific quarterly asthmatic hospital discharge rates – 27 quarters available for analysis	Discharge rates among 1- to 4-year-olds related to TSP. No significant association to air pollutants for 0–1 years. For 4–15 and >15 years only negative association with SO ₂ and NO _x .
Xu et al, 1995 (198) - Beijing (China) 1988	25 370 women, ≥20 years	1-week mean TSP 375	Preterm delivery	OR 1.10 (95% CI 1.01–1.20) per 100 µg/m ³ . Similar effect for SO ₂
Wang et al, 1997 (199) - Beijing (China) 1988–1991	74 671 live first-parity births	3 rd trimester median TSP 399	Low birthweight	OR 1.10 (95% CI 1.05–1.14) per 100 µg/m ³ . Reduction in birthweight 6.9 g (95% CI 4.2–9.6) per 100 µg/m ³ . Somewhat weaker effect for SO ₂ .
Auliciems et al, 1987 (200) - Brisbane (Australia) 1967–1981	369 SIDS cases	Visibility index, lag times up to 30 days before or after tested	SIDS	On average, decreasing visibility index in week before SIDS death, from slightly elevated levels.
Knöbel et al, 1995 (201) - Taiwan, 1981–1991	3816 SIDS cases	Visibility, lag times up to 0 days or 1–9 days	SIDS	OR 3.8 (95% CI 2.8–5.1) for lowest versus highest visibility category. Slightly stronger using 9-day mean visibility.
Penna & Duchade, 1991 (202) - Rio de Janeiro (Brazil) 1985	27 study areas in Rio de Janeiro, mortality ~40/1000 (about ½ of which neonatal)	Annual mean TSP 74–227	Total mortality 0–1 years; pneumonia mortality 0–1 years; diarrheal mortality 0–1 years	Roughly 3–4% increase in pneumonia mortality per 10 µg/m ³ TSP. No significant effect on total or diarrheal mortality.
Bobak & Leon, 1992 (203) - Czech Republic, 1986–1988	~222 000 births; mortality 12.1/1000 (neonatal 8.2, postneonatal 3.9)	Annual mean PM ₁₀ 69	Total neonatal mortality, total postneonatal mortality, respiratory postneonatal mortality	Total neonatal mortality: OR 1.2 (95% CI 1.0–1.4). Total postneonatal mortality: OR 1.4 (95% CI 1.1–1.8). Respiratory postneonatal mortality: OR 2.4 (95% CI 1.1–5.3) – for highest to lowest quintile of PM ₁₀ exposure (>84.7 versus <53.6 µg/m ³). Similar results for SO ₂ .

(continued)

Table 5. Continued.

Study	Characteristics of study population	Exposure measure and levels ^a	Outcome	Results
Woodruff et al, 1997 (204) -US, 1989–1991	3 788 079 births; total postneonatal mortality 3.39/1000 (SIDS 1.10/1000, ie, ~4200 SIDS cases)	Individual 2-month mean PM ₁₀ 31, range 12–69	Total postneonatal mortality; respiratory postneonatal mortal- ity (among normal birthweight and low birth- weight babies separately); SIDS	Total postneonatal mortality: OR 1.4 (95% CI 1.05–1.85); SIDS: OR 1.26 (95%CI 1.14–1.39) for high to low PM ₁₀ exposure (3 categories) (PM ₁₀ mean 44.5 versus 23.6 mg/m ³). Total postneonatal mortality: +4% (95% CI +2–+7), respiratory postneonatal mor- tality (normal birthweight): +20% (95% CI +6–+36), respiratory postneonatal mortal- ity (low birthweight): +5% (95% CI -9– +22), SIDS: +12% (95% CI +7–+17) per 10 mg/m ³ PM ₁₀ in a continuous analysis.

^a Short-to-medium-term air pollution levels [averaged over day(s), week(s), month(s), year or other period] with mean or range of values across study period, if available.

Table 6. Cross-sectional and cohort studies focusing on long-term health effects in relation to particulate air pollution. (For any abbreviations not found in the footnotes, see page 4.)

Study	Characteristics of study population	Exposure measure and levels ^a	Outcome ^b	Results
Cross-sectional studies				
<i>Mortality</i>				
Lave & Seskin, 1977 (210) Lave & Seskin, 1979 (212) - >100 SMSA 1960–1961 & 1969 Mendelsohn & Orcutt, 1979 (213) - Entire US in 404 county groups 1970 Lipfert, 1978 (211) Lipfert, 1980 (214) - 189 central cities 1969–1971 & 89 central cities 1959 Chapple & Lave, 1982 (215) - 104 SMSA 1975 Lipfert, 1984 (216) - 111 SMSAs 1970 Evans et al, 1984 (217) - Summarizes many cross-sectional studies on >100 US cities or SMSA 1960s–1970s Özkaynak & Thurston, 1987 (218) - 1980 US mortality rates (100 SMSAs)	Up to entire US popula- tion in ages relevant to analysis (up to ~150 million). Analysis units were cities, counties or SMSA.	Various particulate measures. Levels moderately high to high, declining over time.	Total mortality. Some studies also examined age-specific and cause-specific mortality.	Mean mortality effect of particles estimated at 3–8% of total mortality. Effect estimates often sensitive to choice of study area and model, including choice of demographic, social and other variables in the model. Some evidence for a stronger effect at ages >65 years, more inconsis- tent results for different causes of death. Suggested positive association for infant mortality [Lave & Seskin (210), Lipfert (211)]. See also 1996 US EPA report for further discussion (1).
Archer, 1990 (219) - Utah Valley (UT) 1950–1987	Three counties with low smoking rates.	TSP 40–93 (multiyear means), declining over time.	Cross-sectional and longitudinal differences in respiratory mortality, and the effect of a steel mill opening in 1 county.	In the most polluted county, 30–40% of respiratory disease deaths were associated with air pollution. Lung cancer death rates increased in the steel mill county in the decade after the mill opened.
<i>Respiratory symptoms or disease</i>				
Euler et al, 1987 (220) Euler et al, 1988 (221) - California 1966–1976	≥25 years, 7445 nonsmoking Seventh-Day Adventists	TSP; 25% of subjects had >750 hours per year at >200 mg/m ³	COPD	COPD associated with TSP, but also with oxidants and SO ₂ . Individual cumulative air pollution exposure estimated in this study.
Ware et al, 1986 (222) - Six US cities, 1976–1980	7–10 years, 8327 subjects	TSP R _i 39–114	Cough, bronchitis, LRI chest illness, wheeze.	Cough, bronchitis, LRI associated with TSP across cities.

(continued)

Table 6. Continued.

Study	Characteristics of study population	Exposure measure and levels ^a	Outcome ^b	Results
Dockery et al, 1989 (223) - Six US cities, 1980–1981	10–12 years, 5422 white children	TSP R ₁ 34–80, PM ₁₅ R ₁ 20–59	Cough, bronchitis, chest illness, asthma, wheeze, hay fever, earache.	Cough, bronchitis, chest illness associated with various particulate measures. Of these, PM ₁₅ provided significant estimates.
Portney & Mullahy, 1990 (224) - US (Health Interview Survey 1979)	17–93 years, 1318 subjects, 42% male	TSP, 6-year mean (1974–1979) R ₁ 35–140	Chronic bronchitis/asthma/emphysema, sinusitis, hay fever	Individual-level data on air pollution. Chronic bronchitis/asthma/emphysema associated with TSP.
Schwartz, 1993 (225) - 53 US urban areas (NHANES I)	30–74 years, 3874 subjects	TSP R ₂ 48–131	Diagnosed respiratory illness, reported bronchitis, reported asthma, reported dyspnea	Diagnosed respiratory illness and reported bronchitis, but not asthma or dyspnea, associated with TSP.
Walters et al, 1995 (249) - 24 UK electoral wards, 1988–1990	All ages & <5 years, 24 electoral wards	BS, levels not given	Respiratory admission rates, asthma admission rates	Weak nonsignificant association between BS and respiratory admissions. Only significant association was all respiratory admissions <5 years with NO ₂ .
Scarlett et al, 1995 (226) - 53 UK counties, 1981	23 years, 11 552 subjects	BS R ₁ 2–55	Phlegm, cough, wheeze	Only phlegm significantly associated with BS but not with SO ₂ .
Dockery et al, 1996 (227) - 24 communities in US & Canada, 1988–1991	8–12 years, 13 369 subjects, 50% male	PM ₁₀ R ₁ 15–33, H ⁺ R ₁ 0–52	Bronchitis, asthma, wheeze, cough, phlegm	Bronchitis related to particles, most strongly to H ⁺ (OR 1.7, 95% CI 1.1–2.5), and similarly to O ₃ and SO ₂ (neither significant). No other associations.
Braun-Fahrlander et al, 1997 (228) - Switzerland, 1992–1993	6–15 years, 4470 subjects, 50% male	PM ₁₀ R ₁ 10–33	Bronchitis, asthma, allergy, cough	Bronchitis, cough associated with PM ₁₀ , but not asthma or allergy.
Xu & Wang, 1993 (229) - Beijing, China 1986	40–69 years, 1576 never-smokers, 25% male	TSP 5-year mean R ₁ 261–449	Bronchitis, asthma, wheeze, cough, phlegm, dyspnea	OR for any symptom: 2.5 (95% CI 1.3–4.8) per ln(TSP) unit (ie. OR ~1.6 across range 261–449). Clearest effects for bronchitis, wheeze and cough.
<i>Lung function</i>				
Ware et al, 1986 (222) - Six US cities, 1974–1980	7–10 years, 8327 subjects	TSP R ₁ 39–114	FVC, FEV _{1.0}	No particle effect on FVC, FEV _{1.0} .
Dockery et al, 1989 (223) - Six US cities, 1980–1981	10–12 years, 5422 white children	TSP R ₁ 34–80, PM ₁₅ R ₁ 20–59	FVC, FEV _{1.0} , MMEF, PEFR	No effect on FVC, FEV _{1.0} , MMEF, PEFR.
Raizenne et al, 1996 (230) - 22 communities in US & Canada, 1988–1991	8–12 years, 10 251 subjects, 51% male	PM ₁₀ R ₁ 15–33	FVC, FEV _{1.0} , MMEF, PEFR	2–3% decrements of FVC, FEV _{1.0} , MMEF, PEFR for 1 standard deviation increase in PM ₁₀ .
Schwartz, 1989 (231) - 44 US locations (NHANES II) 1976–1980	6–24 years, 1849 subjects	TSP R ₃ 43–95	FVC, FEV _{1.0} , PEFR	Small significant particle effect on FVC, FEV _{1.0} , PEFR (but O ₃ effect stronger).
Chestnut et al, 1991 (232) - 49 US urban areas (NHANES I)	25–75 years, 963 subjects	TSP R ₁ 40–155	FVC, FEV _{1.0} , FEV _{1.0} /FVC, MMEF	Effect on FVC, FEV _{1.0} , but not FEV _{1.0} /FVC, MMEF.
Xu et al, 1991 (233) - 3 Beijing areas, China, 1986	40–69 years, 1440 subjects, ~25% male	TSP 5-year mean R ₁ 261–449	FVC, FEV _{1.0}	Effect on FVC, FEV _{1.0} by both TSP and SO ₂ . Study areas were residential, suburban and industrial.
Ackermann-Lieblich et al, 1997 (234) - 8 areas, Switzerland, 1991–1993	18–60 years, 3115 never-smokers, 39% male	PM ₁₀ R ₁ 10–33	FVC, FEV _{1.0}	Effect on FVC, FEV _{1.0} by NO ₂ , SO ₂ and PM ₁₀ , most consistently for PM ₁₀ .

(continued)

Study	Characteristics of study population	Exposure measure and levels ^a	Outcome ^b	Results
Cohort studies^b				
Abbey et al, 1991 (235) CA, LCA, MI, MORT, AS, CB, OD	27–95 years, 6338 subjects	1973–1977:	<i>Mortality:</i> MORT CPDM RESPM LCAM	Follow-up to 1982, 1986, 1987: CA (men), MI, MORT: no effect. <i>Relative risks (and 95% CI) per 1000 hours/year above 200 µg/m³ TSP:</i> CA (women): 1.37 (1.05–1.80) LCA: 1.72 (0.81–3.65) CB: 1.33 (1.07–1.65) OD: 1.36 (1.11–1.66) AS: 1.74 (1.11–2.71)
Mills et al, 1991 (236) CA, LCA	36% male	59% of population had TSP mean above 100 µg/m³	<i>Incidence:</i> MI CA LCA	
Abbey et al, 1993 (237) CA, MI, MORT, AS, CB, OD	<i>Mortality 1977–1986:</i> 6303 subjects, 56576 person-years.	53% of population had PM ₁₀ mean above 50 µg/m³	<i>Respiratory symptoms/disease:</i> CB OD AS	RR for long-term average exposure, estimated per 50 (CA, LCA) or 60 (CB, OD, AS) µg/m³ TSP, and 40 µg/m³ PM ₁₀ (CB, OD, AS) were similar. The analyses also suggested the following: LCA: stronger effect of O ₃ . AS: stronger effect of SO ₂ .
Abbey et al, 1993 (238) AS, CB, OD	<i>Incidence 1977–1982:</i> 6303 subjects, 34431 person-years.			
Greer et al, 1993 (239) AS	<i>Respiratory symptoms 1977–1987:</i> 3914 subjects, no person-years calculated as date of onset unknown.			
Abbey et al, 1993 (240) AS, CB, OD	<i>Mortality and lung cancer incidence 1977–1992:</i> 6338 subjects, person-years not given.		For CB, OD, AS, incidence of new symptoms, as well as exacerbation 1987 compared with exacerbation in 1977, was evaluated.	Follow-up to 1992: <i>relative risks (and 95% CI) per 42 µg/m³ PM₁₀:</i>
Abbey et al, 1995 (241) AS, CB, OD			<i>Lung function:</i> PPFEV _{1,0} FEV _{1,0} /VC PEF Lab	Men MORT 1.11 (1.0–1.3) CPDM 1.10 (0.9–1.3) RESPM 1.23 (0.9–1.6) LCAM 3.36 (1.6–7.2) LCA 5.21 (1.9–14) LCA* 4.72 (1.7–13)*
Abbey et al, 1995 (242) Method to estimate PM _{2.5}				Women 0.94 (0.8–1.0) 0.92 (0.8–1.1) 1.10 (0.9–1.4) 1.33 (0.6–3.0) . 1.25 (0.6–2.7)*
Abbey et al, 1995 (243) AS, CB, OD				* per 78 days/years above 60 µg/m³. LCA & LCAM: Men: similar for O ₃ and SO ₂ , but PM ₁₀ most consistent for LCA. Women: SO ₂ stronger, more consistent.
Abbey et al, 1995 (244) CA, LCA, AS, CB, OD (summary of results)				
Beeson et al, 1998 (245) LCA				
Abbey et al, 1998 (246) Lung function				
Abbey et al, 1999 (247) MORT, CPDM, RESPM, LCAM	<i>All outcomes:</i> Smaller numbers of subjects and person-years occur in some analyses due to missing air pollutant or other covariates.			
- Cohort of nonsmoking California Seventh-Day Adventists, 1977–1992 (93)				
Dockery et al, 1993 (88) - Six US cities, 1974–1991	25–74 years, 8111 subjects, 45% male; 111 076 person-years	PM _{2.5} R ₁ 11–29.6	MORT CPDM LCAM	MORT RR 1.26 (95% CI 1.08–1.47) CPDM RR 1.37 (95% CI 1.11–1.68) LCAM RR 1.37 (95% CI 0.81–2.31) (for 18.9 µg/m³ range in PM _{2.5}).
Pope et al, 1995 (89) - 151 US metropolitan areas, 1982–1989	≥30 years, 295 223 subjects, 44% male (PM _{2.5} analysis) 552 138 subjects, 44% male (SO ₄ analysis)	PM _{2.5} R ₁ 9–33.5 SO ₄ R ₁ 3.6–23.5	MORT CPDM LCAM	MORT RR 1.17 (95% CI 1.09–1.26) CPDM RR 1.31 (95% CI 1.17–1.46) LCAM RR 1.03 (95% CI 0.80–1.33) (for 24.5 µg/m³ range in PM _{2.5}). LCAM RR 1.36 (95% CI 1.1–1.7) for SO ₄ range.

b Abbreviations for the cohort studies: MORT = total mortality, CPDM = cardiopulmonary disease mortality, RESPM = nonmalignant respiratory mortality, LCAM = lung cancer mortality, MI = myocardial infarction, CA=cancer, all, LCA = lung cancer, CB = chronic bronchitis, OD=obstructive pulmonary disease, AS = asthma, PPFEV_{1.0} = percentage of predicted FEV_{1.0}, FEV_{1.0}/VC = FEV_{1.0} percentage of vital capacity, PEF Lab = PEF lability.

Regarding infant mortality in general, two early US cross-sectional analyses suggested an association be-

between annual averages of some particulate indicators and infant mortality (mentioned in table 6 on pages 73-75) (210, 211). The adequacy of annual averages as exposure measures for deaths before 1 year of age may, however, be questioned from a temporal point of view.

in particular for neonatal deaths. Three more recent studies have also examined infant mortality (table 5), two of them also using annual averages. In Rio de Janeiro, mortality from pneumonia (14% of infant deaths) but not total infant mortality (dominated by perinatal mortality) was associated with TSP levels (202). In the Czech Republic, neonatal mortality likewise showed only a suggested association, whereas postneonatal mortality, in particular respiratory mortality, was more associated with the annual PM_{10} levels (203). In the more elaborate US study already mentioned, individual estimates of PM_{10} exposure during the first 2 months of life were similarly associated with total and, especially, respiratory postneonatal mortality (204), whereas the OR per $10 \mu g/m^3$ for all other causes was 1.00 (95% CI 0.99—1.00).

Evaluation

Population-based cross-sectional studies have suggested an association between restrictions in activity, leading to work and leisure-time loss, as well as bed disability among children, and particulate air pollution levels over several previous weeks. Similar associations have been observed for school absences and lung function decrements among children and also suggested for respiratory hospital admissions among both children and adults. Preterm delivery and low birthweight has been associated with particulate air pollution during the week of delivery and 3 months before, respectively. A relation between sudden infant death syndrome and particulate air pollution has also been suggested, but data are not convincing, partly due to unclear exposure specifications regarding an appropriate particulate measure, averaging time, and exposure timing. Similar caveats apply regarding neonatal and postneonatal mortality, although the suggestion of an association particularly for respiratory postneonatal mortality is strong.

Health effects of long-term exposure

Long-term effects have been studied mainly with cross-sectional methodology and in a few cohort studies, as illustrated in table 6 (on pages 73-75) (88, 89, 203, 204, 210—247). Although the aim in cross-sectional studies is often to investigate long-term effects on health, observed effects can be due to short-term as well as long-term exposure. Long-term exposure may have effects that become manifest in the human organism as either chronic or acute diseases. In addition, the prevalence of an outcome is affected by both its incidence and its duration. Cross-sectional studies are therefore often problematic to interpret. Nevertheless, the more extensive evidence from cross-sectional studies has been reviewed first in this section, followed by the few cohort studies reported to date. It has been pointed out that,

since the variance in air pollution concentrations decreases as sampling (averaging) time increases, long-term studies intrinsically have less power than short-term studies. Unless individual long-term exposure can be adequately ascertained and there is sufficient mobility among the subjects, studies of long-term changes in health will tend to be studies of spatial differences in exposure with a longitudinal measure of health effects (248). Even so, a longitudinal follow-up will correctly observe the disease incidence, regardless of variations in disease duration, which may be desirable. Selection by the "healthy worker effect" (ie, sensitive persons avoid areas with high exposure) may be problematic, particularly in cross-sectional studies.

Cross-sectional studies

Mortality. Most of the early studies were large cross-sectional studies utilizing population mortality data and long-term average air pollution measurements from public monitoring networks in the United States (210—218). These cross-sectional analyses found that a proportion of total mortality (generally some 3—8%) appeared to be attributable to air pollution, especially SO_4 or fine particulate matter, despite attempts to control for demographic, social, health and other factors in the population in statistical modeling. It was, however, also shown that these results could be sensitive to the variables introduced into the models, and one conclusion by the mid-1980s was that individual-level data were needed for adequate control of confounding. One late analysis of this type suggested that $PM_{2.5}$ and SO_4 levels were more significantly and consistently associated with increased mortality than PM_{10} and TSP concentrations. The ranges of estimated effects for the various particulate measures on total mortality were 4—9% for SO_4 , 3—8% for $PM_{2.5}$, and 0—6% for PM_{10} and TSP (218). A more local study from Utah among chiefly nonsmokers found both nonmalignant and malignant respiratory mortality to be associated with variations in air pollution between the three studied areas over time, attributing 30—40% of respiratory mortality to air pollution (219).

Respiratory symptoms or disease. Two of the cohort studies to be described in this section have also reported cross-sectional results. The study of Seventh-Day Adventist nonsmokers in California included people who were resident within 8 km of their 1977 residence for at least 10 years and who completed the respiratory symptom questionnaires of the National Heart and Lung Institute in 1977 and again in 1987. Individual cumulative exposures (hours/year) to air pollutants above four threshold levels were estimated using residence zip codes and interpolated dosages from air-monitoring stations. Cross-sectional analyses of 1977 questionnaire

data were presented for SO₂ and TSP (220) and oxidants and NO₂, as well as combined analyses of all pollutants and interactions (221). The TSP thresholds were 60, 100, 150, and 200 µg/m³. The OR for COPD symptoms was 1.22 per 750 hours/year of exposure above a TSP concentration of 200 µg/m³ ($P < 0.00001$). Associations were also statistically significant for oxidants above 100 ppb and SO₂ above 40 ppb. In a multiple regression using all three air pollutants, TSP remained significant ($P < 0.01$), a finding suggesting that TSP was either more strongly associated with symptoms of COPD or was the best surrogate representing the mix of highly correlated pollutants (221). From the US Six Cities Study, an analysis of health examinations in 1975–1978 and air pollution levels in the previous year found that cough, bronchitis, and lower respiratory illness were significantly associated with mean TSP levels across cities — with OR values of 1.11, 1.11, and 1.08 (all three $P < 0.05$) for a 10 µg/m³ increase, respectively (222). Surprisingly, however, the within-city analysis (for year-to-year and region-to-region variability) produced negative associations for all the outcomes. A later analysis of 1980–1981 questionnaire data from this cohort found that the prevalence of reported chronic cough, bronchitis, and chest illness was associated with all the particle measures (TSP, PM₁₅, PM_{2.5}, SO₄). For PM₁₅ the OR values were 3.7 (95% CI 1.0–13.5), 2.5 (95% CI 1.1–6.1), and 2.3 (95% CI 0.8–6.7) for the most, compared with the least, polluted city (40 µg/m³ difference) (223).

Portney & Mullahy (224) used the US National 1979 Health Interview Survey, in which 80 000 persons nationwide responded to questionnaires. The analyses concerned only 1318 persons who resided within 20 miles (about 32 kilometers) of the nearest O₃ and TSP monitoring stations and were also in the subset that answered questions on chronic respiratory illnesses and smoking habits. The results suggested that sinusitis and hay fever were associated with O₃ exposure but that more serious chronic respiratory disease (chronic bronchitis, emphysema and asthma) were associated with average TSP levels over the previous 6 years. In a similar survey, the first National Health and Nutrition Examination Survey (NHANES I), 3874 adults answered a detailed questionnaire and were examined by a physician (225). The OR associated with a 10 µg/m³ increment in annual average TSP was 1.07 (95% CI 1.02–1.12) for reported chronic bronchitis and 1.06 (95% CI 1.02–1.11) for a respiratory diagnosis by the examining physician, whereas asthma showed no association.

In the United Kingdom, nontrivial positive regression coefficients, adjusted for ethnicity and poverty score, were obtained in an analysis for respiratory admissions to hospitals in relation to 2-year electoral ward averages of BS, NO₂, and, for children, also SO₂. For asthma, only NO₂ and, for children, SO₂ showed posi-

tive associations. Only the association of all respiratory admissions among children <5 years of age with NO₂, however, was statistically significant (249). The prevalence of phlegm among 23-year-olds, as reported in questionnaire studies, showed OR values of up to 1.5 and a significant trend over five exposure categories of annual averages of BS (median 30.2 in highest versus 11.0 in lowest category) (226). Cough did not show a significant association, and no association was found for wheeze with BS or for any outcome with SO₂. In a study of children in 24 communities in the United States and Canada (250), respiratory symptoms (227) and lung function (230) were investigated in relation to annual air pollution levels. Bronchitis was related to all the particulate measures (H⁺, SO₄, PM_{2.1}, PM₁₀), most strongly to H⁺, and also with similar strength to O₃ and SO₂ (not significant) (227). No other associations were found. Similarly, a Swiss study across 10 communities found bronchitis to be associated with PM₁₀ levels with an OR of 2.2 (95% CI 1.2–4.9) between the most and least polluted community. An OR of 3.1 (95% CI 1.6–5.8) was observed for chronic cough and was very similar for nocturnal dry cough, but, in this situation too, no association was found for asthma or for allergy (228). A study of adults in Beijing, with very high particulate levels, found several symptoms to be associated with particle levels in the three compared areas, with the strongest effect on cough and wheeze (229).

In a Dutch study investigating exposure contrasts near roads to elucidate air pollution effects, children's symptoms of cough, wheeze, runny nose and asthma, but not bronchitis or atopy, were related to living close to freeways, density of truck traffic, and BS measured in schools (251). The effect was found mainly among girls. Outdoor BS levels ranged from 14.9 µg/m³ close to the freeways to 7.4 µg/m³ at greater distances, whereas no gradients were found for PM₁₀ or PM_{2.5}. The indoor BS levels were in the same range. Several other studies have also found an elevated prevalence of respiratory symptoms or asthma (251–257) or hospitalization for wheezing bronchitis or asthma among young children (258, 259) to be associated with living near busy roads, measures of traffic intensity, or modeled NO₂ concentrations. Other studies found no association for asthma-related respiratory symptoms (260) or the prevalence of active asthma (261). In all of these studies, some measure of road traffic intensity rather than air pollution measurements was used in the analyses, most were cross-sectional studies but some were case-referent.

Lung function. Children in the US Six Cities Study were studied cross-sectionally on two occasions, in 1974–1977 and 1980–1981. Neither study found any association between pulmonary function levels and

particulate measures (TSP and SO_4 , in the latter study also PM_{15} and $\text{PM}_{2.5}$) (222, 223). In an analysis of lung function in relation to annual mean air pollution levels for US and Canadian children (230), $\text{FEV}_{1.0}$ was related to particulate measures (H^+ , SO_4 , $\text{PM}_{2.1}$, PM_{10}), most strongly to H^+ (OR -3.5% , 95% CI -2.0 – 4.9% for a 52 nmol/m^3 increase in H^+). The percentage decrement was similar (more than -3%) for FVC, MMEF (maximum midexpiratory flow), and PEF (peak expiratory flow) and, for all four pulmonary function measures, was around -2% for a $17.3 \text{ } \mu\text{g/m}^3$ increase in PM_{10} . Spirometric measurements and questionnaire data from young people in 44 cities from the US NHANES II National Health Survey were analyzed against annual mean levels of SO_2 , NO_2 , TSP and O_3 in the preceding year (231). Due to an insufficient overlap of pollution monitoring stations, each pollutant was considered in a separate regression. TSP, O_3 , and NO_2 were all significantly associated with FVC, $\text{FEV}_{1.0}$ and PEF in regression models, the TSP relationship being the least significant and also a magnitude smaller than for O_3 over the range of exposure (approximately -0.05% versus -0.1%).

Two of the previously mentioned studies of road traffic and children's health also investigated lung function and found impairments to be associated with traffic density (254, 262). Only in the more recent study were air pollution measurements made, and the association was observed also with BS measured indoors in schools (262).

Among adults, a study based on the US NHANES I survey found that the quarter-yearly average of TSP exposure was associated with FVC (-2.25% for a $34 \text{ } \mu\text{g/m}^3$ increase in TSP at the mean of $87 \text{ } \mu\text{g/m}^3$) and $\text{FEV}_{1.0}$, but not MMEF or the $\text{FEV}_{1.0}/\text{FVC}$ ratio (232). In another study of adults with exposure to very high particulate levels in Beijing, a clear decrease in adult FVC and $\text{FEV}_{1.0}$ was associated with increases in both TSP and SO_2 (233). Likewise, in a Swiss study of adults, significant and consistent effects on FVC and $\text{FEV}_{1.0}$ were found for PM_{10} , SO_2 , and NO_2 , most consistently for PM_{10} with a 3.4% decrease in FVC per $10 \text{ } \mu\text{g/m}^3$ (234).

Case-referent studies and cohort studies

The long-term effect of air pollution, including particles, on the incidence of lung cancer has been studied with both case-referent and cohort methodology. This evidence has been recently evaluated (263, 264) and will not be reviewed in detail in our report, although the cohort results are discussed briefly under the relevant study. Overall, the observed excess risk for lung cancer of 20–40% in areas with high particulate levels does not appear inconsistent with extrapolations based on occupational data, primarily including workers exposed to

diesel exhaust particulate (263). Apart from lung cancer, the case-referent approach, which requires incident disease data, has rather seldom been applied to other chronic respiratory health effects in relation to long-term air pollution exposure, and, when it has, measurements or estimates of air pollution exposure, including exposure to PM, are usually lacking. One example is a study of COPD in Athens, which noted an OR of 2.0 (95% CI 1.2–3.3) for subjects with long-term urban residence, compared with rural or mixed residence, adjusted for gender, age, smoking, and socioeconomic indicators (265). PM exposure was not measured or estimated, but it was known to be elevated in the urban area.

Only three cohort studies have been reported on the health effects on adults as a result of long-term particulate air pollution. In the Californian Seventh-Day Adventist cohort, Cox regression (for mortality and incident disease), logistic regression (for symptom data), and linear regression (for lung function) methods were used for analyses in a cohort of 6338 subjects. The incidence of lung cancer, based on follow-up to 1982 (17 cases), was related to both TSP (RR 1.72, 95% CI 0.81–3.65, see table 6) and O_3 (236, 244); in a multi-pollutant analysis, O_3 was possibly superior (236). With extended follow-up to 1992 (16 men, 20 women), the relation to PM_{10} was strong for the men and was weaker and nonsignificant for the women (245). Associations were similar for O_3 and SO_2 for the men and appeared to be stronger for SO_2 for the women. The authors observed that the gender differences for O_3 and PM_{10} appeared to be partially due to gender differences in exposure, mainly in that men spent more time outdoors, particularly in the summer. In the 1982 follow-up, the incidence of all malignant neoplasms combined showed an elevated risk for the women only (244), whereas myocardial infarction and total natural-cause mortality did not show any relationship to TSP, O_3 , or NO_2 (235, 237). With mortality follow-up to 1992, a weak, nonsignificant association with PM_{10} was observed for total mortality only for the men. The PM_{10} associations appeared to be due to nonmalignant respiratory disease (RR 1.18, 95% CI 1.02–1.36 per 43 days/year above $100 \text{ } \mu\text{g/m}^3$ for both genders combined) and to lung cancer, particularly among the men (247). The results for lung cancer mortality regarding other air pollutants and gender differences were similar to those for lung cancer incidence. In 1987, 3914 subjects received a 10-year follow-up questionnaire on new symptoms. Whereas bronchitis and total COPD were associated chiefly with TSP (RR 1.33 and 1.36 per 1000 hours/year above $200 \text{ } \mu\text{g/m}^3$ in 1973–1977, respectively), the development of asthma showed some association with O_3 (RR 1.40 per 500 hours/year above $200 \text{ } \mu\text{g/m}^3$ 1977–1987, 95% CI 0.99–2.34) (240), mainly observed for men (3.12, 95% CI 1.61–5.85), possibly because they spent more time

outdoors (239). For both genders, asthma development was, however, similarly associated with TSP (RR 1.74 per 1000 hours/year in excess of 200 $\mu\text{g}/\text{m}^3$ 1973–1977, 95% CI 1.11–2.72) and SO_4 (RR 2.85, 95% CI 1.03–7.40, per average annual increase of 7 $\mu\text{g}/\text{m}^3$) (240, 244). Multipollutant analyses could not differentiate clearly between these pollutants in relation to asthma (240). For a subset of this cohort, $\text{PM}_{2.5}$ was estimated from airport visibility data (242). This particulate measure showed an especially strong relationship to all malignant neoplasms among women (244). For a subcohort that performed spirometry in 1993, a decrement of 7.2% in $\text{FEV}_{1.0}$, compared with the predicted level, per 54 days/year when PM_{10} exceeded 100 $\mu\text{g}/\text{m}^3$, was observed for the men whose parents had asthma, bronchitis, emphysema, or hay fever, but not for the men without this familial background or for the women (246). A similar decrement (6.3%) was associated with O_3 . The authors suggested that this gender difference could be due to the marked gender differences in time spent outdoors and in exposure to occupational air pollutants or to a stronger “healthy worker effect” among the women, as suggested in this cohort. PEF lability was similarly increased among all the women and men (0.8% and 0.6% per 54 days/year above 100 $\mu\text{g}/\text{m}^3$ PM_{10} , respectively).

Two other US cohort studies have examined mortality in relation to particulate air pollution using Cox proportional hazard regression modeling. In the US Six Cities Study, a 14- to 16-year follow-up was conducted for 8111 adults in the six cities (88). The adjusted total mortality rate ratio for the most polluted city compared with the least polluted city was 1.26 (95% CI 1.06–1.50). Plotting of the city-specific total mortality rate ratios against various pollutants suggested that $\text{PM}_{2.5}$, PM_{10} , and SO_4 particles best described the rate gradient across the cities, whereas TSP, H^+ , SO_2 , and O_3 correlated less well with the city-specific rate ratios. An analysis with $\text{PM}_{2.5}$ levels instead of simple city indicator variables in the model gave a rate ratio of 1.26 (95% CI 1.08–1.47) across the range of $\text{PM}_{2.5}$ in the most versus the least polluted city (18.6 $\mu\text{g}/\text{m}^3$), and the results were very similar for PM_{10} and SO_4 . The estimate was 1.37 (95% CI 0.81–2.31) for $\text{PM}_{2.5}$ and lung cancer mortality and 1.37 (95% CI 1.11–1.68) for cardiovascular mortality, whereas for all other mortality the rate ratio was not elevated.

The second study linked air pollution data from 151 US metropolitan areas in 1980 with individual risk factors for 552 138 persons resident in these areas when enrolled in the second American Cancer Society Cancer Prevention Study. Mortality was followed until December 1989 (89). The adjusted mortality risk ratios for the most polluted versus the least polluted area were 1.15 (95% CI 1.09–1.22) for 19.9 $\mu\text{g}/\text{m}^3$ SO_4 and 1.17

(95% CI 1.09–1.26) for 24.5 $\mu\text{g}/\text{m}^3$ $\text{PM}_{2.5}$ when SO_4 and $\text{PM}_{2.5}$ were used in the model. Whereas SO_4 was associated with an increased risk of cardiopulmonary and lung cancer death (1.26, 95% CI 1.16–1.37, and 1.36, 95% CI 1.11–1.66) and $\text{PM}_{2.5}$ was related to cardiopulmonary but not lung cancer mortality (1.31, 95% CI 1.17–1.46, and 1.03, 95% CI 0.80–1.33), there was no association for either particulate measure with mortality from other causes.

Evaluation

Large cross-sectional studies in the United States provided an initial impetus for research on the health effects of particles, but they were unable to answer questions regarding short-term versus long-term effects. The lack of individual data also makes these studies vulnerable to confounding. Cross-sectional studies of symptoms rather consistently suggest that chronic bronchitis, cough, and related symptoms are related to particulate air pollution, whereas the data regarding asthma or allergy provide less clear support for an association. From the cross-sectional studies on pulmonary function, there is some evidence for a long-term effect of particulate air pollution, especially for adults. In comparison, the evidence regarding the pulmonary function effects of O_3 appears to be stronger for children, and it may be that this difference between adults and children reflect different time scales for the long-term effects of these two pollutants. Two major cohort studies from the United States have strengthened the conclusion that cardiopulmonary mortality, perhaps including lung cancer, is associated with long-term particulate exposure. A 10 $\mu\text{g}/\text{m}^3$ increase in the long-term $\text{PM}_{2.5}$ level was related to an excess total mortality of roughly 10%. Over the range of $\text{PM}_{2.5}$ levels from the least to the most polluted city, the studies estimated increases in total mortality of 26% (over 18.6 $\mu\text{g}/\text{m}^3$) and 17% (over 24.5 $\mu\text{g}/\text{m}^3$). Calculations using Dutch and US male life-table data and the RR estimates from these studies have estimated a possible effect on average life expectancy on the order of 1 to 1.5 years lost (266). The longitudinal follow-up in the third US cohort study, the Seventh-Day Adventist study, found an association between total mortality and PM_{10} levels of similar magnitude among men, but not among women. The broad category of cardiopulmonary mortality did not show a stronger association, but mortality due to nonmalignant respiratory disease and lung cancer did, particularly among men. SO_2 for both genders and O_3 for men also showed strong associations to lung cancer mortality. This study also confirmed a previously reported cross-sectional association of bronchitic symptoms with particle levels and suggested that asthma may be associated with both O_3 and particles or possibly other pollutants.

Summary and concluding remarks

There is consistency in the findings of increased mortality in association with levels of particulate air pollution on the previous day or days. Different gravimetric measures, such as TSP and PM₁₀, and reflectance or visibility measures such as BS or CoH have been used with similar results. It has lately been suggested that the smaller particulate fractions (eg, PM_{2.5} or even smaller) are primarily responsible for the health effects observed. The possibility that particles are a surrogate for other pollutants cannot be completely dismissed. However, the association has been consistently observed even in locations with low levels of other pollutants. The most recent analyses have modeled several pollutants simultaneously, usually with the effect of particles remaining. The size of the effect is around a 0.5–1% increase in mortality for a 10 µg/m³ increase in PM₁₀, and it appears generally to be stronger for respiratory deaths and cardiovascular deaths than when the totality of death counts is considered. Associations have been observed at particulate levels well below 100 µg/m³, and some studies indicate weaker relationships at higher levels.

The studies on hospital admissions and emergency-room visits provide additional evidence for adverse health effects of short-term exposure to particles. Increases in daily admissions range from 0.5% to 3% per 10 µg/m³ of PM₁₀ in most studies. An effect has been found for many respiratory end points and, in some studies, also for cardiovascular conditions. Generally the estimated effect is stronger for respiratory disease such as COPD and pneumonia and lower for cardiovascular disease or specific cardiac disease end points. The results regarding asthma admissions show a larger variability, possibly due partly to a smaller sample size, but asthma visits, particularly of children, appear to be rather consistently associated with particulate air pollution levels, with increases of roughly 1% to 4% reported per 10 µg/m³ of PM₁₀. The results from recent European studies of hospital admissions (0.4–0.9% increase per 10 µg/m³ of PM₁₀ for different end points in different subgroups) are weaker than previous findings from the United States and elsewhere.

Particulate air pollution has also been found to be related to both respiratory symptoms and lung function among healthy persons. Mostly children have been studied. The lung function decrements are only about 0.5–1.5% per 50 µg/m³ increase in PM₁₀ levels. The most consistent effects have been found for PEFR. The decrements are often more strongly related to longer averaging or lag times than to previous-day levels, and therefore there is a possibility of persistent, chronic effects. The results for symptoms are rather inconsistent, although many studies reported high OR values. For the most part the results have been more consistent for lower

respiratory symptoms and cough than for upper respiratory symptoms, with generally a 10–40% excess RR in association with a 50 µg/m³ increase in PM₁₀ levels when an effect was observed. For asthmatics, a somewhat stronger effect on pulmonary function has often been observed, while this stronger effect does not hold true for symptoms. Extra asthma medication, generally bronchodilator use, has mostly been associated with particulate exposure and may modify the observed effect on symptoms and lung function.

Several studies on both mortality and morbidity have convincingly shown that the effect of particles is stronger among the elderly. There still appears, however, to be an effect also in younger age groups. The stronger effect on the elderly is to be expected if the exposure affects susceptible subgroups of persons with underlying disease. An argument has been made that the effect on mortality only represents a harvesting effect of hastening death by a few days. There is scant evidence to elucidate this hypothesis, but available data suggest that it may be partly true but that the effect is also partly more long-term. There is also overall evidence for stronger effects on respiratory and cardiovascular admissions to hospitals and emergency rooms and mortality than on total admissions and mortality, causal association therefore being suggested.

Cross-sectional studies of symptoms rather consistently suggest that chronic bronchitis, cough, and related symptoms are related to particulate air pollution, whereas the data regarding asthma or allergy provide less support of an association. The longitudinal follow-up in one US cohort study confirmed a previously reported cross-sectional association of bronchitic symptoms with particle levels and suggested that asthma may be associated with both O₃ and particulate exposure or possibly exposure to other pollutants. From the cross-sectional studies on pulmonary function, there is some evidence for a long-term effect of particulate air pollution, especially for adults; this evidence received some support from the mentioned US cohort study. Two recent major cohort studies from the United States have strengthened the conclusion that cardiopulmonary mortality is associated with long-term particulate exposure. A 10 µg/m³ increase in the long-term PM_{2.5} level was related to an excess total mortality of roughly 10%. Over the range of PM_{2.5} levels from the least to the most polluted city, the studies estimated increases in total mortality of 26% (over 18.6 µg/m³) and 17% (over 24.5 µg/m³). A possible effect on average life expectancy on the order of 1 to 1.5 years lost was estimated from these data. The longitudinal follow-up in the first US cohort study mentioned found little association between total mortality and particles, although associations were observed for mortality due to nonmalignant respiratory disease and lung cancer, particularly among men.

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Appendix

Recalculation of regression estimates to a common metric

In tables 1—3 of the review, results from various types of analyses have been recalculated to a percentage increase per 10 $\mu\text{g}/\text{m}^3$. In so doing, the following procedure has been followed.

Original data from each publication were extracted in principle in the following order of priority: (i) for point estimates: published beta-coefficient, relative risk or odds ratio (OR), percentage increase; (ii) for random error: standard error (SE) or confidence interval (CI) of beta, SE or CI of the relative risk or OR, SE or CI of the percentage increase, exact P-value, t-value, P-limit (eg, $P < 0.05$). In a few cases the order of priority was altered to retain as many decimals as possible. In all cases the original numbers were first recalculated to beta per unit of exposure and the SE of the beta for the function relating air pollutant x to outcome y . The slope of the function in a single point was obtained by taking the derivative of this original function. For linear regressions, a relative increase was obtained by dividing by the mean of the outcome (median if mean not available). The derivative function was then evaluated at the mean concentration of the air pollutant (median if mean not available). The result was converted to the PM_{10} (particulate matter $< 10 \mu\text{g}/\text{m}^3$) metric by applying the conversion factors given previously (see the Introduction of the review). Finally the relative risk for the chosen increment (10 $\mu\text{g}/\text{m}^3$) was evaluated as $\exp[10 \times (\text{PM}_{10} \text{ derivative at mean})]$, that is, by assuming an relative risk function-

al form, whether the original function assumed this form (log-linear regression models, generally assuming the Poisson distribution) or a linear absolute risk (linear regression models). The percentage increase was then obtained as $(\text{relative risk} - 1) \times 100$. The result may, in principle, be interpreted as the proportional increase in the outcome due to a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{10} from any level, remembering that it is estimated *based on the association (slope) observed at the mean air pollutant concentration in each study*. All the calculations were performed in an Excel spreadsheet, with no rounding of intermediate steps beyond what was built into the program.

It should be noted that the numbers obtained may differ slightly from those of other reviews. Apart from calculation errors in one place or the other and different conversion factors to PM_{10} , several other explanations are possible. A point estimate may also be obtained as the midpoint (directly or on the log scale as appropriate) between published confidence limits. This procedure may even give point estimates that are as consistent and may perhaps even asymptotically more accurately reflect the "true" nonrounded point estimates obtained in a large number of studies. However, after rounding, such indirectly calculated point estimates will in some cases result in a rounded point estimate that differs from the one published in the paper, which we deemed undesirable. Similarly, the choice of using pub-

lished SE or CI values when both are available for calculating the CI may give slightly different results. The rounding of numbers taken from the publications or of intermediate results can also produce noticeable differences in the final result. Furthermore, an alternative method of evaluating the effect of a $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} is to evaluate the original function at, for example, the mean air pollution level and (mean + 10) and take the difference. This procedure will also often produce slightly different results (except in the case of log-linear, including Poisson, models relating the outcome to untransformed air pollutant levels because these assume a constant relative risk independently of the baseline outcome value and of air pollution levels between which the relative risk is evaluated). However, the choice of (mean + 10) minus mean, or mean minus (mean - 10), or even (mean + 5) minus (mean - 5) for a $10 \mu\text{g}/\text{m}^3$ difference near the mean is arbitrary. Therefore, we chose the method which evaluates the effect *at the mean* (eg, using the instantaneous slope of the function *at the mean* by taking the derivative). Finally, as already noted, others may have retained the linear absolute risk assumption for linear models and evaluated the percentage increase for a $Z \mu\text{g}/\text{m}^3$ increase in such models as simply $[Z \times (\text{PM}_{10} \text{ derivative at mean})] \times 100$ rather than $\{\exp[10 \times (\text{PM}_{10} \text{ derivative at mean})] - 1\} \times 100$. As long as $Z \times (\text{PM}_{10} \text{ derivative at mean})$ is smaller than 0.1 (10%), as is the case for most studies evaluated for a difference of $10 \mu\text{g}/\text{m}^3$ PM_{10} , it will make very little difference. Note, however, for example, the larger numbers for Wordley et al (1) in table 2 of the review; these numbers differ very slightly from percentage increases given in the paper as a result of the constant relative-risk assumption we assumed in our calculations. When evaluated over a larger difference than $10 \mu\text{g}/\text{m}^3$ PM_{10} , such discrepancies will be more noticeable. For

the interested reader, percentage increases for a $Z \mu\text{g}/\text{m}^3$ increase in PM_{10} based on the slope at mean air pollution levels and on the assumption of a linear absolute risk can be obtained from our numbers by taking $\{[\ln(\text{tabular value})/100] + 1\}/10 \times Z \times 100$. Assuming a constant relative risk, as we have done, one computes $\{[(\text{tabular value})/100] + 1\}^{(Z/10)} - 1 \times 100$.

As mentioned in the main text, several sensitivity analyses have shown that results are not overly sensitive to regression type or functional form (variable transformations) when the air pollution effect is expressed as the slope at the mean. If one considers that any regression analysis in a sense "pivots" around the bulk of data, which naturally centers around the mean, and that most reasonable functional forms have moderate curvature near the mean, it is perhaps not surprising that the slope at the mean is relatively insensitive to model specification. The differences between linear or log-linear models or different functional forms for dose-response interpretations become more important when the effect at high air pollution levels are considered, and even more so at low levels, or when extrapolation is done beyond the data range. However, from a practical point of view, the major interest is in present-day averages and possible realistic changes and variations around these levels, and, for that purpose, the different models generally produce qualitatively similar estimates of dose-response.

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