Long-Term Exposure to Traffic-Related Air Pollution and Mortality

BACKGROUND

Increases in urbanization and motor vehicle use have raised questions about the health effects of exposure to pollutants, such as oxides of nitrogen and black smoke (a measure of fine particulate matter), that are emitted from motor vehicle exhaust pipes. Measurements at regional monitoring stations, however, may not reflect the actual concentrations of pollutants related to automobile, bus, and truck traffic to which the surrounding population is exposed. Some studies indicate that living near roads with heavy traffic may increase the risk of adverse health effects associated with air pollution. In Europe, most studies of traffic-related air pollution and health before 2000 focused on short-term variations in pollutant concentrations and acute outcomes in very young populations. Assessments of the risks of long-term exposure were often based on ambient air pollution levels and on results from large cohort studies that did not include specific information on traffic exposure.

In the current study, which began in July 2001, Dr. Bert Brunekreef and colleagues examined associations between long-term exposure to pollution from motor vehicles and mortality in a large cohort in the Netherlands. This expanded the work of a pilot study, reported in the *Lancet* in 2002, in which Gerard Hoek, Bert Brunekreef, and others used state-of-the-art methods based on geographic information systems to estimate black smoke and nitrogen dioxide (NO$_2$) concentrations at the home addresses of 5000 older adults, a randomly selected subcohort within the ongoing Netherlands Cohort Study (NLCS) on diet and cancer. The investigators found variations in concentrations of these traffic-related pollutants among the addresses of study participants; however, the results for the two pollutants were highly correlated at both regional and local levels. In 8 years of follow-up, the relative risk of cardiopulmonary mortality was found to be significantly higher for those who lived near a major road. For the current study, the investigators refined the methods of exposure assessment, included more traffic data, and extended the mortality analysis to the full NLCS cohort. They also added exposure estimates for several other pollutants, collected pollutant data for the 10 years before the NLCS began, and extended the follow-up to 10 years.

STUDY SUMMARY

The objectives of this study were to estimate exposure to traffic-related air pollution for all subjects in the full NLCS cohort, to evaluate associations between exposure and mortality, as well as the incidence of lung cancer, to determine whether exposure was associated with death from specific causes, and to determine whether mortality risks were influenced by the characteristics of individual subjects. The NLCS was originally created to study possible connections between nutritional patterns and the development of cancer. The cohort used for the current study, known as NLCS-AIR, contained 120,852 subjects, who were 55 to 69 years of age in September 1986. During the follow-up period from January 1, 1987, through December 31, 1996, there were 17,674 deaths from natural causes recorded for this cohort.
For the NLCS-AIR study, Dr. Brunekreef’s team conducted full-cohort analyses, in which they examined exposure information and mortality data for the entire cohort, but computerized information on potential individual-level confounding variables was very limited. Detailed personal information from questionnaires completed when the cohort was formed was available for the 5000-person NLCS subcohort on which their pilot study had been based and also was entered for all cohort members who died during follow-up. The investigators used this information in case–cohort analyses in which data for the subcohort were compared with data for study participants who died (cases), with adjustment for a substantial number of potential confounders, to estimate relative risk of mortality. They also analyzed data for the subcohort alone, using the current study methods, to generate results that can be directly compared with those of their pilot study.

Exposure assessment was the most complicated aspect of data collection and analysis. Using available measurements from 1976 through 1996, the investigators calculated long-term exposure levels for black smoke, NO₂, sulfur dioxide (SO₂), and particulate matter equal to or less than 2.5 µm in aerodynamic diameter (PM_{2.5}), at the 1986 home address of each study participant. Calculations were based on a complex system, including regional, urban, and local components of overall exposure for each pollutant. The investigators also used indicators of traffic-related air pollution, including traffic intensity on the nearest road, living near a major road, and sum of traffic intensity in a surrounding 100-m buffer, as variables for local exposure. For analyses including the local variables, a combination of the regional and urban components (called the background exposure) was also included to control for the effects of exposure from sources that were not local.

The health endpoints analyzed in this study were death from all natural causes and death from cardiovascular or respiratory causes, lung cancer, or other natural causes, as well as lung cancer incidence. For the full cohort, analyses were adjusted for age, sex, and smoking status at baseline, determined from the questionnaire, and for information on socioeconomic status in the participant’s neighborhood and regional area, derived from public sources.

Brunekreef and his team chose the well-known Cox proportional hazards method to calculate relative risks of mortality associated with traffic-related air pollution. They also used a newly developed method of Cox-Poisson mixed model analysis, which enabled them to incorporate statistical corrections for spatial autocorrelation (the nonindependence of exposure and health-status observations for people living close together) in the results.

**RESULTS AND INTERPRETATIONS**

The results discussed here, unless stated otherwise, are of the full-cohort analyses, which displayed greater statistical precision than those of the case–cohort analyses because of the much larger number of subjects. Of particular interest are analyses of associations between specific traffic variables and the relative risk (RR) of death from cardiopulmonary causes. In a model that included two variables, reflecting exposure to background air pollution and to local traffic-related air pollution, the RR (95% confidence interval [CI]) was 1.13 (0.99–1.29) for exposure to background black smoke and 1.07 (0.96–1.19) for living near a major road (defined as a road with traffic intensity of more than 10,000 motor vehicles/day). In a model with one variable for exposure to the overall concentration of black smoke, calculated from estimated background exposure and local exposure from traffic using a land-use regression model, the RR was 1.07 (95% CI, 0.98–1.15).

In the pilot study, Brunekreef and colleagues previously reported considerably higher risks for death from cardiopulmonary causes, obtained using similar models: for exposure to background black smoke, the RR was 1.34 (95% CI, 0.68–2.64); for living near a major road, the RR was 1.95 (1.09–3.51); and for overall black smoke exposure, the RR was 1.71 (1.10–2.67). These results were obtained for 8 years of follow-up in the 5000-person NLCS subcohort, compared with 10 years of follow-up in the full cohort of 120,852 members for the current study. Though the relative risks of mortality were higher in the pilot study, the confidence intervals were much wider than those in the current study, reflecting less precision in the estimated risks. The discrepancy between the results is partially due to the difference in statistical power between the two studies resulting from their sample sizes, although other factors such as the longer follow-up period are also likely to have been important. Given the prominence of the pilot study results, the lower risk estimates in the current study, especially for the traffic variable, are noteworthy.
Of further interest are the relative risks of cardiopulmonary mortality for the subjects who lived in the three largest cities, which were higher, for the most part, than those reported for the full cohort. This finding raises questions about whether the higher risk estimates in these three cities are related to the effects of traffic and urbanization, or reflect exposure estimates that were more precisely modeled in urban areas than in other areas.

**DISCUSSION**

A spatial relationship between air pollution and mortality has been reported for decades, both in the United States and in Europe, but attempts to assign risk based on spatial patterns have the potential for serious confounding from local social and economic factors. Though excess mortality due to pollutant exposure has been observed in cohort studies in the United States, evidence from Europe has been sparse. Consequently, European assessments of the health effects of air pollution have relied on results from U.S. studies. The current study in the Netherlands adds to the available information about exposures encountered by European populations.

The large size of the cohort makes the study by Brunekreef and his team noteworthy, in part because effects are detected with greater statistical precision than in a small cohort. Well-designed cohort studies also have the potential to be able to control for confounding factors at the individual level. In the current study control for potential individual-level confounders was very limited in the full-cohort analyses. In contrast, the case-cohort and subcohort analyses were adjusted for an extensive list of potential confounders, but the risk estimates were less precise because of the smaller sample sizes. Sensitivity analyses suggested, however, that the inclusion of the more detailed individual variables would not have substantially changed the risk estimates for the full cohort.

One of the most challenging aspects of this study was the modeling of exposure for specific addresses with limited primary data on local pollutant concentrations and traffic. Several methods were used, including interpolation from pollutant measurements of the national monitoring network and land-use regression models to characterize exposure at residences. The calculations involved considerable manipulation of data and incorporated regression models developed in other studies. Taken as a whole, the data and methods used for exposure assessment result in some uncertainty about the exposure estimates and, consequently, about the associations between exposure and mortality. This is particularly true when quantitative exposure estimates at participants’ residences were not calculated using data from quantitative studies, but based instead on default assumptions about traffic intensity on nearby roads. Uncertainty resulting from a chain of assumptions about exposure (rather than measurement of exposure) may be an issue in this study, particularly when traffic intensity was converted to quantitative local estimates of traffic-related pollutant exposures. Despite these concerns, the exposure assessment in this study was innovative and based on sound principles. Brunekreef’s team made excellent use of advanced technology involving geographic information systems and a wide variety of data sources and types, pushing available techniques for modeling exposure to their limits.

Overall, the results of the mortality analyses should be regarded as suggestive rather than conclusive. The estimates of relative risk were small, in many cases not statistically significant, and often consistent with chance. Also, in any observational study in which the exposure is estimated, rather than measured, residual confounding by unknown factors is possible. Internal inconsistencies in the study are the higher risks of mortality for residents of the three largest cities and for subjects who had a lower level of education or ate less fruit. These results could be explained by differences in these subjects’ vulnerability to air pollution or in the toxicity of the air pollutants to which they were exposed, or they may point toward some type of confounding specific to these groups.

There are also features of the study that might bias the results toward a smaller effect. The authors concluded that exposure misclassification was likely to be higher for subjects who did not live in the major urban areas where more traffic information was available, and might be responsible for their lower risk estimates. Consistent with this theory is the greater risk of death estimated for those who had not changed residence over the period of observation and were thus assumed to have more accurate exposure assessments.
The most intriguing difference is the considerably lower risk of cardiopulmonary mortality associated with measures of traffic-related air pollution in the current study of the full NLCS cohort compared with the pilot study of 5000 persons drawn from the same cohort. The exposure assessment in the current study was more refined. In particular, changes in the way subjects were classified with respect to living near a major road led to substantial changes in exposure assignment for this variable. It seems reasonable to accept the authors’ conclusion that the main explanation for the discrepancy in results lies in the random variation in the selection of the pilot study cohort from the full cohort, and in the longer follow-up period in the current study – although the findings remain puzzling. This experience indicates that caution is necessary in analyzing results from small cohort studies.

Two previous studies of the health effects of traffic-related air pollution in large U.S. cohorts, the American Cancer Society Study and the Harvard Six Cities Study, found stronger associations with cardiovascular mortality than with respiratory mortality, but little association with death from other causes. In contrast, the current study in a large Dutch cohort found higher risks for respiratory mortality than for cardiovascular mortality, and the risks for cardiovascular mortality were similar to those for deaths not related to either respiratory or cardiovascular causes. All three cohort studies found associations with lung cancer mortality, although the risks in the Dutch cohort were not significant. As mentioned above, the precision of the estimates should be taken into account when interpreting such patterns.

The Netherlands, a country half the size of the state of South Carolina, is exposed to a high and fairly homogeneous regional background concentration of particulate matter. This background pollution constituted by far the greatest proportion of the Dutch cohort’s exposure to the pollutants investigated in this study. Though the variation in air pollution exposure estimates was mainly related to traffic sources, the traffic-related variability in exposure was small. Therefore, the estimated mortality risks associated with air pollution were based on a narrower range of exposures than was the case in the U.S. studies, in which average estimates for cities, rather than individuals, were derived directly from measurements of air pollution concentrations.

This major cohort study provides evidence that long-term exposure to air pollution is likely to reduce life expectancy in Europe. The study found evidence of an increased risk of death in subjects living near a busy road, albeit at much lower levels of risk than were found in the pilot study. Though the study did not estimate the city-specific effects of the cohort’s exposure to air pollution, and in this respect differs from cohort studies based on city-level differences in exposure, the estimated effects of air pollution on mortality appear similar in scale to those observed in large U.S. cohort studies. The findings of this study are potentially important for environmental policy decisions and pollution prevention and warrant further investigation.