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Invited Commentary—Beyond the Body Count: Air Pollution and Death

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The link between air pollution and death was established many years ago by a series of infamous air pollution "disasters" (Meuse Valley, Belgium, 1930; Donora, Pennsylvania, 1948; London, United Kingdom, 1952) (1). In all of these episodes, stagnant weather conditions made concentrations of smoke, sulfur oxides, and other noxious substances rise to levels that were extremely high compared with current conditions in the developed world. In the London episode, the number of deaths rose to severalfold the usual number for more than a week, rivaling the fatality rate of the great cholera epidemic of 1854 and the great influenza epidemic of 1918. Most of the fatalities were thought to occur among "a susceptible group of patients whose life expectancy, judging from their preexisting diseases must, even in the absence of fog, have been short" (2, p. 1). However, a certain number of previously healthy subjects were also dying within days or even hours after the beginning of these episodes.

A series of abatement measures have reduced current pollution levels to a mere fraction of what they were during these episodes. For a while, effects of air pollution on mortality were believed to be a thing of the past. Indeed, 20 years ago, a complete issue of this journal was filled with an intelligent report by a group of well-known epidemiologists from the United Kingdom who argued that the air quality standards for particulate matter that were being proposed at the time in the United States were unnecessarily low (3). From their point of view, the standards could be relaxed without jeopardizing public health in any significant way.

Since then, the issue of air pollution and death has risen as a phoenix from its ashes. It is beyond the scope of this commentary to discuss the reasons for this, but one of them is the steady sharpening of the epidemiologic tools that are used to investigate acute effects of air pollution on mortality. In the early episodes, one could see and smell the pollution, and the number of deaths per day was increased to several times the expected number. Remarkably, the original report on the London episode of 1952 mentions that the highly increased mortality rates were not immediately noted, as opposed to the heavy demand for hospital beds. The event was reported to be a "supreme example of the way in which a metropolis of eight and a quarter million people can experience a disaster of this size without being conscious all the while of its occurrence" (2, p. 1). Nevertheless, with effects as immediate and dramatic as these, one could do without sophisticated statistical tools to demonstrate a relation. Nowadays, the relative risks reported in air pollution epidemiology papers are on the order of a few percentage points' increase in mortality over realistic exposure ranges (4). Time series analysis, imported into epidemiology from fields such as econometrics, has been the tool of choice for distinguishing the small effects we're currently seeing from the "noise" caused by season, influenza epidemics, weather changes, etc. Were it not for the large number of reports from all over the world that have documented associations between day-to-day variations in air pollution and day-to-day variations in mortality, such small relative risks could easily have been dismissed as being probably due to some unmeasured confounding factor(s)—and indeed, some skeptics remain unconvinced that there is a real effect (5). However, the causality of the associations has been largely accepted by regulatory agencies such as the US Environmental Protection Agency and the European Union. Both bodies have now promulgated air quality standards for particulate matter (which is seen as the most likely culprit, either alone or in combination with gaseous pollutants) that are far lower than the standards that were criticized 20 years ago (3).

There is one question in all this that has received relatively little attention so far: By how many days (or weeks, months, or years) is death in an individual advanced by air pollution? The question is by no means unimportant. If the mortality displacement is short and deaths are advanced by only a few days, no relation between air pollution and mortality would exist on time

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scales of several weeks or more. In other words, if the association between air pollution and death amounts to little more than a reduction in a terminally ill patient's suffering by a day or two, each increase in air pollution and its associated increase in mortality would be followed by a *decrease* in mortality within a few days. The total number of people dying during a longer period of, say, a month or a year would be unaffected, as the patients in question would have died very soon anyway. Curiously enough, the 1952 London report did suggest that persons who died because of the episode had had little life left in them, but it failed to bring this argument to its logical conclusion—that if this were true, there should have been far *fewer* deaths than expected during the weeks after the episode. In fact, such a death "deficit" was completely absent from the statistics of the month following the episode. Nevertheless, the question of how much *life expectancy*, rather than the *daily number of deaths*, is affected by air pollution episodes is as important now as it was then, and it is a question that we should try to answer in greater detail than we have so far.

In this issue of the *Journal*, Schwartz (6) presents analyses in which he has tried to provide an answer on the basis of time series data. His argument is that the extent of mortality displacement by air pollution can be analyzed in time series studies by using time scales of increasing lengths. If the mortality displacement is short and deaths are advanced by a few days only, this would cancel out the relation between air pollution and mortality. If, however, death is advanced by substantially more days, the relation would remain, or even become stronger if additional damage were done by cumulative exposures beyond that caused by the daily fluctuations. Schwartz therefore separates the time series of mortality, air pollution, and confounding factors into three components: long term (trend and season), midscale (varying from 15 days to 60 days), and short term (days). While the usual time series studies analyze the short term component, Schwartz analyzes the midscale component. The results are remarkable. For all-cause mortality, the effect size does not decrease, but it increases steadily with increasing "window size." For ischemic heart disease deaths, the pattern is essentially the same. For deaths due to chronic obstructive pulmonary disease, however, the effect size tends toward zero with increasing "window size," a pattern consistent with the original "harvesting" hypothesis. For pneumonia deaths, finally, there seems to be some harvesting, but the effect sizes then increase again with window sizes greater than 30 days.

How do we interpret these findings? One important conclusion is that for all-cause mortality and ischemic heart disease death, mortality displacement in this data set seems to be at least 2 months. Only for the less frequent chronic obstructive pulmonary disease deaths did harvesting seem to take place. The overall impact of air pollution on mortality was therefore far from trivial. However, as Schwartz acknowledges (6), his approach does not allow conclusions about mortality displacements of more than approximately 2 months. Because adjustment for season (by using a 120-day window in the basic analysis) in this type of analysis is always needed, it seems that this is how far the time series approach can take us in answering the harvesting question. In other words, *how* substantial the impact is remains unclear, other than "more substantial than 2 months." Since, on the basis of cohort studies (7, 8), the effect of long term exposure on life expectancy has been estimated to be in the order of at least 1 year (9), a substantial gap remains that the time series approach alone cannot fill.

Even more intriguing than the absence of harvesting is the finding that most effect estimates even *increased* with increasing window sizes. The implication seems to be that cumulative exposures over periods of 1–2 months are actually more harmful (in terms of the daily number of deaths associated with them) than shorter exposures of similar magnitude. Schwartz argues that this can be interpreted not only as an indication of more damage being done to an individual's health but also as an indication of a larger number of individuals' being moved into the "pool of susceptibles" from which air pollution takes its toll (6). The quoted time series studies on the effects of air pollution on hospital admissions speak to the plausibility of the latter interpretation. Early studies of the effects of air pollution on lung function in healthy subjects showed effects to persist for weeks in some cases (10, 11). Earlier work by Schwartz suggested that deaths associated with air pollution were found primarily among older individuals whose health was somehow already compromised, but not necessarily to the extent that they were institutionalized (12). To us, the current results suggest that the gap between the time series analyses and the cohort studies can conceivably be filled by studying carefully selected groups of presumably "susceptible" individuals over periods of several years in communities characterized by different long term air pollution concentrations. This would allow for more detailed documentation of what happens at the individual level to subjects who experience different long term average concentrations as well as (inevitably) short term peak concentrations. For example, a recent study from Scotland (13) investigated the association between air pollution and health in subjects who had already had a cardiorespiratory emergency hospital admission. Such approaches are useful models for future studies.

One potential problem with the approach suggested by Schwartz is an increased risk of confounding in

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comparison with the analysis carried out on the short time scale of days. Is the stronger association found at the "midscale times" really due to air pollution, or is it due to other slowly changing risk factors such as influenza epidemics? Adjustment for seasonality has been sufficiently made using the generalized additive model, and the author observed that using a shorter span resulted in overadjustment (6). Nevertheless, several investigators observed that after careful adjustment for seasonality, mortality was still associated with influenza epidemics (14, 15). It would be interesting to study the robustness of the present findings to the inclusion of data on influenza or, alternatively, to restriction of the analysis to the summer season.

As with all epidemiology, one would like to see the results of the current analysis replicated in other data sets. A recent publication by Zeger et al. (16) also addressed the harvesting problem using data on total suspended particulate matter and total mortality in Philadelphia, Pennsylvania; these authors also found that removal of the shortest term fluctuations from their time series increased rather than decreased the pollution effect estimates. Unfortunately, no data on cause-specific mortality were provided.

Studies like those of Schwartz (6) and Zeger et al. (16) help us move beyond the "body count" approach that has been so prevalent in (especially) the popular press' interpretations of time series studies on air pollution and death. What's really important is the impact of air pollution on life expectancy, and further research is needed to firmly establish the magnitude of this impact. The cost associated with significant loss of life expectancy, as well as with further reductions of air pollution concentrations, is very high. Investment in a few cohort studies specifically designed to test such hypotheses as can be derived from Schwartz' latest contribution to the field seems a very reasonable proposition.

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