AIR POLLUTION RISK

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Abstract

This article reviews the literature on health effects of air pollution, with a primary focus on time series studies but also covering prospective studies and case-crossover designs. It also covers some of the controversies created by these studies and concludes with a brief review of air pollution standards in the U.S.

Keywords. Bayesian random effects, Case-control studies, Generalized Additive Models, Generalized Linear Models, Morbidity, Mortality, Ozone, Particulate matter, Prospective studies, Time series, TLNISE.

Concern about air pollution risk takes two main forms. The first is the greenhouse effect — the collective contribution of a group of gases (known as greenhouse gases), which results in global warming and has potentially catastrophic consequences for our climate. The best known greenhouse gas, and the one on which most emission-reduction attempts are focussed, is carbon dioxide (CO_2). However, since this encyclopedia contains a separate entry on global warming, we shall not consider it any further here. The second major risk, and the focus of this article, is the effect of air pollution on human health.

As an illustration of one of the major recent studies of this phenomenon, Fig. 1 (taken from [1]) shows the results of a time series study based on 88 U.S. cities. For each city, plotted is the regression coefficient and 95% confidence interval for the estimated percentage increase in mortality corresponding to a 10 μg/m^3 rise in particulate matter of aerodynamic diameter less than 10 microns (PM_{10}), a size at which particles are capable of penetrating directly into the lungs. Other studies have focussed on $PM_{2.5}$, which has the same definition with a maximum diameter of 2.5 microns.

The cities are grouped into seven regions, and the figure also shows a posterior mean and 95% posterior interval of the pooled effect across each region. Finally, at the bottom the figure shows the estimated national effect: this shows a posterior mean increased mortality of 0.21% with a posterior standard deviation of 0.06%. Other results from the so-called NMMAPS (National Morbidity and Mortality Air Pollution Study) have included a similar study of ozone [2] and the effect of $PM_{2.5}$ on hospital admissions [3]. These and other results have been extensively cited in recent years as evidence for tightening the U.S. air pollution standards.

The remainder of this article covers the background and history of this subject, followed by a detailed description of time series studies. Other study designs are also covered, followed by some of the caveats that have been expressed about this whole area of research.

1 Background and History

The first studies of the human health impact of air pollution were done in the 1950s, as a result of several dramatic incidents of extremely high air pollution causing widespread death. Possibly the best known of these incidents was the London "smog" of December 5–8, 1952, during which the level of "British Smoke" rose to over 3,000 $\mu g/m^3$ and the result was around 4,000 excess deaths over what would normally have been expected during this period. Similar incidents in other places led to global concern about the consequences of high air pollution, and motivated the introduction of legislation such as the (British) Clean Air Act of 1956 and the (U.S.) Clean Air Act of 1970, which were the first attempts to deal with the issue by regulation.

Despite the success of these early attempts at eliminating very high pollution events, concern persisted that even at much lower levels, pollution was still responsible for adverse health effects, including premature death. Analysis of long-term data records from London ([4], [5], amongst others) prompted researchers to start compiling and analyzing time series from several U.S. cities (e.g. [6], [7], [8], [9]). Most of these showed that after adjusting for effects due to seasonal variation and meteorology, a strong correlation remained between PM and mortality. Other studies showed similar associations with various measures of morbidity, for example, hospital admissions or asthma attacks among children. However, some authors focussed on the sensitivity of these results to modeling assumptions and suggested they were not statistically reliable [10,11].

This background led to a number of large-scale research efforts, of which NMMAPS is the best known. In the next section, we outline the methodology behind these studies.

2 Time Series Analyses

Although there are many variants on the basic methodology, most are close to the following.

The analyses depend on multiple regressions in which the dependent variable $y_t,\ t = 1, ..., n$ is either the death count or some measure of morbidity (e.g. hospital admissions) on day t. Typically the death counts exclude accidental deaths and they may be stratified by cause of death or by age group. The regression may be ordinary least squares (sometimes y_t is transformed, e.g. log or square root deaths) but a more common analysis assumes that y_t has a Poisson distribution with mean μ_t, expressed in terms of covariates x_{tj} by a formula such as $\log \mu_t = \sum \beta_j x_{tj}$, and fitted through generalized linear model (GLM) software. Some studies include a correction for overdispersion ($\text{Var}(y_t) = c\mu(t)$, some $c > 1$) or for autocorrelation, but these are usually not major issues.

The regressors $x_{tj}, j = 1, ..., p$ typically represent three types of explanatory variable: (a) air pollution, (b) meteorology, (c) seasonality and long-term trends. Of course (a) is the main object of interest but (b) and (c) are included as well to adjust for possible confounding: deaths are higher in extreme meteorological conditions and there are seasonal effects or long-term trends caused by factors such as flu epidemics, demographic changes, etc.

For (a), the covariate is usually the air pollution variable of interest (e.g. PM_{10} or ozone) taken from the nearest monitor or the average over all monitors within a given study area. Very often lagged variables are included to allow for the possibility of delayed effects of up to 7 days. In recent years the "distributed lag model" has become fashionable, in which a separate covariate is included for each lag (typically up to day 7) and the sum of corresponding regression coefficients taken as the overall pollution-mortality effect. Some attempts have been made to model longer-term lagged effects and to deal with the so-called "harvesting" issue. (Harvesting refers to the possibility that those killed by a high air pollution event are already very sick and would have died anyway within a few days. However if such an explanation were true, there should be observed negative correlations to account for the temporary decrease in the population of susceptible individuals. Studies have repeatedly failed to demonstrate such correlations [12,13].) Sometimes other pollutants than the main one of interest are included as possible "co-pollutants", e.g. in a study of PM_{10}, we may include SO_2 as a co-pollutant to adjust for the possible confounding of those two effects.

For (b), temperature is almost always included, as well as at least one variable representing humidity, and there may also be lagged values as well. The NMMAPS papers have used temperature and dewpoint as the two variables of interest, both current day and the average of the three previous days to accommodate lagged effects. Other authors have used either specific or relative humidity instead of dewpoint, and some have also included atmospheric pressure.

For (c), it is conventional to assume that one component of the regression function is some nonlinear function of time, that has sufficient degrees of freedom to incorporate both seasonal and long-term trend effects. The nonlinear effect may be modeled as a linear sum over K spline basis functions [14]; here K is the number of "knots" and is the most critical parameter. Typically authors use between 4 and 12 knots per year. Similar representations are sometimes used to treat other variables nonlinearly, such as temperature and dewpoint, though typically with much smaller K (in the range 3–6).

In addition to the above covariates, the NMMAPS analyses have typically included a day-of-week effect and additional nonlinear terms to represent the interaction of long-term-trend with age group.

The alternative "generalized additive model" or GAM approach [15] has also been used for non-linear effects. Some erroneous results were reported due to inappropriate use of default convergence criteria and standard error formulae [16], though subsequent research resolved these difficulties and strengthened the methodology [17].

2.1 Combining Estimates Across Cities

Although the initial application of time series regression analysis was to one city at a time, it has been generally recognized that to obtain definitive results, it is necessary to combine analyses across many cities. A typical assumption is that the critical parameter of interest (for example, the regression coefficient relating mortality to PM_{10}) is a random effect for each city, say, θ_c in city c, drawn independently from a normal distribution with mean θ^* and variance τ^2. However the *estimate* in city c, denoted $\hat{\theta}_c$, is also treated as random with mean θ_c with a presumed known standard error. Based on these assumptions we could, for example, estimate the national parameters θ^* and τ^2 by restricted maximum likelihood, followed by smoothed (or "shrinkage") estimates of the individual θ_c's. Alternatively, researchers have taken a Bayesian approach to the whole analysis, for example using the TLNISE software of Everson and Morris [18]. Some attempts have been made to extend the basic random effects model to allow for spatially dependent effects (see e.g. [19]).

The results of Fig. 1 result from application of this methodology to data on 88 U.S. cities from 1987–2000. The air pollution variable was daily PM_{10}, lagged one day. Other covariates at each city include long-term trend, temperature and dewpoint (current day plus average of the three previous days, using splines to allow for a nonlinear effect), day of week and an interaction term between the long-term trend and age group. Most of the attention has focussed on the regional and national "overall" results, in which point and interval estimates are given for θ^*.

3 Alternative Study Designs

3.1 Prospective studies

Apart from time series analysis, there are two other commonly used study designs. *Prospective studies* take a specific cohort of individuals and follow them through a long time period. This has the advantage of allowing researchers to measure long-term effects, which time series studies do not. However, unlike time series studies in which regression parameters are computed for each city, and only later combined across cities to achieve greater precision, in prospective studies the regressions themselves rely on between-city comparisons, typically estimating a standardized mortality rate for each city and regressing on some city-wide measure of air pollution. This raises issues associated with ecological bias, or in other words, the possibility that between-city variations may be due to effects that have nothing to do with air pollution.

The paper [20] presented results from the Harvard Six Cities study, a long-term study of over 8,000 individuals in six U.S. cities. Survival rates were conducted using the Cox regression model and showed that., after adjusting for smoking and other known risk factors, there was a statistically significant association between air pollution and mortality. A subsequent paper [21] showed similar results based on a much larger study (the American Cancer Society or ACS study), which involved over 500,000 individuals from 154 U.S. cities. However, although the study involved many more participants, in other respects it was inferior to the Six Cities study, for example in using participants recruited by volunteers rather than a randomized sample, and in relying essentially on air pollution measures at a single point in time. A third study is the Adventist Health Study of Smog (AHSMOG) which showed similar results for a cohort of over 6,000 nonsmoking California Seventh-day Adventists [22].

Given the importance of these studies for regulation, the Health Effects Institute commissioned an independent reanalysis of the six-cities and ACS studies [23]. This study recreated the datasets and largely confirmed the correctness of the original analyses. However, they also conducted many sensitivity analyses, some of which raised doubts about the interpretation of results. We refer to these in more detail in Section 4.

3.2 Case-crossover studies

A third paradigm for the design of air pollution-mortality studies is the *case-crossover design.* The idea is that the exposure of an individual to a pollutant immediately prior to some catastrophic event (e.g. death, heart attack) is compared with the exposure of the same individual to the same pollutant at other, control or “referent” times. Making plausible assumptions about how the risk of the catastrophic event depends both on time and covariates, it is possible to write down likelihood estimating equations (for a regression coefficient between the pollutant and the risk of the catastrophic event) that look very similar to the Poisson regression equations that arise in time series studies. However, a source of bias is the time interval between the catastrophic event and the selected referent times: too long and the analysis may be biased due to trend, too short and it could be affected by autocorrelation. The papers [24] and [25] used (respectively) simulation and theoretical arguments to examine the bias issue. The case-crossover methodology was applied [26] to out-of-hospital sudden cardiac arrest in the Seattle region, finding no significant relationship between high air pollution and mortality, which the authors attributed to the lack of prior history of coronary artery disease in the subjects under study, in contrast with other studies that have included patients with such history.

4 Issues and Controversies

Despite the enormous amount of research that has been done on air pollution and health, the scientific community is by no means unanimous about the interpretation of these studies, especially in the context of regulations about air quality standards. Extended commentaries have been provided [27,28]; here we summarize a few of the issues that have been raised.

None of the study designs we have discussed are controlled, randomized studies of the sort that are common in, for instance, drug testing. Therefore, they are all vulnerable to possible confounders or “effect modifiers”. Despite serious efforts to include such effects as covariates in the regression analyses, the results typically remain sensitive to exactly which covariates are included or certain *ad hoc* decisions about how to include them (for example, when long-term trends are modeled nonlinearly using splines, how many degrees of freedom to include in the spline representation). See [11,29] for issues related to model selection or model averaging; the recent paper [30] contains a particularly comprehensive discussion of the degrees of freedom issue.

Most studies have assumed a linear relationship between dose and response (possibly after transformation, e.g. $\log \mu_t$ in the case of Poisson-regression time series analysis). But this is arguably inappropriate for regulatory decisions in which it is critical to assess the likely benefit of a specific reduction in pollution (for example, if the 8-hour ozone standard were reduced from 80 to 60 parts per billion). [31] presented nonlinear models for ozone; earlier authors did the same for PM [32,33,34] with varying conclusions.

The question of "fine or coarse particles?" is another one that has caused much argument. Much of the research and regulatory effort over the past decade has been focussed on fine particles ($PM_{2.5}$), which penetrate deeper into the lungs and are therefore widely believed to have a more significant health effect. But to take one example, [34] reached the opposite conclusion in analyzing epidemiological data from Phoenix, Arizona.

The criticisms that have been raised of cohort studies are somewhat different, but ultimately raise similar issues over whether the associations found in studies are indicative of a true causal effect. [23] introduced a number of "ecological covariates" at a city-wide scale to try to determine whether the inter-city PM effects that had been observed in earlier studies could be due to other sources. In the case of the ACS dataset, they examined some 20 possible ecological covariates; all but two were not statistically significant, but one of those that was significant was gaseous sulfur dioxide (SO_2). The picture was further clouded when spatial correlations were introduced into the model; in one analysis, involving both SO_2 and sulfate particles in a model with spatial dependence, the "particles" effect was not statistically significant, though the SO_2 effect still was significant. It has been speculated [35] that these inconsistencies in the results of different cohort studies may be due to an inappropriate assumption of proportional hazards in the Cox regression model.

5 Summary and Conclusions

At the time of writing, the EPA has recently finalized a new $PM_{2.5}$ standard — controversially from the point of view of some epidemiologists, it did not lower the long-term average level permitted from the standard of 15 μg/m^3 that was introduced in 1997. A possible lowering of the ozone standard, from its present value of 80 parts per billion, is still under consideration. Other countries have similar standards in force that in some cases are lower than in the U.S. Both advocates and opponents of tightened standards draw heavily on the epidemiological studies that have been discussed in this article, so their interpretation has significant political and societal implications. In the view of the present writer, new research over the past decade has added enormously to the information available about health effects, but there remain fundamental controversies that may never be fully resolved.

6 References

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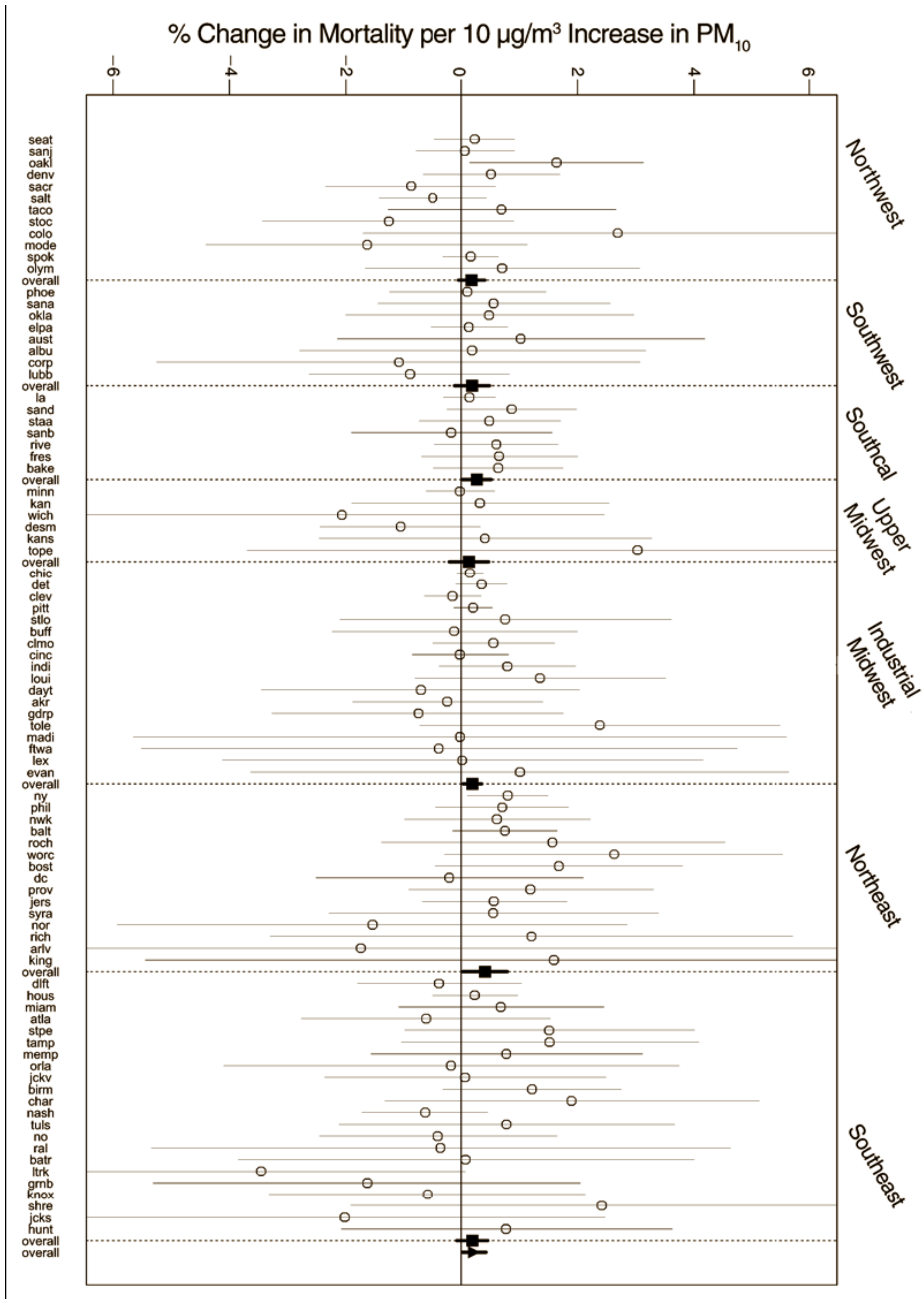
Figure 1


% Change in Mortality per 10 µg/m³ Increase in PM10
−6
−4
−2
0
2
4
6
Northwest
Southwest
Southcal
Upper Midwest
Industrial Midwest
Northeast
Southeast
seat
sanj
oakl
denv
sacr
salt
taco
stoc
colo
mode
spok
olym
overall
phoe
sana
okla
elpa
aust
albu
corp
lubb
overall
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sand
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sanb
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minn
kan
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chic
det
clev
pitt
stlo
buff
clmo
cinc
indi
loui
dayt
akr
gdrp
tole
madi
ftwa
lex
evan
overall
ny
phil
nwk
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