HEALTH EFFECTS INSTITUTE

STATEMENT

Synopsis of Research Report 171

Multicity Study of Air Pollution and Mortality in Latin America (the ESCALA Study)

BACKGROUND

For nearly two decades, scientists seeking to understand the role that air pollution might play in population health effects have relied heavily on epidemiologic studies known as time-series studies. Time-series studies use information on daily changes in air pollutant concentrations and daily counts of mortality and morbidity. Although initially conducted at the individual city level, coordinated analyses across many cities have recently emerged as the tool of choice for developing more reliable and comparable estimates of the short-term effects of air pollution on health in regions around the world. HEI has a long-standing interest in these coordinated analyses; it has funded studies such as the National Morbidity, Mortality, and Air Pollution Study; Air Pollution and Health: A European and North American Approach; and Public Health and Air Pollution in Asia.

The present study, referred to hereafter by its Spanish acronym ESCALA (Estudio de Salud y Contaminación del Aire en Latinoamérica), was initiated to address underlying data and methodologic limitations in the epidemiologic literature on the health effects of air pollution in Latin America that had been identified in a 2005 review by the Pan American Health Organization. The William and Flora Hewlett Foundation, which has a strong interest in understanding air pollution and health in Latin America, provided HEI with supplemental support to address gaps in the evidence necessary to inform regulatory decisions, and in the process to build a network of health experts capable of carrying out research on air pollution in the future. The multicenter study was led by Dr. Isabelle Romieu, then at the Instituto Nacional de Salud Pública in México, in collaboration with Dr. Nelson Gouveia in Brazil and Dr. Luis Cifuentes in Chile.

APPROACH

The primary objective of the ESCALA study was to estimate the effect of daily exposures to PM_{10} (particulate matter $\leq$ 10 µm in aerodynamic diameter) and to ozone on daily mortality from several causes (all natural causes, cardiopulmonary disease, respiratory disease, cardiovascular disease, cerebrovascular–stroke, and chronic obstructive pulmonary disease) and for several age groups (all-age, $\geq$ 65 years, < 1 year, 1–4 years, 1–14 years) in nine Latin American cities, and for the region as a whole, using a common analytic framework. The nine cities were Monterrey, Toluca, and Mexico City in México; Rio de Janeiro, São Paulo, and Porto Alegre in Brazil; and Santiago, Concepción, and Temuco in Chile. Of these, three cities (Porto Alegre, Concepción, and Temuco) were excluded from the ozone analyses because of the lack of adequate ozone monitoring data.

In the first stage of the analyses, the investigators estimated the percentage change in the risk of mortality per 10-µg/m^3 increase in PM_{10} or ozone for each combination of age group and cause of death for the individual cities in each country. They followed a common protocol for fitting the widely used Poisson regression models to the air pollution and mortality time-series data in each city while controlling for other factors that might also explain the temporal patterns of mortality (e.g., temperature, humidity, season, day-of-the-week, holidays). The investigators also carried out analyses to test the sensitivity of the results to various details of the models. Ultimately, the final models used in the individual cities were chosen to fit specific patterns of mortality in those cities.

With the individual city data, the investigators also explored two-pollutant models, in which PM_{10} results were controlled for the presence of ozone and vice versa; whether the association of ozone with mortality differed by warm and cold season;

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and whether lower socioeconomic status might increase the susceptibility of different age groups to the effects of air pollution.

In the second stage of the analyses, the investigators used two meta-analytic statistical techniques to analyze further the effect estimates from individual cities. First, meta-analysis was used to combine the individual city results, providing a weighted average effect of PM_{10} and ozone on the various categories of mortality for the region. These analyses were conducted for the all-age and the ≥ 65 age groups where sufficient data were available. Next, meta-regression was used to explore whether variables representing different aspects of city geography, density of the monitoring network, weather, age structure, smoking patterns, and health status could explain the varying effects of PM_{10} on individual categories of mortality that were observed across the nine cities. Meta-regression analyses were not conducted for ozone because data were available for only six of the nine cities.

RESULTS AND INTERPRETATION

In the individual city analyses, the ESCALA investigators found daily increases in PM_{10} to be associated with small percentage increases in daily mortality from all natural causes, cardiopulmonary disease, respiratory disease, cardiovascular disease, cerebrovascular–stroke, and chronic obstructive pulmonary disease in most of the cities studied; although the strength of the associations varied from city-to-city. In two-pollutant models, in which ozone was included as the second pollutant, the mean PM_{10} effects on mortality were not significantly different from those observed with PM_{10} alone. In some cities (for example, in Santiago) the effects appeared slightly strengthened, while in others they were slightly weaker (for example, in Mexico City).

The investigators observed a pattern of small, but positive, associations between daily increases in ozone and increases in cardiopulmonary and cardiovascular mortality in most cities except Toluca. Significant associations were least often observed for respiratory disease (only in São Paulo and Mexico City), cerebrovascular–stroke (only São Paolo), and chronic obstructive pulmonary disease (only in Mexico City). The associations were generally weaker and more variable across cities than were those for PM_{10} but were most consistently observed in the three largest cities — São Paulo, Rio de Janeiro, and Mexico City. When adjusted for PM_{10} in two-pollutant models, the estimated effects of ozone were weaker and no longer significant in most cities and for most causes of death (except in Santiago where they appeared stronger in several cases) than in models with ozone alone. The investigators reported seasonal effects of ozone on mortality; the effects were generally stronger in the warm season in São Paulo, Rio de Janeiro and Monterrey but were stronger in the cold season in Mexico City.

When the analyses were restricted to the population 65 years or older in each city, effects of both PM_{10} and ozone on mortality were, on average, slightly stronger than when all ages were included. These findings are consistent with those from other studies; however, the differences between age groups did not appear to be statistically significant in ESCALA.

The investigators also looked specifically at the effects of PM_{10} and ozone on respiratory mortality and on a subcategory of respiratory mortality, lower respiratory infection, among infants and children for the three largest cities — São Paulo, Santiago, and Mexico City. The results varied substantially among cities. With exposure to PM_{10}, significantly increased respiratory mortality was observed in infants (< 1 year) and children 1–4 years in Santiago, but not in São Paulo or Mexico City. The PM_{10}-associated risk of mortality from lower respiratory infection was significantly increased for infants only in Mexico City. For children 1–14 years, the risk of mortality from lower respiratory infection was increased in all three cities, but significantly so only in Santiago. Exposure to ozone was associated with significant increases in the risk of respiratory mortality in children 1–4 years and in the risk of mortality from lower respiratory infection in both infants and in children 1–14 years in Mexico City, but not in the other two cities. As in the analyses with adults, the seasonal effects of ozone on mortality were strongest in the cold season in Mexico City and in the warm seasons in the other two cities.

The meta-analyses pooled the results from the individual cities, providing estimates of the overall mean effects of increases in PM_{10} and ozone on mortality for the region. For PM_{10}, the investigators reported positive and statistically significant increases in all-natural-cause (0.77%), cardiopulmonary (0.94%), respiratory (1.19%), cardiovascular (0.72%), cerebrovascular–stroke (1.10%), and chronic obstructive pulmonary disease (2.44%) mortality in the all-age group, with similar findings in individuals 65 years and older. For ozone, small positive and significant associations with increased mortality were observed for cardiopulmonary (0.23%), respiratory (0.21%), and cardiovascular (0.23%) disease mortality in the all-age group, with similar findings in the older age group. The HEI Health Review Committee concluded that the ESCALA study results were broadly consistent with findings from similar coordinated multicity time-series studies of air

pollution and mortality in the United States, Canada, Europe, and Asia. The effect of PM_{10} on all-natural-cause, all-age mortality in ESCALA was also similar in magnitude to a result (0.61%) reported from a meta-analysis of 17 separate studies of Latin American cities by the Pan American Health Organization in 2005.

The HEI Health Review Committee thought that the meta-regression analyses, which were conducted to evaluate whether different city characteristics could explain differences in PM_{10} mortality in adults, were appropriate and well-done. However, it cautioned that conclusions identifying some city characteristics as "significant" predictors of the size of a city's PM–mortality coefficients should be considered suggestive rather than definitive. These few associations emerged from a large number of predictors considered and therefore might have arisen by chance. They also did not fit an obvious causative pattern. The Committee could not rule out the possibility that unidentified factors that could not be accounted for in the analyses might have affected the results in individual cities differently, thus causing spurious evidence of effect modification.

The investigators' evaluation of whether socioeconomic status could modify the adverse effects of PM_{10} and ozone on mortality was also well-conducted and an important facet of the study. The investigators reported patterns of higher risks of respiratory mortality among people with low socioeconomic status and higher risks of cardiovascular mortality among people with medium or high socioeconomic status, but these patterns were not consistently observed from city to city. Despite the ESCALA investigators' careful efforts, the Committee concluded that their analyses did not provide convincing evidence on this issue.

The HEI Health Review Committee concluded that the most robust estimates of the effect of air pollution on health were those for the larger cities, the larger age groups, and the causes of mortality with the larger number of deaths. For PM_{10}, this means greater confidence might be placed in the relative risks for all-natural-cause, all-age mortality (in particular for the Brazilian and Mexican cities) and for cardiovascular and cardiopulmonary mortality in the all-age and the ≥ 65 groups. For ozone, the more robust associations were also with all-natural-cause, all-age mortality and with cardiovascular and cardiopulmonary mortality in both the all-age and the ≥ 65 age groups. The high sensitivity of the main results to model choice for many of the other causes of death and age groups, particularly among children, suggests that caution should be exercised in their interpretation.

CONCLUSIONS

The ESCALA study is an important extension of coordinated multicity time-series methods to the study of the effects of ambient PM_{10} and ozone in a region of the world where these methods had not yet been applied — Latin America. The ESCALA investigators found small but significant effects of daily exposure to PM_{10} and ozone on daily mortality that were largely similar to those from other coordinated multi-city studies around the world. The relatively high degree of rigor used in carrying out ESCALA, with common protocols for data collection and analysis, and sensitivity analyses to test alternative model assumptions, should provide policymakers with reasonable assurance that the main findings of a relationship between air pollution and common types of mortality have a solid foundation and are the most reliable estimates for the region to date. Given the potential uncertainties associated with interpretation of specific results, caution should be exercised in the interpretation of the more complex patterns observed in these studies such as the patterns of results between cities, between socioeconomic status levels, and in the degree of effect modification by different covariates in the meta-regression analyses. The ESCALA investigators have established an important methodologic foundation for future work in Latin America. The ESCALA study could be readily expanded to include other cities in Latin America, used to explore alternative analytic methods, and improved upon by taking into account both the recommendations of the HEI Review Committee and the many insights gained by the investigators in the course of the study.

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