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Effects of Short-Term Exposure to Air Pollution on Hospital Admissions of Young Children for Acute Lower Respiratory Infections in Ho Chi Minh City, Vietnam

HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City
(Le Truong Giang, Long Ngo, Sumi Mehta, et al.)

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with a Critique by the HEI Health Review Committee

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ABOUT HEI

The Health Effects Institute is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the effects of air pollution on health. To accomplish its mission, the institute

- Identifies the highest-priority areas for health effects research;
- Competitively funds and oversees research projects;
- Provides intensive independent review of HEI-supported studies and related research;
- Integrates HEI's research results with those of other institutions into broader evaluations; and
- Communicates the results of HEI's research and analyses to public and private decision makers.

HEI receives its core funds for the Health Effects of Air Pollution program from the U.S. Environmental Protection Agency and the worldwide motor vehicle industry. Frequently, other public and private organizations in the United States and around the world support major projects and research programs. The study by the HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City was supported with funds from HEI's Public Health and Air Pollution in Asia (PAPA) Program, the Poverty Reduction Cooperation Fund of the Asian Development Bank (Technical Assistance 4714-VIE), and in-kind support from the government of Vietnam.

HEI has funded more than 280 research projects in North America, Europe, Asia, and Latin America, the results of which have informed decisions regarding carbon monoxide, air toxics, nitrogen oxides, diesel exhaust, ozone, particulate matter, and other pollutants. These results have appeared in the peer-reviewed literature and in more than 200 comprehensive reports published by HEI.

HEI's independent Board of Directors consists of leaders in science and policy who are committed to fostering the public–private partnership that is central to the organization. The Health Research Committee solicits input from HEI sponsors and other stakeholders and works with scientific staff to develop a Five-Year Strategic Plan, select research projects for funding, and oversee their conduct. The Health Review Committee, which has no role in selecting or overseeing studies, works with staff to evaluate and interpret the results of funded studies and related research.

All project results and accompanying comments by the Health Review Committee are widely disseminated through HEI's Web site (*www.healtheffects.org*), printed reports, newsletters and other publications, annual conferences, and presentations to legislative bodies and public agencies.

ABOUT THIS REPORT

Research Report 169, *Effects of Short-Term Exposure to Air Pollution on Hospital Admissions of Young Children for Acute Lower Respiratory Infections in Ho Chi Minh City, Vietnam,* presents a research project supported by HEI and others; it was conducted by the HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City. This report contains three main sections.

The HEI Statement, prepared by staff at HEI, is a brief, nontechnical summary of the study and its findings; it also briefly describes the Health Review Committee's comments on the study.

The Investigators' Report, prepared by the HEI Collaborative Working Group, describes the scientific background, aims, methods, results, and conclusions of the study.

The Critique is prepared by members of the Health Review Committee with the assistance of HEI staff; it places the study in a broader scientific context, points out its strengths and limitations, and discusses remaining uncertainties and implications of the study's findings for public health and future research.

This report has gone through HEI's rigorous review process. When an HEI-funded study is completed, the investigators submit a draft final report presenting the background and results of the study. This draft report is first examined by outside technical reviewers and a biostatistician. The report and the reviewers' comments are then evaluated by members of the Health Review Committee, an independent panel of distinguished scientists who have no involvement in selecting or overseeing HEI studies. During the review process, the investigators have an opportunity to exchange comments with the Review Committee and, as necessary, to revise their report. The Critique reflects the information provided in the final version of the report.

HEI STATEMENT

Synopsis of Research Report 169

Air Pollution and Ho Chi Minh City Pediatric Hospital Admissions for Acute Lower Respiratory Infections

BACKGROUND

In the past decade HEI has made a substantial commitment to furthering air pollution science in Asia by funding studies that provide science for decision making as they develop the abilities of local scientists to conduct research on air pollution and public health. This report describes a study by the HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City, Vietnam, that was financed by HEI, the Poverty Reduction Cooperation Fund of the Asian Development Bank, and in-kind support from the government of Vietnam. The study was led by Dr. Le Truong Giang of the Ho Chi Minh City Department of Public Health; Dr. Long Ngo, a biostatistician at Beth Israel Deaconess Medical Center in Boston, Massachusetts; and Dr. Sumi Mehta, who was at HEI during the study and currently is director of programs at the Global Alliance for Clean Cookstoves. It focused on associations between pediatric hospital admissions for acute lower respiratory infection (ALRI) and air pollution levels. This is the first study of health and air pollution conducted in Vietnam and one of the first studies in the region to focus on the important question of air pollution and children's health.

HEI directed this study under its Public Health and Air Pollution in Asia (PAPA) Program, which supports new science in understudied areas in the developing countries of Asia, in combination with technical capacity building for local investigators. The model for this study was also based on the Asian Development Bank's model of supporting collaborative research through technical-assistance grants. Capacity-building projects develop the abilities of new investigators and train local personnel to organize and conduct future studies. Such projects are designed to answer scientific questions that are relevant to regional decisions about air quality, health, and related issues. Although the studies are designed to be achievable within the constraints of data and technical capacity often found in developing countries, they are subject to the full peer-review procedures of HEI, which are intended to assess the quality and utility of the study.

The HEI International Scientific Oversight Committee (ISOC) reviewed the Collaborative Working Group's original proposal and provided technical expertise and oversight for this project. In typical HEI-funded studies, investigators identify and propose projects that are carried out with supervision by the HEI Health Research Committee and HEI staff. The Ho Chi Minh City projects involved deeper participation by ISOC and HEI staff in the design and conduct of the research.

ALRI, a disease category comprising bronchiolitis and pneumonia, is the chief cause of death among children under the age of 5 years worldwide. Pediatric ALRI cases in developing countries are often bacterial, and without antibiotic therapy they can progress rapidly, sometimes leading to death. Poverty is associated with the incidence of ALRI and with mortality from the disease; malnutrition is the primary risk factor for ALRI.

Although exposure to indoor air pollution from burning solid fuel has been shown to increase the risk of ALRI, the relationship of outdoor air pollution to ALRI has not been widely studied in the developing world. In the developed world, the U.S. Environmental Protection Agency has determined that there is some evidence that exposure to nitrogen dioxide (NO_2) reduces resistance to respiratory infection. The current study in Ho Chi Minh City attempted to explore relationships among outdoor air pollution, hospital admissions of young children with ALRI, and poverty in a developing Asian country.

This Statement, prepared by the Health Effects Institute, summarizes an HEI project conducted by the HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City. Research Report 169 contains both the detailed Investigators' Report and a Critique of the study prepared by the Institute's Health Review Committee.

APPROACH

The study focused on the short-term effects of daily average exposure to NO_2, particulate matter (PM) $\leq$ 10 μg/m^3 (PM_{10}), sulfur dioxide (SO_2), and ozone (O_3) in Ho Chi Minh City. Its specific aims were to assess the effects of such exposure on the hospitalization of young children for ALRI and to compare these effects in poor children with those in other children.

The investigators collected data on admissions for ALRI to Ho Chi Minh City's two major pediatric hospitals in 2003, 2004, and 2005. Their analysis focused on admissions of children who were between 28 days and 5 years of age and resided in an urban district. Because hospital staff did not always distinguish between bronchiolitis and pneumonia, the investigators created a single category for both diagnoses. ALRI cases were identified by the child's hospital identification (ID) number and by the case ID number, admission date, discharge date, and discharge diagnosis.

Air pollution data were obtained from four of the air quality monitoring stations that the Ho Chi Minh City Environmental Protection Agency operates with assistance from the Norwegian Institute for Air Research. These four stations, considered to monitor residential levels of air pollution, measured levels of NO_2, SO_2, and O_3 every 5 minutes and collected 24-hour filter samples for PM_{10}. The investigators then calculated mean daily levels for NO_2, SO_2, and PM_{10} and daily 8-hour maximum mean levels for O_3. Hourly weather data from a local forecasting center were used to calculate mean daily temperature and humidity and to track rainfall.

The investigators used both time-series and case–crossover analyses to search for statistical associations between ALRI cases and pollution levels. In the time-series analyses, they used Poisson regression to assess the impact of short-term changes in pollutant levels on ALRI admissions. The daily count of admissions was modeled as a function of average pollutant concentration and meteorologic conditions for the day of admission, for each of the preceding 10 days (lags 0–10), and over the range of days (lags 1–6) they considered to include the probable time of onset of ALRI. Variables for season, holidays, and long-term time trend were included, and natural spline smoothing functions were used for temperature, relative humidity, and day, and fixed effects for weekdays and holidays.

In the case–crossover analyses the investigators linked each ALRI case to average pollutant levels for the date of admission, for individual lag days, and for the range of lags 1–6. To calculate the excess risk of ALRI associated with these pollutant levels, they compared levels on the specific lag day or the average of lags 1–6 with the mean daily pollutant levels recorded every 7th day before and after, and within the same month as, the admission date — times that would not be associated with disease onset.

Financial information from patients' hospital records was used to assign an individual-level indicator of socioeconomic position. The poverty rate for each child's district of residence, based on 2004 district estimates from a poverty mapping project by the Institute of Economic Research in HCMC, the General Statistics Office of Vietnam, and the World Bank, was used to assign a district-level indicator. The investigators explored the potential role of socioeconomic position as a modifier of the effects of pollution in separate time-series and case–crossover models using the individual-level and district-level data. They created four quartiles of socioeconomic position using the district-level data and performed analyses stratified by quartile and by season.

RESULTS AND INTERPRETATIONS

For PM_{10}, ALRI admissions were found to increase with increases of 10 μg/m^3 in pollutant levels in the case–crossover analyses, but not in the time-series analyses. In contrast, during the rainy season, increases in PM_{10} levels appeared to be associated with reduced ALRI hospitalization in both types of analyses. Full-year results were consistent with those of studies of childhood respiratory morbidity and PM_{10} from other countries.

Levels of NO_2 demonstrated the most consistent relationships to hospital admissions for ALRI, and the results were broadly consistent with results from studies of respiratory morbidity from other countries. The excess risks of hospitalization associated with an increase of 10 μg/m^3 in NO_2 concentration were significant and equivalent in magnitude for lag days 2 and 3 and in both types of analyses. Except for lag day 3, these associations were also found in the overall time-series analyses (in which rainy and dry season data were combined). In the rainy season NO_2, like PM_{10}, showed a negative association with ALRI hospitalization for some lag periods, but only in the case–crossover analyses.

ALRI admissions were not associated with increased SO_2, except for two significant findings of excess risk with a 10-μg/m^3 increase in SO_2 concentration for specific lag periods in the dry season case–crossover analysis and the overall time-series analysis. As with the other pollutants, SO_2 had significant negative associations with ALRI admissions in the rainy season case–crossover analyses.

A 10-μg/m^3 increase in the level of O_3 had no significant positive associations with the risk of ALRI admissions in any analysis, but multiple significant negative associations in the rainy season case–crossover and time-series analyses and the overall time-series analyses were found.

In two-pollutant analyses the investigators found significant excess risks of ALRI hospitalization with a 10-μg/m^3 increase in NO_2 concentration in the dry season when they controlled for SO_2, O_3, and PM_{10} levels in time-series analyses and for SO_2 and O_3 levels in case–crossover analyses. Significant excess risks were associated with a 10-μg/m^3 increase in SO_2 when the overall time-series and dry season case–crossover analyses were adjusted for PM_{10} and O_3, but not when they were adjusted for NO_2.

To investigate the confusing disparity between rainy season and dry season results, the investigators conducted a simulation using the hypothetical prevalence of respiratory syncytial virus (RSV) infection, based on known seasonal patterns, as a possible confounding variable in the PM_{10} analysis. RSV is an independent, viral cause of ALRI. Its incidence peaks during the rainy season, when air pollution levels are low in Vietnam. This simulation analysis demonstrated that the study's results for the rainy season may well have been confounded by hospital admissions due to RSV infection.

The investigators' attempts to analyze the data when stratified by an individual-level indicator of poverty were inconclusive, owing to the small proportion (1%) of patients identified as being poor. When they used the district-level indicator of poverty, they found an elevated risk of ALRI associated with 10-μg/m^3 increases in NO_2 and SO_2 levels in the dry season for patients who lived in the wealthiest districts.

CONCLUSIONS

This study of air pollution and children's health in Vietnam provides interesting information on associations between individual pollutants and hospital admissions for ALRI. Overall, the data were sound, and the study was well conducted. The associations between NO_2 concentration and hospital admissions for ALRI during the dry season, in particular, suggest a potential role of pollution exposure in the development of ALRI. Further work is needed to verify these findings in developing countries.

The lack of information recorded in individual hospital records made it difficult to study the role of socioeconomic position in ALRI hospitalization. The small number of patients identified as poor was inconsistent with the known poverty rate in Ho Chi Minh City, and the reliability of the results was not much improved by using district-level data. Furthermore, strongly seasonal and unmeasured confounding variables possibly produced some contradictory results. These difficulties underscore the need for capacity-building initiatives in developing countries, since investigators' familiarity with the environments that they study increases the likelihood that they will be able to design studies that consider local disease trends, social factors, and environmental conditions.

INVESTIGATORS' REPORT

Effects of Short-Term Exposure to Air Pollution on Hospital Admissions of Young Children for Acute Lower Respiratory Infections in Ho Chi Minh City, Vietnam

HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City (Le Truong Giang, Long Ngo, Sumi Mehta, et al.)

ABSTRACT

There is emerging evidence, largely from studies in Europe and North America, that economic deprivation increases the magnitude of morbidity and mortality related to air pollution. Two major reasons why this may be true are that the poor experience higher levels of exposure to air pollution, and they are more vulnerable to its effects — in other words, due to poorer nutrition, less access to medical care, and other factors, they experience more health impact per unit of exposure. The relations among health, air pollution, and poverty are likely to have important implications for public health and social policy, especially in areas such as the developing countries of Asia where air pollution levels are high and many live in poverty. The aims of this study were to estimate the effect of exposure to air pollution on hospital admissions of young children for acute lower respiratory infection (ALRI*) and to explore whether such effects differed between poor children and other children. ALRI, which comprises pneumonia and bronchiolitis, is the largest single cause of mortality among young children worldwide and is responsible for a substantial burden of disease among young children in developing countries. To the best of our knowledge, this is the first study of the health effects of air pollution in Ho Chi Minh City (HCMC), Vietnam. For these reasons, the results of this study have the potential to make an important contribution to the growing literature on the health effects of air pollution in Asia.

The study focused on the short-term effects of daily average exposure to air pollutants on hospital admissions of children less than 5 years of age for ALRI, defined as pneumonia or bronchiolitis, in HCMC during 2003, 2004, and 2005. Admissions data were obtained from computerized records of Children's Hospital 1 and Children's Hospital 2 (CH1 and CH2) in HCMC. Nearly all children hospitalized for respiratory illnesses in the city are admitted to one of these two pediatric hospitals. Daily citywide 24-hour average concentrations of particulate matter (PM) $\leq$10 μm in aerodynamic diameter (PM_{10}), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) and 8-hour maximum average concentrations of ozone (O_3) were estimated from the HCMC Environmental Protection Agency (HEPA) ambient air quality monitoring network. Daily meteorologic information including temperature and relative humidity were collected from KTTV NB, the Southern Regional Hydro-Meteorological Center.

An individual-level indicator of socioeconomic position (SEP) was based on the degree to which the patient was exempt from payment according to hospital financial records. A group-level indicator of SEP was based on estimates of poverty prevalence in the districts of HCMC in 2004, obtained from a poverty mapping project of the Institute of Economic Research in HCMC, in collaboration with the General Statistics Office of Vietnam and the World Bank. Poverty prevalence was defined using the poverty line set

This Investigators' Report is one part of Health Effects Institute Research Report 169, which also includes a Critique by the Health Review Committee and an HEI Statement about the research project. Correspondence concerning the Investigators' Report may be addressed to Dr. Long Ngo, Harvard Medical School, Department of Medicine, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Room 130, Boston, MA 02215; *lngo@bidmc.harvard.edu*. For information on the members of the Collaborative Working Group and their institutions, see "About the Authors" at the end of this Investigators' Report (p. 71).

The study by the HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City was supported with funds from HEI's Public Health and Air Pollution in Asia (PAPA) Program, the Poverty Reduction Cooperation Fund of the Asian Development Bank (Technical Assistance 4714-VIE), and in-kind support from the government of Vietnam. The contents of this document have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties and no endorsement by them should be inferred.

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

by the People's Committee of HCMC of 6 million Vietnamese dong (VND) annual income. Quartiles of district-level poverty prevalence were created based on poverty prevalence estimates for each district.

Analyses were conducted using both time-series and case–crossover approaches. In the absence of measurement error, confounding, and other sources of bias, the two approaches were expected to provide estimates that differed only with regard to precision. For the time-series analyses, the unit of observation was daily counts of hospital admissions for ALRI. Poisson regression with smoothing functions for meteorologic variables and variables for seasonal and long-term trends was used. Case–crossover analyses were conducted using time-stratified selection of controls. Control days were every 7th day from the date of admission within the same month as admission.

Large seasonal differences were observed in pollutant levels and hospital admission patterns during the investigation period for HCMC. Of the 15,717 ALRI admissions occurring within the study period, 60% occurred in the rainy season (May through October), with a peak in these admissions during July and August of each year. Average daily concentrations for PM_{10}, O_3, NO_2, and SO_2 were 73, 75, 22, and 22 $\mu g/m^3$, respectively, with higher pollutant concentrations observed in the dry season (November through April) compared with the rainy season.

As the time between onset of illness and hospital admission was thought to range from 1 to 6 days, it was not possible to specify a priori a single-day lag. We assessed results for single-day lags from lag 0 to lag 10, but emphasize results for an average of lag 1–6, since this best reflects the case reference period. Results were robust to differences in temperature lags with lag 0 and the average lag (1–6 days); results for lag 0 for temperature are presented.

Results differed markedly when analyses were stratified by season, rather than simply adjusted for season. ALRI admissions were generally positively associated with ambient levels of PM_{10}, NO_2, and SO_2 during the dry season (November–April), but not the rainy season (May–October). Positive associations between O_3 and ALRI admissions were not observed in either season. We do not believe that exposure to air pollution could reduce the risk of ALRI in the rainy season and infer that these results could be driven by residual confounding present within the rainy season. The much lower correlation between NO_2 and PM_{10} levels during the rainy season provides further evidence that these pollutants may not be accurate indicators of exposure to air pollution from combustion processes in the rainy season.

Results were generally consistent across time-series and case–crossover analyses. In the dry season, risks for ALRI hospital admissions with average pollutant lag (1–6 days) were highest for NO_2 and SO_2 in the single-pollutant case–crossover analyses, with excess risks of 8.50% (95% CI, 0.80–16.79) and 5.85% (95% CI, 0.44–11.55) observed, respectively. NO_2 and SO_2 effects remained higher than PM_{10} effects in both the single-pollutant and two-pollutant models. The two-pollutant model indicated that NO_2 confounded the PM_{10} and SO_2 effects. For example, PM_{10} was weakly associated with an excess risk in the dry season of 1.25% (95% CI, −0.55 to 3.09); after adjusting for SO_2 and O_3, the risk estimate was reduced but remained elevated, with much wider confidence intervals; after adjusting for NO_2, an excess risk was no longer observed. Though the effects seem to be driven by NO_2, the statistical limitations of adequately addressing collinearity, given the high correlation between PM_{10} and NO_2 ($r = 0.78$), limited our ability to clearly distinguish between PM_{10} and NO_2 effects.

In the rainy season, negative associations between PM_{10} and ALRI admissions were observed. No association with O_3 was observed in the single-pollutant model, but O_3 exposure was negatively associated with ALRI admissions in the two-pollutant model. There was little evidence of an association between NO_2 and ALRI admissions. The single-pollutant estimate from the case–crossover analysis suggested a negative association between NO_2 and ALRI admissions, but this effect was no longer apparent after adjustment for other pollutants. Although associations between SO_2 and ALRI admissions were not observed in the rainy season, point estimates for the case–crossover analyses suggested negative associations, while time-series (Poisson regression) analyses suggested positive associations — an exception to the general consistency between case–crossover and time-series results.

Results were robust to differences in seasonal classification. Inclusion of rainfall as a continuous variable and the seasonal reclassification of selected series of data did not influence results. No clear evidence of station-specific effects could be observed, since results for the different monitoring stations had overlapping confidence intervals.

In the dry season, increased concentrations of NO_2 and SO_2 were associated with increased hospital admissions of young children for ALRI in HCMC. PM_{10} could also be associated with increased hospital admissions in the dry season, but the high correlation of 0.78 between PM_{10} and NO_2 levels limits our ability to distinguish between PM_{10} and NO_2 effects. Nevertheless, the results support the presence of an association between combustion-source pollution and increased ALRI admissions. There also appears to be evidence of uncontrolled negative confounding within the rainy season, with higher incidence of ALRI and lower pollutant concentrations overall.

Exploratory analyses made using limited historical and regional data on monthly prevalence of respiratory syncytial virus (RSV) suggest that an unmeasured, time-varying confounder (RSV, in this case) could have, in an observational study like this one, created enough bias to reverse the observed effect estimates of pollutants in the rainy season. In addition, with virtually no RSV incidence in the dry season, these findings also lend some credibility to the notion that RSV could influence results primarily in the rainy season.

Analyses were not able to identify differential effects by individual-level indicators of SEP, mainly due to the small number of children classified as poor based on information in the hospitals' financial records. Analyses assessing differences in effect by district-level indicator of SEP did not indicate a clear trend in risk across SEP quartiles, but there did appear to be a slightly higher risk among the residents of districts with the highest quartile of SEP. As these are the districts within the urban center of HCMC, results could be indicative of increased exposures for residents living within the city center. It remains possible that poorer children systematically experience higher exposures to air pollution per unit of reported air quality on any given day compared with other children, regardless of district of residence. Since in these analyses a single daily measurement of pollution was assigned to all children for a particular day, however, we were not able to estimate daily differences in individual exposures across districts or socioeconomic groups.

INTRODUCTION

A growing body of epidemiologic evidence shows that exposure to particles generated by emissions from diverse sources results in significant adverse health effects in urban populations (Cohen et al. 2004). Children that live close to heavily trafficked roads have been shown to experience more adverse respiratory episodes than children that live farther away (Kim et al. 2008). In addition, in vitro and in vivo toxicologic studies have shown that exposure to particles from traffic emissions results in inflammatory responses (HEI Panel on the Health Effects of Traffic-Related Air Pollution 2010).

In Asia, however, the composition of the emitted particles differs considerably from that in North America and Europe, where the majority of studies on the health effects of air pollution have been performed. Vehicle fleets in Asia are dominated by two- and three-wheeled vehicles, and automobiles and trucks are significantly older or use old technology (Han et al. 2005). In addition, a number of local sources that contribute to exposures in Asia are not present in North America and Europe. A significant fraction of households and roadside vendor stalls rely on solid fuels for cooking and heating, trash is frequently burned in the street, and a large percentage of the population continues to use tobacco products in the home (HEI International Scientific Oversight Committee 2004).

With a large proportion of the world's population living in highly polluted areas of Asian cities, the effects of air pollution on health in these areas have significant public health impact and highly relevant policy implications. Although a systematic review revealed 421 studies on the health effects of air pollution in Asia (Health Effects Institute 2006), to date no studies have been conducted in many of the poorer Southeast Asian countries such as Laos, Cambodia, and Vietnam. The ability to conduct such studies is currently compromised by the relative lack of reliable and easily accessible data on health outcomes, routinely collected air quality data, and collaboration between the health and environmental sectors in the region.

AIR POLLUTION AND ALRI

Background

The capacity for combustion-derived air pollution to affect resistance to infection is well documented (Thomas and Zelikoff 1999). More recent studies suggest a role for fine particles (PM $\leq$ 2.5 μm [$PM_{2.5}$]) (Zelikoff et al. 2003). Effects on airway resistance, epithelial permeability, and macrophage function have been associated with a variety of components in the complex mixture of air pollution generated by indoor and outdoor sources. There has also been considerable interest in the role of particle-associated transition metals, including iron, in producing oxidative stress in the lung (Ghio 2004; Ghio and Cohen 2005), which has been hypothesized to be a common factor in a range of adverse effects of air pollution on the cardiovascular and respiratory systems (Kelly 2003). PM-associated transition metals have also been associated with altered host defenses in rats (Zelikoff et al. 2002).

ALRIs, including pneumonia, bronchitis, and bronchiolitis, are the largest single cause of mortality among young children worldwide, and thus account for a significant global burden of disease (Williams et al. 2002; World Health Organization 2004). These infections have been estimated to cause nearly one-fifth of mortality in children under the age of 5 years, with 90% of deaths from ALRI being directly attributable to pneumonia (World Health Organization 2004). A substantial fraction of the burden is experienced by populations in Asia and Africa. The annual incidence of lower respiratory infections for all ages is

134 million in Asia and 131 million in Africa; the overall global annual total is 429.2 million cases. In Vietnam more than 33,000 ALRI deaths occur each year (World Health Organization 2004).

Recent reviews of the epidemiologic literature reveal a consistent association between ALRI in young children and exposure to air pollution from indoor and outdoor sources. Fourteen studies in developing countries have associated exposure to air pollution from indoor combustion of solid fuels with increased risk and incidence of mortality (Smith et al. 2004). A meta-analysis found that young children exposed to indoor air pollution resulting from household use of unprocessed solid fuel had a 1.8 (95% CI, 1.5–2.2) times greater risk of pneumonia than unexposed children (Dherani et al. 2008). Two of these studies attempted to measure the levels of air pollution (Ezzati and Kammen 2001; Ezzati 2005), but the majority of these studies relied on qualitative indicators of indoor air pollution.

In developing countries outdoor air pollution is also associated with increased ALRI mortality, symptoms, hospital admissions, and visits to emergency departments (Romieu et al. 2002). In developed countries, where pollution concentrations are lower, pneumonia-related mortality and hospital admissions have also been linked to exposure to outdoor air pollution (Zanobetti et al. 2000; Braga et al. 2001). The confounding and modifying roles of host, environmental, and social factors have not, however, been extensively assessed. In addition, the epidemiologic studies have not, for the most part, been conducted in the regions that are most affected. Of the 42 studies reviewed by Smith et al. (2004) and Romieu et al. (2002), only 3 were conducted in developing countries of Asia, although the highest exposures and the greatest burden of disease due to indoor and outdoor air pollution are borne by the populations in these regions (Cohen et al. 2004; HEI International Scientific Oversight Committee 2004; Smith et al. 2004).

In summary, although outdoor air pollution has been associated with increased ALRI morbidity and mortality, very few studies have been conducted in developing countries of Asia, where populations are exposed to much higher levels of air pollution and experience the greatest burden of disease due to ALRI. As such, the results of this study have the potential to make an important contribution to the growing literature on the health effects of air pollution in Asia.

Evidence from Short-Term Studies

A systematic review of the literature identified six time-series or case–crossover studies that investigated the association between short-term exposure to ambient PM and ALRI morbidity in young children. Two of these studies were conducted in Brazil (Gouveia and Fletcher 2000; Braga et al. 2001). The others were conducted in Mexico (Hernández-Cadena et al. 2007), the United States (Karr et al. 2006), Australia (Barnett et al. 2005), and France (Segala et al. 2008). The time-series studies found increased risks of hospital admissions or emergency department visits for ALRI associated with increased PM_{10} concentrations, with stronger effects observed among the younger age groups (Gouveia and Fletcher 2000; Braga et al. 2001; Hernández-Cadena et al. 2007). These studies were conducted at annual average PM_{10} concentrations ranging from 39 to 67 μg/m^3. With every increase of 35 μg/m^3 (interquartile range) in PM_{10} exposure, Braga et al. (2001) observed a 9% increase in respiratory admissions (relative risk [RR], 1.09; 95% CI, 1.08–1.11) for children under 3, and a 3% increase (RR, 1.03; 95% CI, 1.00–1.06) for children ages 3 to 5. Gouveia and Fletcher (2000) identified a 9% higher risk of infant pneumonia (RR, 1.09; 95% CI, 1.01–1.18) and a somewhat lower 5% risk among the group under 5 years of age as a whole, which was not statistically significant (RR, 1.05; 95% CI, 0.98–1.12), for every 98.1-μg/m^3 increase (from 10th to 90th percentile) in ambient PM_{10}. Hernández-Cadena et al. (2007) found a slightly increased risk in Mexican infants and children below age 6 associated with a 20.0-μg/m^3 increase (interquartile range) in PM_{10} exposure, although this risk was not statistically significant (RR, 1.01; 95% CI, 0.98–1.06).

Although the published evidence from case–crossover studies of young children is more limited than the evidence from time-series studies, case–crossover studies in the United States, France, Australia, and New Zealand have found a positive association between PM exposure and ALRI admissions among children below 5 years of age (Barnett et al. 2005; Karr et al. 2006; Segala et al. 2008) at lower annual average pollutant concentrations, ranging from 11 to 23 μg/m^3 for PM_{10} and 9 to 24 μg/m^3 for $PM_{2.5}$.

Two studies on PM_{10} and respiratory mortality also showed a positive association between ALRI and PM_{10} (Conceição et al. 2001; Ha et al. 2003). Ha et al. (2003) observed a 14% greater risk of respiratory mortality in Korean infants (RR, 1.14; 95% CI, 1.10–1.19) for each 42.9-μg/m^3 increase (interquartile range) in PM_{10} exposure. Conceição et al. (2001) found a significant but smaller association between per-unit increases in PM_{10} exposure and mortality in Brazilian children below age 5. Another study conducted in Brazil (Saldiva et al. 1994), however, did not find an association between PM_{10} and respiratory mortality in children under 5 years of age, but observed strong effects associated with nitrogen oxide exposure.

Studies on pollution and ALRI have also explored the potential for effect modification by season, with the strongest effects generally observed in the winter, but the definition of season used has varied from study to study (Gouveia and Fletcher 2000; Barnett et al. 2005; Karr et al. 2006; Hernández-Cadena et al. 2007).

AIR POLLUTION, POVERTY, AND HEALTH

There is emerging evidence, largely from studies in Europe and North America, that economic deprivation increases the magnitude of morbidity and mortality resulting from air pollution (Krewski et al. 2000). There are two major reasons why this may be true (O'Neill et al. 2003): one is that the poor experience higher levels of exposure to air pollution; the other is that the poor, owing to poorer nutrition, less access to medical care, and other factors, are more vulnerable to air pollution — that is, they experience more health impact per unit of exposure. Effect modification by group characteristics, such as living in slums (Gouveia et al. 2004) or highly polluted areas (Jerrett et al. 2004), has also been observed. Yet, because of the challenges of explaining observed group-level effects, studies have continued to use individual estimates of exposure and SEP. Previous studies using individual characteristics to assess effect modification by SEP suggest that low levels of educational attainment (Krewski et al. 2000; Gouveia et al. 2004; Jerrett et al. 2004) and family income (Gouveia et al. 2004) are associated with increased health effects related to air pollution. Evidence that group-level indicators such as residence in a poor neighborhood could be a risk factor above and beyond the SEP of an individual (Malmström et al. 2001) underscores the importance of using hierarchical models that integrate individual and group-level indicators of SEP.

Relations among health, air pollution, and poverty are likely to have important implications for public health and social policy, especially in areas where air pollution levels are high and many live in poverty. However, few studies of the interaction between poverty and the health effects of air pollution have been conducted in developing countries in general, or in Asia in particular. In developing areas the sources of exposure are likely to be very different, and the impacts of exposure — and the influence of economic deprivation on those impacts — may be greater. Therefore, results from Western studies can only be extrapolated to other areas with considerable uncertainty (Cohen et al. 2004).

If poor children are more susceptible to air pollution, or experience higher exposures, or both, then poverty could act as an effect modifier. If higher risks were observed among the poor in HCMC, it would suggest that poverty is modifying the effect of air pollution on health through one or more risk factors that increase susceptibility among the poor. Differential effects at a given level of exposure could reflect differential susceptibility among poor children mediated via mechanisms involving nutritional deficiencies, differences in access to or quality of medical care, or other biosocial factors.

STUDY LOCATION

HCMC, formerly known as Saigon, is the largest city in Vietnam and home to over 6 million people. Located northeast of the Mekong River, it occupies 910 square miles of flat land along the Saigon River and is bordered by Cambodia on the west and the South China Sea on the east. HCMC is a major industrial and commercial center of the country. The city has hot and humid weather year round, with the mean temperature averaging between 23°C and 32°C. There are two seasons in HCMC, a dry season from November through April and a rainy season from May through October. The urban area of HCMC, occupying only about 10% of the total land in the city, is divided into 19 districts where most people in the city live (Table 1). Figure 1 shows a map of the districts. Note that the urban districts cluster in the middle and the rural districts are farther outside the city's center.

The Vietnamese economic reforms of 1989 transformed the city into a magnet for foreign investments and tourism. Currently, more than 1000 large-scale enterprises and over 30,000 small factories operate in the city. Rapid economic development has also brought more migrants to the city, contributing to traffic congestion and urban crowding. With daily average PM_{10} levels routinely ranging from 30 to 150 μg/m^3 and higher, HCMC provides a unique opportunity to evaluate the health effects of short-term changes in air pollution across a wide range of the exposure–response curve.

Major Air Pollution Sources in HCMC

Transport HCMC has the largest vehicle fleet of any city in Vietnam, and the number of motor vehicles is rapidly increasing. On average, 1000 new vehicles are registered every day in HCMC (Viet Nam Register 2002). In October 2002, there were 2,225,000 motorcycles and 189,000 cars, trucks, and buses officially registered in HCMC. Many of the trucks and buses are old and use obsolete technology; the majority of the motorcycles, cars, and vans are relatively new, but tend to use old technology and have no pollution control devices. The vast majority of transportation demand is met by two-wheeled vehicles — motorbikes or motorcycles (56%) and bicycles (30%). The remainder is met by public buses (3%), cars (3%), and pedestrian travel

Table 1. HCMC Area, Population, and Population Density, by District, 2004[a]

District	Number of Wards /Communes	Area (km^2)	Population	Population Density (People/km^2)
All Districts	317	2095.01	6,062,993	2,894
Urban Districts				
District 1	10	7.73	199,247	25,776
District 2	11	49.74	123,968	2,492
District 3	14	4.92	201,425	40,940
District 4	15	4.18	182,493	43,659
District 5	15	4.27	171,966	40,273
District 6	14	7.19	241,902	33,644
District 7	10	35.69	156,895	4,396
District 8	16	19.18	359,194	18,728
District 9	13	114.00	199,150	1,747
District 10	15	5.72	235,442	41,161
District 11	16	5.14	229,837	44,715
District 12	10	52.78	282,864	5,359
Go Vap	12	19.74	443,419	22,463
Tan Binh	15	22.38	392,521	17,539
Tan Phu	11	16.06	361,747	22,525
Binh Thanh	20	20.76	422,875	20,370
Phu Nhuan	15	4.88	175,668	35,998
Thu Duc	12	47.76	329,231	6,893
Binh Tan	10	51.89	384,889	7,417
Rural Districts				
Cu Chi	21	434.5	287,807	662
Hoc Mon	12	109.18	243,462	2,230
Binh Chanh	16	252.69	298,623	1,182
Nha Be	7	100.41	72,271	720
Can Gio	7	704.22	66,097	94

[a] Source: Statistical Office of Ho Chi Minh City 2004.

(8%) (Viet Nam Register 2002). Transportation infrastructure is poor, the density of the roadway system is relatively low at 0.81 km/km^2, and the average traffic speed is only 4 to 5 km/hr. Use of clean liquid propane gas/compressed natural gas or alternative fuel for vehicles in HCMC is mostly limited to some pilot projects.

Energy HCMC accounts for 25% of the total electricity consumption of Vietnam. The city used 12 billion kilowatt-hours (kWh) in 2005, and the annual demand was projected to be 23 billion kWh by 2010. The climate greatly influences power usage. For example, power consumption increased by 20% when HCMC suffered extreme high temperatures in the first quarter of 2003 (Power Engineering International 2003).

Industry As one of Vietnam's largest economic and industrial centers, HCMC contributed approximately 17% of the national gross domestic product (GDP) in 2001 (Le 2003). In 2001, HCMC had 28,573 industrial establishments, of which 128 were centrally state-owned enterprises, 152 locally state-owned enterprises, 27,901 private enterprises, and 390 industrial joint ventures involving foreign investment. Most of the industries are small-scale operations, located mainly within residential areas, and related to the production of rice, coffee, seafood, beverages, tobacco, textiles, paper, chemical products, rubber, plastic, and building materials (Statistical Office of Ho Chi Minh City 2001).

Air quality in HCMC has become a serious problem as a result of industrial emissions. Only a small number of industries use the best available technologies, while most

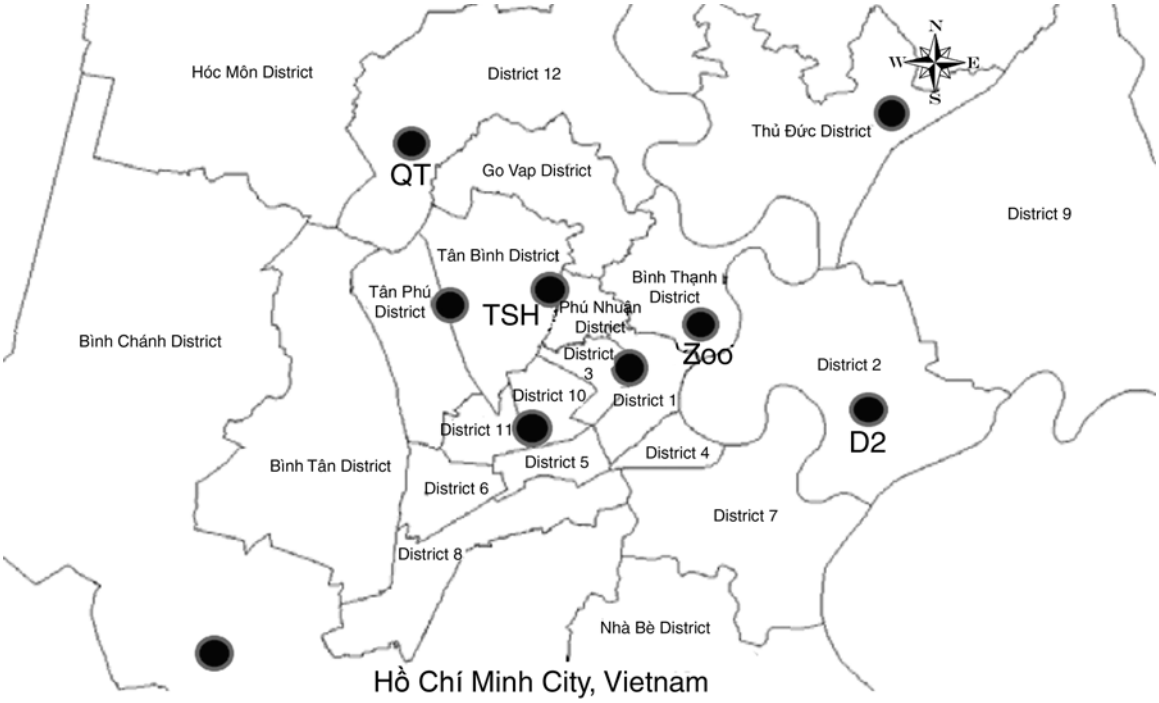

Figure 1. Districts of HCMC. Circles show the nine air quality monitoring stations. The four stations from which data were obtained for this study are labeled: QT (Quang Trung), TSH (Tan Son Hoa), D2 (District 2), and Zoo.

still use older technologies. The lack of investment in environmental protection compounds the problem (Do 2003). To strike a balance between economic and environmental concerns, the city implemented a program to identify polluting industries or plants for relocation, plan relocation zones, and adopt policies and measures to facilitate relocation of these industries (Do 2003).

Localized Sources In addition to neighborhood industries, other key local sources of air pollution include smoking, the use of solid fuels such as wood and coal for cooking (in residences as well as at roadside food stalls), and incense burning for ancestral shrines. Localized sources of pollution are likely to be well correlated with household exposures, because houses are generally well ventilated and open to the outdoor environment. Very few households use air conditioning; in a survey of over 1000 households, only 11% reported the use of air conditioning (HEI Collaborative Working Group on Air Pollution, Poverty, and Health in HCMC, unpublished data).

Poverty in HCMC

Poverty reduction has been a high priority for the government of Vietnam since the mid-1980s, when 75% of the population lived in poverty. At the beginning of the 1990s, after *doi moi* ("reform") was implemented, the country's economy improved quickly, resulting in impressive poverty reduction. From 1990 to 2001, the annual GDP growth rate ranged from 5.1% to 9.5%, exports went from $2.4 billion to $15 billion, imports went from $2.8 billion to $16.2 billion, and annual GDP per capita went from $98 to $404. HCMC's poverty rate went from 33% in 1993 to 8% in 1998 (General Statistics Office of Vietnam 2004). Although the level of poverty has been reduced, the inequality gap between the rich and the poor is thought to be widening.

To the extent that the government's economic reform has been successful, it may have mitigated some of the problems that confer increased susceptibility to the effects of air pollution on the poor (e.g., starting in June 2005, all children under 6 years of age became eligible to receive free medical care). Wealth is currently more equitably distributed in HCMC than in many other cities with similar development profiles. Correspondingly, inequity from risk factors such as lack of clean water and sanitation or limited access to health care is less of a problem in HCMC.

Unlike many other large cities in Asia, HCMC has relatively little residential segregation by SEP, with district-level poverty prevalence ranging from 4.5% to 12.3% (HCMC Bureau of Statistics 2005). Government relocation projects have cleared nearly all of the slums, or shantytowns, previously located along the Mekong River or its canals. Wide swaths of empty ground strewn with rubble

can be observed beside some of the canals where shantytowns previously stood. More often, however, the relocation projects have already renewed the land, and pleasant green spaces now line most of the city's canals.

SPECIFIC AIMS

The first objective of this study was to assess whether increases in exposure to air pollution in the short term (on the order of days) were associated with increased hospitalizations for ALRI among children under 5 years of age in HCMC from 2003 through 2005. Admissions for ALRI, specifically pneumonia and bronchiolitis, were extracted from computerized records of the two pediatric hospitals in HCMC. Daily city-level exposures to PM_{10}, O_3, NO_2, and SO_2 were estimated using data from the HEPA ambient air quality monitoring network. Daily meteorologic information, including temperature and relative humidity, was collected from KTTV NB, the Southern Regional Hydro-Meteorological Center.

The second objective was to compare the effect of air pollution on poor children versus other children using individual and group-level indicators of SEP. The individual-level indicator of SEP was based on the degree of payment exemption according to hospital financial records. Estimates of poverty prevalence for the 19 districts in 2004, determined from a collaborative project of the Institute of Economic Research in HCMC, the General Statistics Office of Vietnam, and the World Bank to map poverty in HCMC, were used as group-level indicators of SEP.

METHODS

PATIENT POPULATION

This study was approved by the institutional review board of the Biological and Medical Ethical Committee of HCMC Department of Public Health (Decision 2751/SYT-NVY). We focused the study on the children of HCMC under the age of 5. Nearly all children admitted for respiratory illnesses in HCMC are hospitalized in one of the two pediatric hospitals. Thus, by involving both pediatric hospitals in the study, we captured nearly all children's admissions for respiratory illness in HCMC.

CH1, a 900-bed hospital located in District 10, had 1,071,756 outpatient visits and 48,854 admissions in 2004. CH2, an 800-bed hospital located in District 1, had 587,718 outpatient visits and 54,629 hospital admissions in 2004 (Table 2). Diseases of the respiratory system are among the leading causes of inpatient admissions in both hospitals (Tables 3 and 4).

Figure 2 illustrates the different pathways by which a child can be admitted to one of the pediatric hospitals. Through visits to primary health clinics, study staff confirmed that these clinics refer all children requiring hospitalization to the pediatric hospitals. In addition, private clinics and private medical practices treating children (often staffed by physicians from the pediatric hospitals) also refer patients to the pediatric hospitals for admission. The extent to which the Integrated Management of Childhood Illness (IMCI) guidelines of the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) are used to inform patient referral to the hospital is unclear. Once patients present to the pediatric hospitals, however, IMCI guidelines are followed to determine their diagnosis.

CH1 is the primary referral center for children in Southern Vietnam, but children in HCMC can visit either CH1 or CH2. The primary health clinics in the city refer patients to the closest hospital, but in reality there are very few patient transfers from the district clinics. In other words, the majority of the cases are resolved at the ward or district health clinic or by a private doctor (point B or C in Figure 2), and the child does not end up at one of the pediatric hospitals (point D). For example, the primary health clinic in District 10 only transferred seven patients to CH1 in 2003, five in 2004, and two in 2005. This suggests that the patients with the most severe respiratory illness — namely, those who require hospital care — are referred directly to the pediatric hospitals. The only exception seems to be children with tuberculosis, who are referred to the respiratory hospital, rather than a pediatric hospital.

Other than severity of illness, we have not been able to identify any major factors that could affect the likelihood of a child's admission.

Despite increasing numbers of beds over the study period, both CH1 and CH2 routinely operated at or beyond capacity (Table 5). These hospitals adhere to the IMCI guidelines for the management of ALRI when determining the need for admission. Clinicians have reassured the investigative team that the availability of hospital beds does not affect admissions for ALRI; when necessary, multiple patients share the same hospital bed.

As ability to pay is determined after admission, family financial status does not influence admission. Occasionally, children who live in a remote province (outside HCMC) may be admitted using less-stringent criteria because of the hardship that traveling back and forth presents to their families. Because we focused only on HCMC residents, this did not affect our study.

Respiratory Outcome Data

Ideally, we would have liked to collect information on ALRI incidence, but only daily aggregate information on outpatient visits was available, so we focused the analysis on hospital admissions. Using incidence of hospital admissions allowed us to identify ALRI cases severe enough to warrant hospitalization, but also limited our ability to ascertain the precise time of clinically relevant disease onset.

Both pediatric hospitals have had computerized record systems for individual hospital admissions for many years. CH1, for example, has had a computerized system for maintaining diagnostic, treatment, and financial records since 1995. Before this study, both hospitals had completed a cooperative study with UNICEF on data abstraction and disease trends from 1995 to 2004 (Children's Hospital 1 and 2 2004), thus demonstrating their ability to manage, extract, and tabulate data from their computerized record systems.

Criteria for ALRI Diagnosis and Hospital Admission

WHO and UNICEF launched the IMCI initiative in 1995 to address five leading causes of childhood deaths in the world: pneumonia, diarrhea, measles, malaria, and malnutrition. The initiative has three main components: improvements in the case-management skills of health care staff; improvements in health care systems; and improvements in

Table 2. Outpatient Visits and Hospital Admissions to HCMC Children's Hospitals, 2000–2004[a]

	Children's Hospital 1			Children's Hospital 2		
		Admissions			Admissions	
Year	Outpatient Visits	*N*	% of Visits	Outpatient Visits	*N*	% of Visits
2000	722,216	40,843	5.7	332,189	41,405	12.5
2001	805,060	41,546	5.2	401,735	42,483	10.6
2002	863,183	39,961	4.6	450,653	43,479	9.6
2003	978,450	45,087	4.6	521,930	51,169	9.8
2004	1,071,756	48,854	4.6	587,718	54,629	9.3

[a] Source: Children's Hospital 1 and 2 2004.

Table 3. Ten Leading Causes of Inpatient Admission to HCMC Children's Hospital 1, 2000 and 2004[a]

2000				2004			
Cause of Admission	ICD-10 Code	*N*	%	Cause of Admission	ICD-10 Code	*N*	%
Acute pharyngitis	J02	3088	7.6	Diarrhea	A09	3346	6.8
Diarrhea	A09	2678	6.6	Acute pharyngitis	J02	3038	6.2
Acute bronchiolitis	**J21**	**2300**	**5.6**	**Acute bronchiolitis**	**J21**	**2494**	**5.1**
Bacterial pneumonia	**J15**	**1742**	**4.3**	**Pneumonia, organism unspecified**	**J18**	**2294**	**4.7**
Asthma	J45	1658	4.1	Dengue hemorrhagic fever (II)	A91-2	2281	4.6
Acute bronchitis	J20	1387	3.4	Acute bronchitis	J20	1502	3.1
Indigestion / viral intestinal infection	K30	1221	3.0	Intussusceptions	K56.1	1362	2.8
Viral infections	B34	859	2.1	Viral infections	B34	1139	2.3
Upper acute respiratory infection	J06	715	1.7	Shigellosis	A03.9	1132	2.3
Shigellosis	A03.9	681	1.7	Asthma	J45	985	2.0

[a] Source: Children's Hospital 1 and 2 2004. **Bold** indicates ICD-10 code included in primary discharge diagnoses for patients in this study.

Table 4. Causes of Inpatient Admission to HCMC Children's Hospital 2, 2000–2004[a]

	2000		2001		2002		2003		2004	
Cause of Admission	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Bacterial and parasitic infections	10,093	24.5	10,604	24.7	10,819	24.9	14,247	27.9	15,470	28.3
Neoplasms	981	2.4	925	2.2	819	1.9	971	1.9	986	1.8
Hematologic diseases and immunologic disorders	287	0.7	347	0.8	418	1	411	0.8	465	0.8
Endocrinal, nutritional, and metabolic diseases	162	0.4	236	0.5	212	0.5	301	0.6	343	0.6
Mental and behavioral disorders	28	0.1	38	0.1	60	0.1	34	0.1	28	0.1
Diseases of the nervous system	759	1.8	692	1.6	577	1.3	580	1.1	726	1.3
Diseases of the eye and adnexa	121	0.3	221	0.5	312	0.7	219	0.4	453	0.8
Diseases of the ear and mastoid process	148	0.4	129	0.3	167	0.4	134	0.3	179	0.3
Diseases of the circulatory system	159	0.4	175	0.4	203	0.5	197	0.4	202	0.4
Disease of the respiratory system	18,505	44.8	19,227	44.8	18,763	43.2	21,666	42.4	22,830	41.7
Diseases of the digestive system	4,098	9.9	4,230	9.8	4,404	10.1	4,756	9.3	4,709	8.6
Diseases of the skin and subcutaneous tissue	616	1.5	674	1.6	725	1.7	794	1.6	839	1.5
Diseases of the musculoskeletal system	312	0.8	364	0.8	374	0.9	411	0.8	471	0.9
Diseases of the genitourinary system	962	2.3	1,055	2.5	1,168	2.7	1,267	2.5	1,252	2.3
Pregnancy, childbirth, and the puerperium	—	0	—	0	—	0	—	0	—	0
Perinatal period	717	1.7	677	1.6	863	2	1,004	2	885	1.6
Congenital malformations	1,510	3.7	1,835	4.3	1,934	4.4	2,098	4.1	2,425	4.4
Symptoms, signs not elsewhere classified	543	1.3	272	0.6	374	0.9	333	0.7	356	0.7
Injury, poisoning, and certain other consequences of external causes	673	1.6	749	1.7	777	1.8	1,119	2.2	1,713	3.1
External causes of morbidity and mortality	588	1.4	498	1.2	449	1	417	0.8	368	0.7
Factors influencing health status and contact with health services	11	0	14	0	51	0.1	92	0.2	56	0.1
Total	41,273	100	42,962	100	43,469	100	51,051	100	54,756	100

[a] Source: Children's Hospital 1 and 2, 2004.

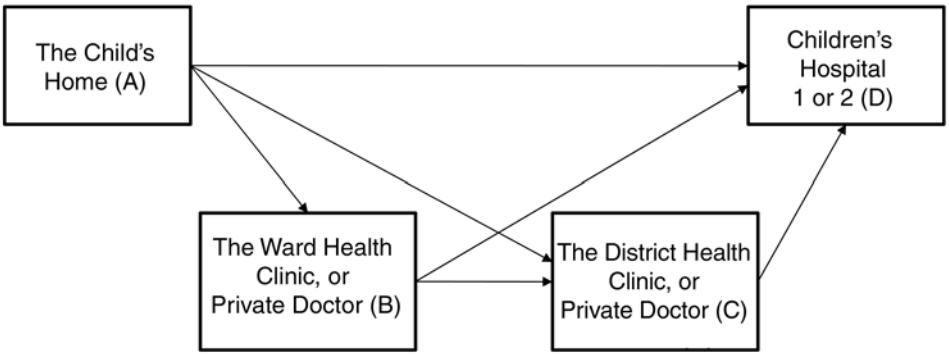

Figure 2. Pathways of admission to children's hospitals.

Table 5. Monthly Occupancy (% of Capacity) at HCMC Children's Hospitals, 2003–2005

Month / Hospital Beds	2003		2004		2005	
	CH1	CH2	CH1	CH2	CH1	CH2
January	102	92	89	96	88	113
February	75	92	97	121	73	79
March	101	116	109	124	104	91
April	116	118	108	129	99	96
May	116	110	111	128	100	103
June	123	132	110	110	113	114
July	122	131	116	134	113	113
August	117	130	116	133	110	100
September	124	115	115	128	103	93
October	122	117	111	137	112	101
November	113	131	112	122	118	106
December	133	133	110	117	108	102
Total number of beds	800	700	850	700	900	800

family and community practices (World Health Organization 1997). Diagnoses for all patients admitted to the HCMC pediatric hospitals for acute respiratory illness are based on standardized IMCI criteria. Both hospitals use *International Classification of Diseases,* 10th revision (ICD-10) codes to report and classify diseases.

Admissions Data Collection and Management Local collaborators at the pediatric hospitals informed us that they did not use objective clinical criteria to distinguish between pneumonia and bronchiolitis. Thus, we created a single outcome category for ALRI, which includes both pneumonia and bronchiolitis. ALRI admissions of children less than 5 years of age during 2003, 2004, and 2005 were extracted from computerized records of CH1 and CH2 using the following criteria:

1. Admission date from January 1, 2003, through December 31, 2005.
2. Age at admission date less than 5 years.
3. Residence in the central area of HCMC on admission date (patients residing in the five rural districts of HCMC were excluded because their exposures are not well reflected by the air quality monitoring network).
4. Primary discharge diagnosis of ICD-10 codes J13, J14, J15, J16, J18, or J21.

5. Age at admission at least 28 days (neonatal admissions were excluded because these are likely to be influenced by perinatal conditions).
6. Consistent with the CRECER (Chronic Respiratory Effects of Early Childhood Exposure to Respirable Particulate Matter) study protocols (available from *http://ehs.sph.berkeley.edu/guat/?page_id=123*), we excluded all repeat visits occurring within 14 days of admission to avoid double counting of the same case. This was only possible for CH1 owing to limitations in the electronic data set for CH2. As this restriction removed only a handful of cases from the CH1 analysis, however, this is unlikely to have major implications for our study results.
7. Aside from repeat visits within the 14-day window, all multiple visits for children within the study period were retrieved.

More details on the construction of the clinical database are available in Appendix E (available on the HEI Web site).

We chose not to include a control disease in our analysis because we were not convinced that we would be able to select an ideal control disease for this study. Moreover, as described above, the pediatric hospitals routinely operate beyond capacity; although we were assured that this does not affect admissions for lower respiratory illness, we were unclear how limited capacity may impact admissions for other conditions.

Definition of Case Reference Period Because we focused on hospital admissions, we used an empirical induction time (Rothman and Greenland 1998).The definition of the case reference period took into consideration induction times for ALRI, as well as time between onset of illness and detection of disease or time of hospitalization. The induction time would likely be on the order of a few days.

Clinicians at the primary health clinics provided information on referral patterns used to inform the choice of an optimal case reference period. One of the primary health clinics used IMCI criteria, or three visits to the clinic, or 6 days of treatment at the clinic without visible improvement as the basis for referral. Hard copies of clinical records were selected at random and reviewed to assess the lag between onset of illness and hospital admission, based on caregiver-reported estimates of when the child first fell ill. The caregivers reported lags ranging from around 2 to 7 days. Physicians at both pediatric hospitals were also interviewed. The consensus of opinion from the physicians was that a child admitted to their hospital for ALRI usually is treated at home first, or at the ward's or district's clinic, but typically is brought to one of the pediatric hospitals within a week of onset.

On the basis of this information, we assumed that the case reference period should be between 1 and 6 days. This has implications for the choice of lag times for average pollutant concentrations. We explored single-day lags from pollution on the day of admission (lag 0) to pollution on the day 10 days before admission (lag 10) and decided to focus on the average of pollution levels 1 to 6 days before admission.

AIR QUALITY DATA

Data Collection and Management

Since 2011, HEPA, with technical assistance from the Norwegian Institute for Air Research, has maintained nine stations that automatically monitor air quality, including levels of PM_{10}, O_3, NO_2, and SO_2, around the city. Figure 1 shows the locations of monitoring stations in HCMC. Of the nine sites, five are intended to measure exposure to traffic-related air pollution. Only data from the four stations intended to reflect background levels of pollution and exposure in residential areas — namely, the District 2 (D2), Ho Chi Minh City Zoo (Zoo), Tan Son Hoa (TSH), and Quang Trung (QT) stations — were considered potentially eligible for inclusion in our analyses.

The monitoring stations generate data every 5 minutes, and HEPA software automatically converts these data to hourly data without any quality assurance procedures. HEPA staff manually clean the air quality data on an hourly basis, using visual checks to identify spurious measurements, suspicious repeated values, and so forth. Initially, we planned to utilize automated algorithms to clean the data, starting with the rawest available form, in other words, the 5-minute data. However, several critical issues precluded construction of daily time series based on the 5-minute data.

The stations put very little emphasis on maintaining the 5-minute data set, mainly because all reporting and standards focus on the hourly data. In fact, the 5-minute data are not maintained in the central HEPA database, so this data set had to be manually reconstructed from spreadsheets used to derive hourly data and from direct downloads from the monitoring stations, resulting in a 5-minute data set with considerable gaps (on the order of months) compared with the HEPA-generated hourly data set. It was evident that statistical approaches to cleaning the raw 5-minute data would not be sufficient to address nuances in the air quality data, so we decided to use the HEPA-generated hourly data as the rawest form of data.

The available 5-minute data did reveal one important aspect of the data cleaning process, however: slightly negative values in the NO_2 data were systematically deleted.

These values probably occurred as a result of instrument zero drift; as they likely indicate near-zero concentrations, they probably should have been reported as is, or as zero. Their deletion could have resulted in slightly higher daily average concentrations being recorded when pollution was at very low levels. In addition, because we set a completeness criterion (discussed in greater detail below) requiring 75% of hourly values to generate each daily estimate, there could also be a bias due to missing daily average concentrations that should have taken very low levels into account. Given the infrequency of these negative values in the 5-minute data set, these practices are unlikely to have had a serious impact on results.

Although reasonable trends and levels were observed in the HEPA hourly pollutant data overall, careful quality assessment revealed a few issues that needed to be addressed in the data cleaning process. Figure 3 provides a brief overview of the process of creating time series for daily average air quality data. First, hourly values for each monitoring station were manually reviewed to flag recurrent values. All strings of four or more repeated values, indicating a problem with the monitoring system, were deleted. Then the station-specific daily time series were reviewed to identify other potential data quality concerns. It should also be noted that PM_{10} data from the TSH station were based on 24-hour gravimetric samples. While these data reflected a slightly different averaging window (around 6:00 AM to 5:59 AM vs. 12:00 AM to 11:59 PM), they appeared to be well correlated with the measurement data from the other stations.

Daily average values were created for each monitoring station by taking the mean of 24 hourly values for PM_{10}, NO_2, and SO_2, and by generating maximum 8-hour moving averages for O_3. A 75% completeness criterion was applied to all hourly data. No additional constraints to the data (i.e., no thresholds) were applied.

Time-series plots and interstation correlations were carefully assessed to inform decisions about the quality and completeness of average daily pollutant concentrations at each station. Citywide estimates for each pollutant were created from the mean of daily averages from each eligible station. More detailed information on the data cleaning process and creation of daily average pollution time series is available in Appendix F (available on the HEI Web site).

Meteorologic Data

Hourly meteorologic data were provided to us in electronic format by KTTV NB and had very few missing values. Mean daily data on temperature and humidity were calculated from these hourly data.

ASSESSMENT OF SEP

There are currently no reliable data on individual income in Vietnam. The government has not instituted a

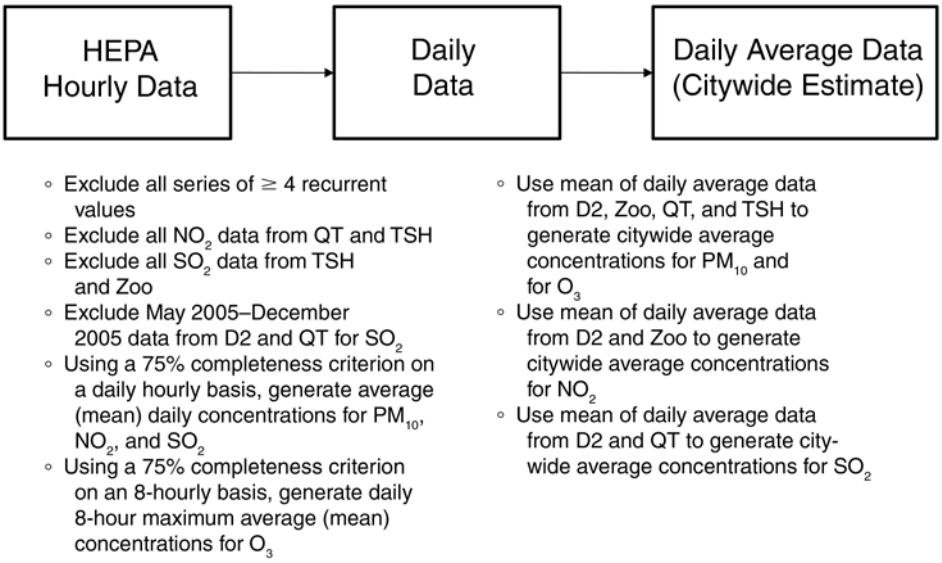

Figure 3. Process for generating daily average pollutant values.

reliable system for reporting personal income. Although government employees are paid a known salary, many also earn money through private work. Physicians at the pediatric hospitals, for example, also work from 5 PM to 8 PM at their private practice and earn substantially more than their official hospital salaries. Business owners report their profits for income tax purposes, but nongovernmental employees working for private businesses do not report their income. In addition, cash is used for almost all small business or person-to-person transactions. Thus, there is no straightforward way to establish poverty status on the basis of individual income.

To determine poverty status for the subjects in our study, we used two potential indicators, one based on individual-level data and the other based on district-level data. All children in HCMC less than 6 years of age became eligible to receive free medical care starting in June 2005; therefore, the analysis based on individual-level data only includes admissions before this date.

Individual-Level Data on SEP

The individual-level poverty indicator we used is based on eligibility for free or reduced-fee health care. At HCMC hospitals, a patient's eligibility for free or reduced-fee health care is determined after admission. A hospital social worker, in consultation with doctors and other relevant caregivers, determines eligibility on the basis of interviews with or observations of the patient's family. Because this assessment is made after admission to the hospital, admissions are not biased on the basis of SEP. There are also rare cases of people who just leave the hospital without paying or discussing payment status. The hospitals' staffs believe strongly that these cases should be classified as poor.

Free medical care is also available through the use of health insurance cards from the HCMC Department of Labor, Invalids and Social Assistance (DOLISA). Working with ward-level authorities, DOLISA applies a government-based definition of poverty to determine which families are eligible for these insurance cards. The staff surveys the neighborhood to examine the conditions of families they deem poor by housing characteristics, possession of transportation means (motorcycles), and household goods. They hold meetings to select families that are considered poor and conduct interviews to gather detailed data on the living conditions, jobs, and incomes of household members. Through visits and conversations with DOLISA staff, we determined that they maintain these detailed socioeconomic data in a computer database. The poverty lines defined by DOLISA changed five times from 1992 to 2003. The 2003 poverty line was monthly income under 250,000 VND (about $17 in the United States at the current exchange of $1 per 15,000 VND) for urban areas, and 200,000 VND (about $13) for rural areas. The poverty line for 2004 and later was increased to 500,000 VND ($34) for the entire city regardless of residential location. While possession of DOLISA insurance cards is likely to be a reasonable indicator of low SEP within each community, few patients presented DOLISA insurance cards to the pediatric hospitals.

Information on payment information from hospital financial records was used to determine whether patients were given free or reduced-fee health care. Financial records include information on payment status (i.e., 1 is paid in full; 2, paid a reduced fee; 3, left without paying; 4, received free medical care; 5, paid by insurance), the total amount owed to the hospital, and the total amount paid to the hospital (Table 6). The financial database from CH1

Table 6. Summary Information on Individual Patient Payment Status, 2003–2005

Payment Status	Children's Hospital 1		Children's Hospital 2		Combined	
	%	*N*	%	*N*	%	*N*
Unknown	0.00	0	9.90	1,036	6.59	1,036
Free	0.46	24	0.07	7	0.20	31
Fully paid	91.58	4807	89.03	9,320	89.88	14,127
Insurance	0.40	21	0.16	17	0.24	38
Ran away[a]	0.63	33	0.18	19	0.33	52
Reduced fee	1.10	58	0.66	69	0.81	127
Under 6 yr old	5.83	306	0.00	0	1.95	306
Total	100	5249	100	10,468	100	15,717

[a] Left without paying or discussing payment status.

also has information which indicates the type of insurance (such as veterans insurance or DOLISA insurance) that the patient has, if any. In theory, every patient record can be directly linked to payment information from the hospital's finance department.

Financial records for CH1 patients could be linked to clinical records by a unique case record identification (ID) and visit number; however, we faced some complications in attempting to link case records and financial records for CH2 patients. The financial database at CH2 includes information on date of admission, name, age, and payment information for each child. It does not include unique case record IDs and visit numbers. Thus, there was no way to link the financial and clinical databases directly. To establish linkage to the clinical database, the financial records were manually extracted, charts were reviewed, and manual checks were used to construct a unique identifier for each child within the financial database.

More details on the linkage between financial and clinical records are available in Appendix E (available on the HEI Web site).

District-Level Data on SEP

The Institute of Economic Research in HCMC, in collaboration with the World Bank and the General Statistics Office of Vietnam, conducted an exercise to map poverty levels in the city (HCMC Bureau of Statistics 2005). Using small area estimation, this project combined expenditure data from the 2002 Vietnam Household Living Standards Survey (VHLSS) with a 10% sample of the HCMC 2004 mid-term population to estimate poverty indices for districts in HCMC. VHLSS collects information on household characteristics including basic demography, employment, and labor force participation, education, health, income, expenditures, housing, fixed assets, and durable goods. The 2002 VHLSS covered 75,000 households, of which 30,000 were asked for detailed information on consumption expenditure. The sample of 30,000 households represents the eight regions of Vietnam. The "South East" region expenditure equation is used for HCMC.

The 10% HCMC population sample was from 2004 census data. From 10,037 city blocks of similar size (between 100 and 120 households), 30 to 40 blocks were randomly selected within each district, and all households in these blocks were interviewed. The interview contained a set of expenditure questions related to housing structure, use of electricity, running water, toilets, television, phone, computer, and Internet access, which were a subset of the expenditure questions asked in the VHLSS study.

A regression model was derived for VHLSS expected expenditure. The regression coefficient estimates from this model were used on the census data to obtain estimated expenditure, which was used to derive the probability of a particular household falling below the poverty line (for example, set at 6 million VND). The poverty estimate was assigned to all individuals living in the same household. The poverty rate of a specific block was the average of all residents' rates in the block. This estimation procedure was repeated for each sampled block in the district. The district poverty rate was estimated by determining the average of all poverty rate estimates of all randomly sampled blocks in the district.

STATISTICAL METHODS

We used two different statistical modeling approaches: the time-series (Poisson regression) approach and the case–crossover approach. In the time-series analyses, the day is the unit of analysis and the impact of short-term changes in air pollution levels on daily counts of ALRI admissions is assessed. Time-varying covariates are adjusted for by modeling these factors as smoothed functions (Health Effects Institute 2003).

The case–crossover method deals with covariates by optimal specification of control and effect periods. Case–crossover studies can be used to examine the acute effects of intermittent exposures to air pollution. Case–crossover studies do not compare the exposure of individuals who become case subjects with the exposure of control subjects. Rather, they estimate relative risk for a case subject by contrasting exposure shortly before the onset of disease with exposure during times when the individual was not affected. In other words, cases of disease are identified, the exposure of each case subject is estimated during a case period and a control period, and then relative risk is calculated based on contrasting the exposure levels during those periods. Other factors that may affect the magnitude of effects from the exposures, such as indicators of poverty, can be included in the analysis as well. The case–crossover approach controls for time-invariant factors by design; in other words, there is no need to address confounding issues from factors such as child-specific demographic conditions that do not vary through time. However, time-varying factors that change slowly over time, such as long-term seasonal trends, can confound the effect of interest.

The rationale for using these two different designs comes from recent findings that evaluated the performance of these methods based on bias and efficiency. Case–crossover estimates are acknowledged to have lower precision (larger standard errors) than time-series estimates (Bateson and

Schwartz 1999; Fung et al. 2003). However, simulation studies have suggested that the case–crossover method, though not as statistically efficient (only 66%) as the time-series (Poisson regression) method, is more advantageous when individual-level data are available because it can add more information to the modeling of the effect of interest (Bateson and Schwartz 1999).

A few studies have been conducted using both methods to analyze data, and they generally gave similar results. For example, Neas and colleagues (1999) reanalyzed data on air pollution and mortality in Philadelphia and found similar results between the time-series and case–crossover approaches for outcomes such as cardiovascular mortality and mortality of subjects over 65 years of age. Luginaah et al. (2005) analyzed data on air pollution and daily respiratory hospitalizations in Windsor, Ontario, Canada, between 1995 and 2000 using both case–crossover and time-series methods and obtained consistent results from both approaches. Perhaps most analogous to this study, Segala and colleagues (2008) explored the association between winter air pollution and infant bronchiolitis in Paris and also found results to be consistent across approaches.

All data in this study were stored and managed using SAS software version 9 (SAS Institute Inc. 2000). All analyses were conducted using SAS/STAT version 9 and R version 2.60 with MGCV version 1.3-29.

Time-Series Analysis

Daily counts of ALRI admissions were merged with the daily pollutant and meteorologic data to form the analysis data set. For each day in the time series, daily counts of ALRI admissions, estimates of exposure, and meteorologic data, as well as potential lags from day 1 to day 10 for each pollutant and for meteorologic variables, were compiled. An indicator variable for the seasonal effect, a variable for long-term trend, and an indicator for holidays were also used in the model. We used Poisson regression with smoothing functions for meteorologic variables (temperature and relative humidity) for lags of 1 to 10 days, and an average of the mean pollutant concentrations for the average lag days (1–6). We specified natural cubic spline smoothing functions with 27 *df* for day, 4 *df* for temperature, and 4 *df* for humidity. Fixed effects of weekdays and holidays were also included in the models. The model and the likelihood function of the Poisson density function have the following forms:

$$L(y_1,\ldots,y_t \mid \mu_1,\ldots,\mu_t) = \prod_{t=1}^{T} \frac{{\mu_t}^{y_t} e^{-\mu_t}}{y_t!}$$

$$\begin{aligned}\mu_t &= E(y_t \mid x_{1t},x_{2t},x_{3t},x_{4t},x_{5t},x_{6t}) \\ &= e^{\beta_0+\beta_1 x_{1t}+f_1(x_{2t})+f_2(x_{3t})+\beta_4 x_{4t}+f_5(x_{5t})+\beta_6 x_{6t}}\end{aligned}$$

$$\begin{aligned}&\log E(y_t \mid x_{1t},x_{2t},x_{3t},x_{4t},x_{5t},x_{6t}) \\ &\quad = \beta_0 + \beta_1 x_{1t} + f_1(x_{2t}) + f_2(x_{3t}) \\ &\quad + \ \beta_4 x_{4t} + f_5(x_{5t}) + \beta_6 x_{6t}\end{aligned}$$

Where μ_t denotes the daily mean number of ALRI cases, x_{1t} the daily average pollutant level, x_{4t} the weekday indicator, and x_{6t} the holiday indicator, and the smoothing functions are x_{2t} for temperature, x_{3t} for humidity, and x_{5t} for days. We used the GAM (generalized additive model; Hastie and Tibshirani 1990) function in R from package MGCV, which uses a penalized, iteratively reweighted, least squares method (Wood 2004; Wood 2006).

After testing for interaction by season, all analyses were conducted for the entire study period, as well as for each season.

Case–Crossover Analysis

The analysis database used individual patient records (identified by ID number and admission date) as the main units of observation. Data on respiratory diagnosis, demographic information, and appropriate meteorologic and exposure data corresponding to predefined case and control periods were linked to each case record.

The ideal control period should be the smallest possible number of days outside the autocorrelation period. Choosing control periods that are too long could introduce bias due to seasonal patterns. Choosing periods that are too short, however, may potentially cause autocorrelation and introduce bias.

Analyses were conducted using a time-stratified design. Although in the past most case–crossover studies have used a symmetric bidirectional design, more recent publications have emphasized the advantages of using a time-stratified design (Lumley and Levy 2000; Levy et al. 2001; D'Ippoliti et al. 2003; Janes et al. 2005; Mittleman 2005). Specifically, the time-stratified design has been shown to produce unbiased estimates, as it enables the removal of overlap bias resulting from time trends in the pollutant data (Janes et al. 2005).

Control days were every 7th day from the induction date within the same month as admission. Children hospitalized on the same day share the same case and control periods. Data were analyzed using conditional logistic regression. The effect of interest (PM_{10} on hospital admission for ALRI) was estimated as follows, using the statistical procedure PHREG in SAS/STAT software version 9:

- Assume that a child could be hospitalized for ALRI on any day from January 1, 2003, through December 31, 2005 (the duration of this study). We denote these potential hospitalization days as t_1, t_2,..., t_M. Let N be the number of case–control pairs.
- Let a $1 \times p$ vector $\boldsymbol{X_{ij}}$ denote the set of p variables, which include the daily gaseous pollutant, and other potential time-varying covariates such as meteorologic variables (including lags) for child i who was hospitalized on day t_j.
- Let a $p \times 1$ vector β denote the regression coefficients that correspond to the p variables. Since the estimation will be done via conditional logistic regression for the 1:M matched case–control design (where M is the number of controls matched per individual case), each of these coefficients represents the adjusted log odds estimate.
- The conditional probability that a child was hospitalized on a particular day, t_k, given that she or he was hospitalized on any of the days t_1, t_2,..., t_M, is

$$p_{ik} = \frac{\exp\left(\beta^T X_{ik}\right)}{\sum_{j=1}^{M} \exp\left(\beta^T X_{ij}\right)}$$

- Therefore the likelihood function for N hospitalized children is

$$\prod_{i=1}^{N} p_{ik} = \prod_{i=1}^{N} \frac{\exp\left(\beta^T X_{ik}\right)}{\sum_{j=1}^{M} \exp\left(\beta^T X_{ij}\right)}$$

- Adjusted maximum likelihood estimate and standard error for the pollutant effect is obtained from the estimated vector β and its variance–covariance matrix.

Note that in the above we assume that each child is hospitalized only once, or that the repeat visits occurred more than 14 days apart and can be treated as independent ALRI episodes.

For the hypothesis of estimating the effect of PM_{10} controlling for the other gaseous pollutants, we examined the correlation among PM_{10} and the other pollutants, since it was likely that positively correlated pollutant levels could pose challenges of multicollinearity.

We checked to see whether the correlation coefficient between PM_{10} and each of the gaseous pollutants exceeded 0.7, since collinearity could introduce a problem in obtaining the adjusted estimate of PM_{10}. With the exception of the 0.78 correlation between PM_{10} and NO_2 in the dry season, none of the correlations exceeded 0.7; however, the correlation between O_3 and PM_{10} was greater than 0.6 in both seasons. We were relatively confident of our ability to assess the effect of PM_{10} in the presence of another pollutant, but maintained caution about our ability to distinguish between the effects of PM_{10} and NO_2.

Effect Modification by SEP

With only approximately 1% of cases being classified as poor using the hospital financial records, there was insufficient power to conduct a time-series analysis stratified by individual measures of SEP. We attempted to model the effect modification of individual-level poverty status in the case–crossover models using stratification.

For the district-level indicator of SEP, we had four economic quartiles, with quartile 1 being the least-poor group, and quartile 4 the poorest group. We also used stratification to obtain the estimates for each of the quartiles in the case–crossover models.

All of the above analyses were stratified by season because of the observed difference in the distribution of the pollutants and meteorologic variables between the dry and rainy seasons.

RESULTS

HOSPITAL ADMISSIONS

Figure 4 summarizes the process of extracting and linking data from the hospitals' clinical and financial records. Of the 15,717 total ALRI admissions, 10,468 occurred at CH2 and 5,249 at CH1. We were able to link individual financial data on payment status to clinical data for 14,681 (more than 93%) of the ALRI admissions for the two hospitals combined (Table 6).

Daily, Monthly, and Seasonal Variations

To explore differences in the characteristics of the patient populations admitted to CH1 and CH2, we stratified

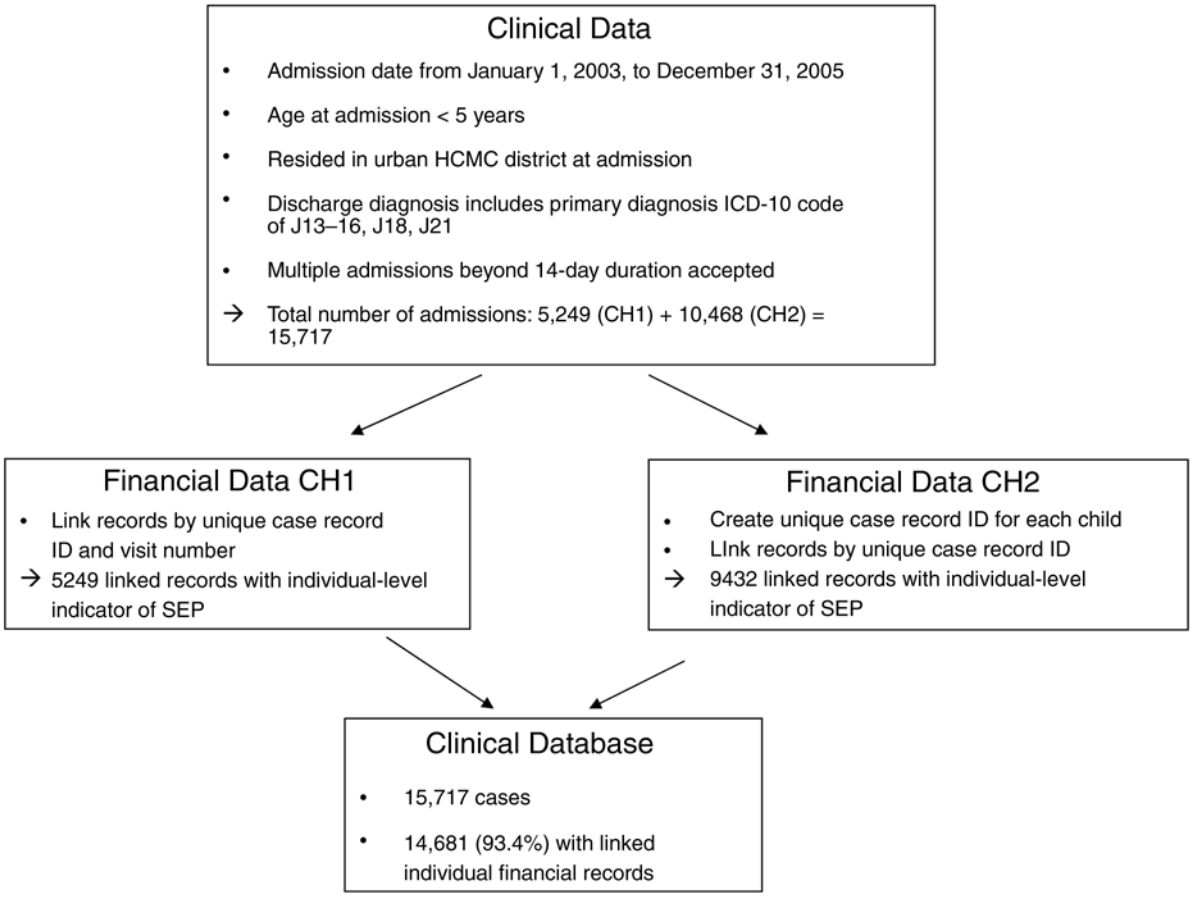

Figure 4. Overview of hospital data extraction and linkage.

the data by hospital and also combined the data from the two hospitals. Table 7 provides a summary of the ALRI admissions to CH1 and CH2 during the study, by year, day of the week, month of the year, and season. CH2 had approximately twice as many ALRI admissions as CH1. Figure 5 shows the time-series plots of daily admissions over time for CH1 and CH2 combined, by season. Admissions tended to peak during July and August each year, most likely reflecting a seasonal effect since this is the peak of the rainy season in HCMC (Table 7).

Admissions by ICD-10 Code at Discharge and Patient Demographics

ALRI classification by ICD-10 code at discharge was relatively consistent between the two hospitals. Approximately 58% of the patients admitted with ALRI were discharged with the diagnosis of pneumonia, and approximately 42% were discharged with the diagnosis of bronchiolitis (Table 8). Nearly 65% of the ALRI admissions were male children, accounting for approximately 72% of all admissions to CH1 and 61% of all admissions to CH2.

Table 7. ALRI Admissions by Year, Day of the Week, Month, and Season, 2003–2005

	Children's Hospital 1		Children's Hospital 2		Combined	
Time Period	%	*N*	%	*N*	%	*N*
2003	35.0	1836	34.9	3,654	34.9	5,490
2004	29.9	1567	29.5	3,086	29.6	4,653
2005	35.2	1846	35.6	3,728	35.5	5,574
Total	100.0	5249	100.0	10,468	100.0	15,717
Monday	10.5	551	11.7	1,221	11.3	1,772
Tuesday	16.9	889	15.8	1,650	16.2	2,539
Wednesday	15.8	827	14.8	1,546	15.1	2,373
Thursday	14.7	774	15.4	1,613	15.2	2,387
Friday	14.4	755	14.8	1,552	14.7	2,307
Saturday	15.4	809	14.8	1,549	15.0	2,358
Sunday	12.3	644	12.8	1,337	12.6	1,981
Total	100.0	5249	100.0	10,468	100.0	15,717
January	6.3	332	6.4	667	6.4	999
February	0.0	265	5.0	520	5.0	785
March	7.3	385	6.2	648	6.6	1,033
April	7.0	370	6.3	664	6.6	1,034
May	7.9	417	8.0	835	8.0	1,252
June	10.3	541	10.2	1,064	10.2	1,605
July	11.5	602	12.4	1,296	12.1	1,898
August	12.5	654	11.2	1,173	11.6	1,827
September	9.1	476	8.7	914	8.8	1,390
October	9.0	474	9.3	975	9.2	1,449
November	6.9	360	8.5	887	7.9	1,247
December	7.1	373	7.9	825	7.6	1,198
Total	100.0	5249	100.0	10,468	100.0	15,717
Rainy Seasons	60.3	3164	59.8	6,257	59.9	9,421
Dry Seasons	39.7	2085	40.2	4,211	40.1	6,269
Total	100.0	5249	100.0	10,468	100.0	15,717

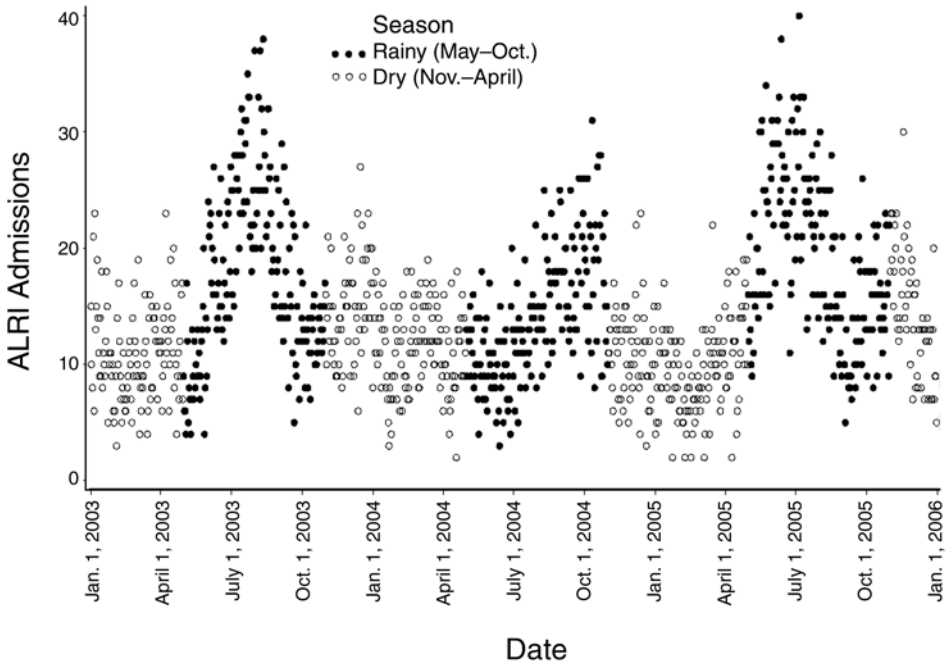

Figure 5. Daily ALRI admissions to the two HCMC children's hospitals combined, 2003–2005.

Approximately 33% of the children admitted for ALRI were under 1 year of age, 41% between 1 and 2 years of age, and 18% between 2 and 3 years of age. The percentage of children under 1 year of age was higher at CH1 (over 38%) than at CH2 (nearly 30%) (Table 8). Tan Binh and Districts 6, 8, 10, and 11 were responsible for the largest proportion of patients at CH1, while the Binh Thanh, Go Vap, and Thu Duc districts were responsible for 43% of admissions to CH2 (Table 8). Data on sex and age for ALRI admissions to the two hospitals are shown by individual-level indicator of SEP (poor, nonpoor, or unknown) in Table 9.

The average length of stay in the hospital differed by outcome as well; patients with pneumonia stayed a median of 7 days, while patients with bronchiolitis were discharged after a median of 6 days (Table 10).

Quality Assurance for Hospital Data

A quality assurance unit led by Dr. Do Van Dzung and composed of staff from CH1 and CH2 conducted manual cross-checks to assess the quality of electronic data in the CH1 and CH2 databases (more details on the construction of the clinical database are presented in Appendix E, available on the HEI Web site).

The quality assurance team randomly selected 300 records from the electronic admissions database of each hospital (approximately 6% and 3% of CH1 and CH2 ALRI admissions, respectively) and cross-checked the electronic information with the information recorded in the clinical charts for these patients. The team also cross-checked the financial data against hard copies of financial records for this same sample, to verify the accuracy of the electronic data. A handful of errors were identified, most of which were of the type that may be of administrative concern, but would not have substantial impacts on scientific research (Table 11). The miscoded ICD-10 codes nearly all reflected miscoding within the group of codes that the single-outcome category comprises. In addition, most of the errors in coding for sex were miscoding of females as males. This was largely due to the similarity between the letters *n* used to indicate *nữ* (Vietnamese for "female") and *m* used to indicate *nam* (Vietnamese for "male").

Table 8. ALRI Admissions by ICD-10 Code at Discharge and Patient Demographics, 2003–2005

ICD-10 Code, Patient Demographics	Children's Hospital 1		Children's Hospital 2		Combined	
	%	*N*	%	*N*	%	*N*
J13. Pneumonia due to *Streptococcus pneumoniae*	0.0	0	0.0	4	0.0	4
J14. Pneumonia due to *Haemophilus influenzae*	0.0	0	0.0	1	0.0	1
J15. Bacterial pneumonia, not elsewhere classified	0.7	37	0.3	33	0.4	70
J16. Pneumonia due to other infectious organisms, not elsewhere classified	0.0	0	0.2	19	0.1	19
J18. Pneumonia, organism unspecified	39.0	2045	66.4	6,955	57.3	9,000
J21. Acute bronchiolitis	60.3	3167	33.0	3,456	42.1	6,623
Total	100.0	5249	100.0	10,468	100.0	15,717
Sex						
Male	71.7	3761	61.4	6,424	64.8	10,185
Female	28.3	1488	38.6	4,044	35.2	5,532
Total	100.0	5249	100.0	10,468	100.0	15,717
Age						
0–1 yr	38.4	2015	29.6	3,101	32.6	5,116
1–2 yr	41.0	2150	40.5	4,243	40.7	6,393
2–3 yr	14.3	750	19.4	2,026	17.7	2,776
3–4 yr	4.3	226	6.7	700	5.9	926
4–5 yr	1.8	92	2.8	289	2.4	381
5–6 yr	0.3	16	1.0	109	0.8	125
Total	100.0	5249	100.0	10,468	100.0	15,717
District of Residence						
District 1	2.5	131	6.2	647	5.0	778
District 2	0.4	23	5.3	555	3.7	578
District 3	5.4	284	3.3	342	4.0	626
District 4	1.2	63	8.5	894	6.1	957
District 5	4.9	257	0.8	81	2.2	338
District 6	9.0	469	0.6	64	3.4	533
District 7	1.8	94	7.5	788	5.6	882
District 8	9.9	518	1.2	122	4.1	640
District 9	0.5	25	7.0	733	4.8	758
District 10	8.5	443	0.8	88	3.4	531
District 11	8.6	449	0.4	46	3.2	495
District 12	6.4	336	6.6	695	6.6	1,031
Binh Tan	3.1	163	0.0	0	1.0	163
Binh Thanh	2.3	122	16.2	1,700	11.6	1,822
Go Vap	3.9	202	14.5	1,516	10.9	1,718
Phu Nhuan	1.5	77	4.4	456	3.4	533
Tan Binh	26.3	1379	4.1	433	11.5	1,812
Tan Phu	2.8	148	0.0	0	0.9	148
Thu Duc	1.1	57	12.5	1,308	8.7	1,365
Total	100.0	5240	100.0	10,468	100.0	15,708

Table 9. Sex and Age of ALRI Patients by Individual-Level Indicator of SEP, 2003–2005

SEP / Sex and Age	Children's Hospital 1		Children's Hospital 2	
	%	*N*	%	*N*
Nonpoor Patients				
Sex				
Male	71.98	3475	61.78	5768
Female	28.02	1353	38.22	3569
Total	100.00	4828	100.00	9337
Age (yr)				
0–1	37.49	1810	28.94	2702
1–2	41.30	1994	41.33	3859
2–3	14.73	711	19.42	1813
3–4	4.27	206	6.63	619
4–5	1.88	91	2.71	253
5–6	0.33	16	0.97	91
Total	100.00	4828	100.00	9337
Poor Patients				
Sex				
Male	65.22	75	57.89	55
Female	34.78	40	42.11	40
Total	100.00	115	100.00	95
Age (yr)				
0–1	48.70	56	37.89	36
1–2	34.78	40	37.89	36
2–3	10.43	12	16.84	16
3–4	5.22	6	5.26	5
4–5	0.87	1	1.05	1
5–6	0.00	0	1.05	1
Total	100.00	115	100.00	95
SEP Unknown[a]				
Sex				
Male	68.95	211	58.01	601
Female	31.05	95	41.99	435
Total	100.00	306	100.00	1036
Age (yr)				
0–1	48.69	149	35.04	363
1–2	37.91	116	33.59	348
2–3	8.82	27	19.02	197
3–4	4.58	14	7.34	76
4–5	0.00	0	3.38	35
5–6	0.00	0	1.64	17
Total	100.00	306	100.00	1036

[a] Patients with unidentified (missing) individual-level indicator of SEP.

Table 10. Average Length of Hospital Stay (Days) by ALRI and SEP Indicators, 2003–2005

ALRI / SEP Indicator	*N*	Mean	SD	Median	Minimum	Maximum
ALRI Classification						
Pneumonia	9094	8.0	6.2	7.0	0.0	129.0
Bronchiolitis	6623	6.4	3.8	6.0	0.0	70.0
District-Level SEP Indicator[a]						
Quartile 1	4618	7.5	5.3	7.0	0.0	123.0
Quartile 2	5474	7.3	5.7	7.0	0.0	129.0
Quartile 3	4976	7.2	5.1	6.0	0.0	104.0
Quartile 4	640	7.5	5.2	7.0	0.0	66.0
Individual-Level SEP Indicator						
Nonpoor						
Children's Hospital 1	4828	7.4	5.7	7.0	0.0	123.0
Children's Hospital 2	9337	7.2	4.2	7.0	0.0	104.0
Poor						
Children's Hospital 1	115	13.7	16.5	8.0	0.0	83.0
Children's Hospital 2	95	14.3	16.9	9.0	0.0	123.0
Unknown						
Children's Hospital 1	306	6.7	6.3	5.0	0.0	49.0
Children's Hospital 2	1036	6.8	7.3	6.0	0.0	129.0

[a] Quartile 1 is the highest quartile of SEP.

Table 11. Quality Assurance Summary for Children's Hospital Admissions Data Sample[a]

	Children's Hospital 1		Children's Hospital 2	
Variable	Number of Discrepancies	Comments	Number of Discrepancies	Comments
Sex	27 (9%) — 5 in 2003, 11 in 2004, 11 in 2005	89% of errors were females miscoded as males, most likely due to the similarity between letters indicating female (*n*) and male (*m*)	8 (2.7%) — 1 in 2003, 4 in 2004, 3 in 2005	75% of errors were females miscoded as males
Name	1 (0.33%) — 2 in 2003, 3 in 2004, 3 in 2005	Important administratively but not critical for scientific aspects of research	1 (0.33%) — in 2003	Important administratively but not critical for scientific aspects of research
District	8 (2.7%)	3 errors were for patients actually residing beyond HCMC	0	
ICD-10 code	10 (3.3%) — 5 in 2003, 3 in 2004, 2 in 2005	4 of the miscoded ICD-10 codes at discharge were within J10–18, J20–22	18 (6%) — 7 in 2003, 7 in 2004, 4 in 2005	1 J18 miscoded as J20, 1 J15 miscoded as J18, 4 J20 miscoded as J18, 12 J18 miscoded as J20

[a] The sample was 600 records, 300 from each hospital.

AIR QUALITY DATA

Station-Specific Pollutant Concentrations and Correlations

Table 12 summarizes the availability of pollutant data by monitoring station, and station-specific summary statistics are provided in Table 13. Station-specific distributions of daily pollutant concentrations are shown in Figure 6. There is a clear seasonal trend in the data, with pollutant levels at their lowest in the rainy season (from May through October) and highest in the dry season.

Mean PM_{10} concentrations ranged from 63.3 μg/m^3 at the TSH station to 91.3 μg/m^3 at the QT station, with similar standard deviations in the data for all of the stations. Mean concentrations of O_3 hovered around 75 μg/m^3, with slightly higher variability in the data from the TSH station, but relatively similar levels across all stations. NO_2 concentrations showed wider variability across monitoring stations, with average mean concentrations of 10.4, 18.6, 24.4, and 26.9 μg/m^3 measured at the TSH, D2, QT, and Zoo stations, respectively (only the D2 and Zoo stations had sufficient data to be included in the final analysis); this station-specific ordering of concentrations remained consistent in both dry and rainy seasons. SO_2 levels varied widely across monitoring stations, with mean concentrations of 19.0, 24.5, and 44.7 μg/m^3 measured at D2, QT, and TSH, respectively, over the study (only the D2 and QT stations had sufficient data to be included in the final analysis). Differences in concentrations between stations were far more pronounced in the rainy season than in the dry season.

The number of days with missing values increased over time, with far more missing data in 2005. No data are available for large gaps of time (on the order of months). According to HEPA, this can be attributed largely to power failures at the monitoring stations. We decided not to impute values for these large data gaps. Also, as there were very few instances of more than two consecutive missing values at the daily level, missing values were not imputed.

Interstation Correlations

Station-specific distributions of daily concentration estimates and pollutant-specific correlations across stations are provided in Tables 13 and 14. In general, the PM_{10} values observed across the different stations were highly correlated, except between the QT and TSH stations. The highest correlations were observed between the Zoo and D2 stations, which had high correlations for PM_{10}, O_3, and NO_2 (r = 0.81, 0.82, and 0.66, respectively). The QT station appeared to have lower correlations with the other stations.

On the basis of interstation correlations, as well as visual inspection of station-specific time-series plots and correspondence with HEPA, we excluded the following data series because data were extremely sparse or considered implausible: NO_2 data from QT and TSH stations; SO_2 data from TSH station; and SO_2 data from QT and D2 stations from May through December 2005 (SO_2 was not monitored at the Zoo station).

A summary of the valid pollutant data available from each monitoring station is provided in Table 13.

Citywide Daily Average Concentrations

Daily citywide concentrations for each pollutant were estimated by taking the mean of daily average data from the D2, QT, TSH, and Zoo stations for PM_{10} and O_3, from the D2 and Zoo stations for NO_2, and from the D2 and QT stations for SO_2.

Table 12. Availability of Pollutant Data, by Monitoring Station, 2003–2005

Station	PM_{10}	NO_2	SO_2	O_3
District 2 (D2)	Jan. 2003–Dec. 2005	Jan. 2003–Dec. 2005	Jan. 2003–April 2005	Jan. 2003–Dec. 2005
Quang Trung (QT)	Jan. 2003–Dec. 2005		Jan. 2003–April 2005	Jan. 2003–Dec. 2005
Tan Son Hoa (TSH)	Jan. 2003–Dec. 2005			Jan. 2003–Dec. 2005
Zoo	Jan. 2003–Dec. 2005	Jan. 2003–Dec. 2005		Jan. 2003–Dec. 2005

Table 13. Distribution of Mean Daily Pollutant Concentrations (μg/m^3), by Monitoring Station, 2003–2005

Pollutant	Station	Mean	SD	*N*	Median	Minimum	Maximum
Overall							
PM_{10}	D2	74.4	31.3	926	66.8	18.4	209.9
	QT	91.3	32.6	188	86.5	23.2	173.5
	Zoo	71.7	28.2	816	65.6	19.2	185.4
	TSH	63.4	32.2	331	52.5	19.0	175.8
O_3	D2	72.4	30.6	982	67.8	0.9	179.9
	QT	76.8	34.0	711	73.7	11.0	218.3
	Zoo	76.9	33.6	955	71.7	3.6	184.1
	TSH	75.2	40.1	663	74.0	0.4	195.0
NO_2	D2	18.6	7.5	897	16.8	2.8	49.1
	QT	24.4	8.6	199	26.3	0.2	42.9
	Zoo	26.9	8.0	727	27.1	5.0	55.2
	TSH	10.4	6.2	257	8.7	0.4	31.1
SO_2	D2	19.0	11.7	571	17.3	2.2	75.0
	QT	24.5	11.5	469	23.2	3.2	80.4
	Zoo	—	—	—	—	—	—
	TSH	44.7	24.8	178	40.4	7.2	112.9
Dry Season							
PM_{10}	D2	84.9	35.6	459	75.5	33.1	209.9
	QT	101.9	32.9	100	102.2	23.2	173.5
	Zoo	82.1	28.5	445	76.2	32.9	181.6
	TSH	73.8	38.6	179	60.1	22.2	175.8
O_3	D2	84.9	30.7	477	81.1	7.3	179.9
	QT	93.8	30.4	378	87.3	24.5	218.3
	Zoo	93.9	31.4	471	91.7	20.2	184.0
	TSH	94.3	35.3	336	91.4	7.1	195.0
NO_2	D2	19.7	8.5	417	17.4	2.8	42.5
	QT	29.5	5.5	106	28.9	12.3	42.9
	Zoo	26.0	8.7	407	25.8	11.5	50.6
	TSH	11.2	6.3	122	8.6	3.8	31.1
SO_2	D2	24.2	12.0	308	22.0	4.6	75.0
	QT	27.3	12.0	307	25.4	5.2	80.4
	Zoo	—	—	—	—	—	—
	TSH	38.1	28.5	98	27.0	7.2	112.9
Rainy Season							
PM_{10}	D2	64.0	21.8	467	60.8	18.4	150.5
	QT	79.4	27.9	88	77.7	25.1	167.4
	Zoo	59.2	22.1	371	55.5	19.2	185.4
	TSH	51.1	15.2	152	49.0	19.0	98.6
O_3	D2	60.6	25.3	505	55.4	0.9	159.3
	QT	57.6	27.0	333	51.5	11.0	163.8
	Zoo	60.4	26.6	484	54.9	3.6	184.1
	TSH	55.5	35.0	327	53.4	0.4	170.6
NO_2	D2	17.6	6.4	480	16.6	4.8	49.1
	QT	18.7	7.9	93	18.3	0.2	37.0
	Zoo	28.0	6.9	320	28.1	5.0	55.2
	TSH	9.7	6.0	135	8.9	0.4	23.8
SO_2	D2	12.9	7.7	263	11.0	2.2	40.5
	QT	19.2	8.2	162	18.8	3.2	40.6
	Zoo	—	—	—	—	—	—
	TSH	52.7	16.3	80	55.2	8.8	82.7

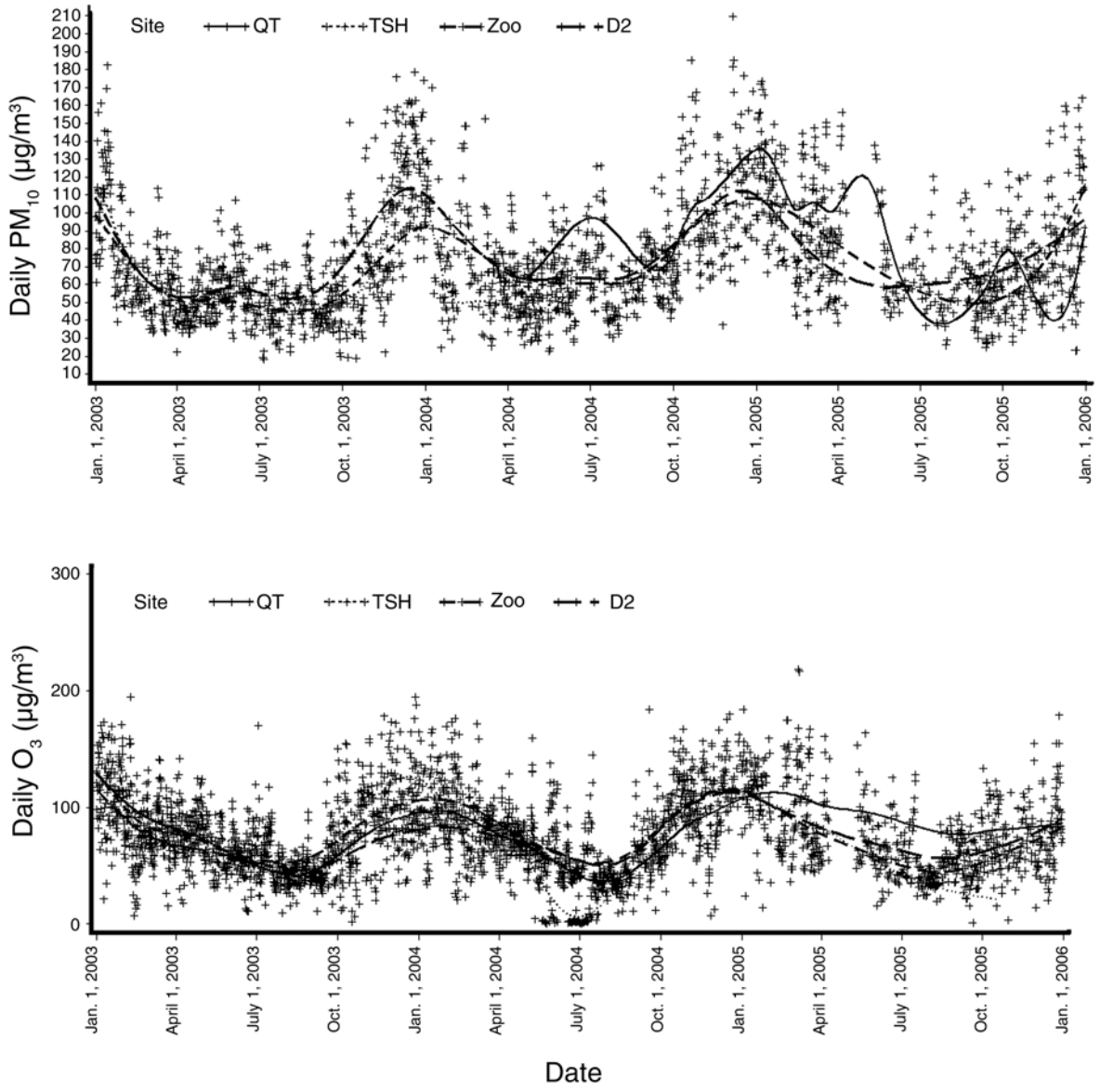

Figure 6. Mean daily pollutant concentrations, by monitoring station, 2003–2005. For each pollutant, only those stations that had sufficient data to be included in the final analysis are shown. (*Figure continues on next page*)

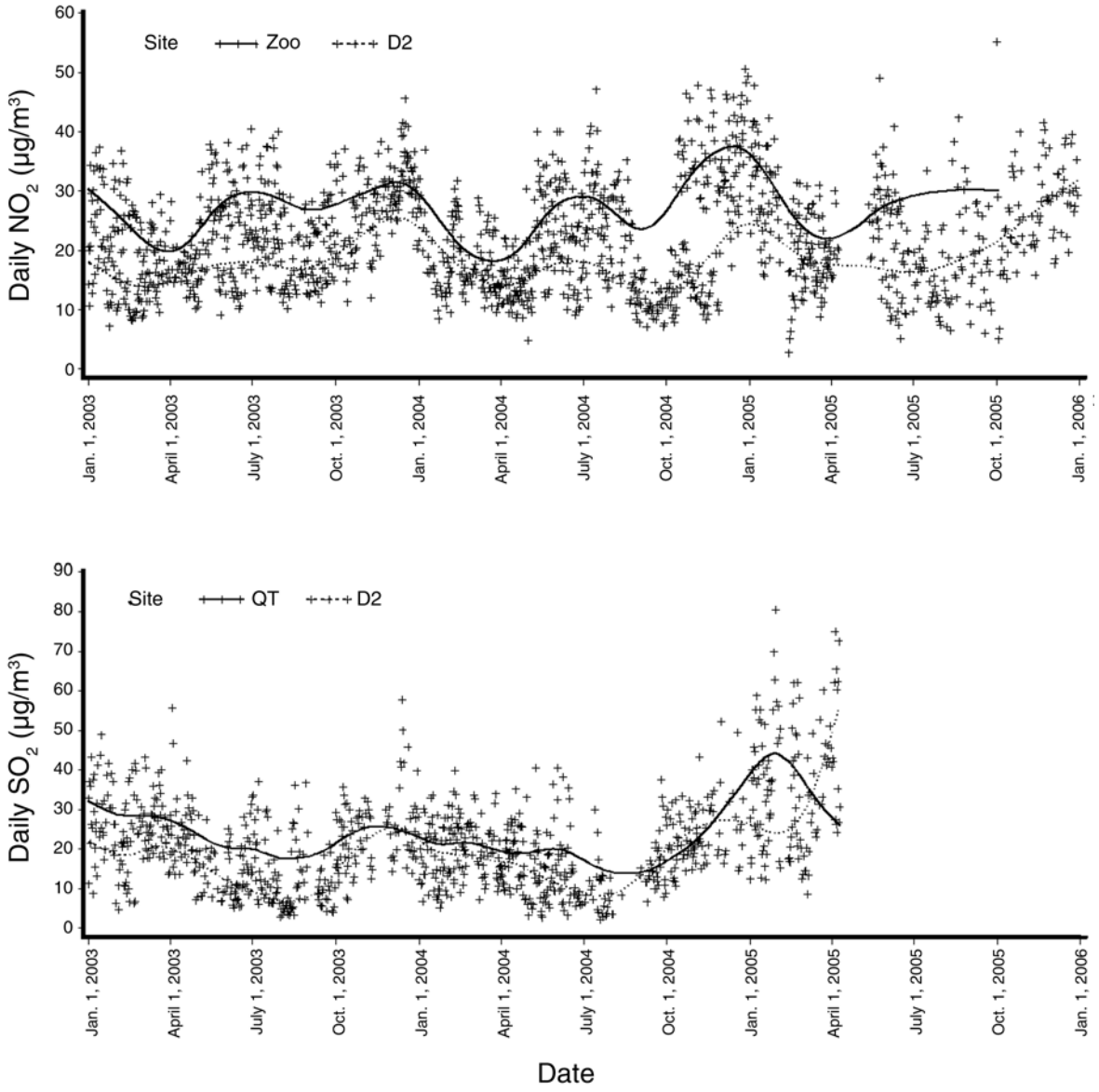

Figure 6 (*Continued*).

Table 15 and Figure 7 show the annual distributions of estimated pollutant concentrations citywide (across all monitoring stations), along with the total number of available daily data points, for the duration of the study. The seasonal trend in the data is evident, with pollutant levels at their highest in the dry season and lowest in the rainy season in HCMC. Mean daily concentrations for the dry season versus the rainy season were 83.6 versus 63.1 µg/m^3 for PM_{10}, 91.8 versus 59.0 µg/m^3 for O_3, 23.1 versus 21.2 µg/m^3 for NO_2, and 26.4 versus 15.0 µg/m^3 for SO_2. The concentrations of all four pollutants, and PM_{10} in particular, showed greater variability in the dry season.

During the dry season, correlations between levels of pollutants were high for PM_{10} and NO_2 (r = 0.78), high for

Table 14. Interstation Pollutant Concentration Correlations, Overall and by Season, 2003–2005

Pollutant	Station	D2	QT	Zoo	TSH
Overall					
PM_{10}	D2	1.00	0.60	0.81	0.75
	QT	0.60	1.00	0.71	0.15
	Zoo	0.81	0.71	1.00	0.66
	TSH	0.75	0.15	0.66	1.00
O_3	D2	1.00	0.67	0.82	0.51
	QT	0.67	1.00	0.68	0.59
	Zoo	0.82	0.68	1.00	0.59
	TSH	0.51	0.59	0.59	1.00
NO_2	D2	1.00	0.02	0.66	0.15
	QT	0.02	1.00	−0.21	0.39
	Zoo	0.66	−0.21	1.00	0.50
	TSH	0.15	0.39	0.50	1.00
SO_2	D2	1.00	0.27	—	0.09
	QT	0.27	1.00	—	0.03
	Zoo	—	—	—	—
	TSH	0.09	0.03	—	1.00
Dry Season					
PM_{10}	D2	1.00	0.60	0.78	0.76
	QT	0.60	1.00	0.61	0.07
	Zoo	0.78	0.61	1.00	0.64
	TSH	0.76	0.07	0.64	1.00
O_3	D2	1.00	0.57	0.77	0.38
	QT	0.57	1.00	0.62	0.34
	Zoo	0.77	0.62	1.00	0.42
	TSH	0.38	0.34	0.42	1.00
NO_2	D2	1.00	0.10	0.70	0.61
	QT	0.10	1.00	0.03	0.39
	Zoo	0.70	0.03	1.00	0.79
	TSH	0.61	0.39	0.79	1.00
SO_2	D2	1.00	0.15	—	0.29
	QT	0.15	1.00	—	0.14
	Zoo	—	—	—	—
	TSH	0.29	0.14	—	1.00
Rainy Season					
PM_{10}	D2	1.00	0.46	0.84	0.44
	QT	0.46	1.00	0.70	0.53
	Zoo	0.84	0.70	1.00	0.42
	TSH	0.44	0.53	0.42	1.00
O_3	D2	1.00	0.61	0.79	0.42
	QT	0.61	1.00	0.52	0.60
	Zoo	0.79	0.52	1.00	0.54
	TSH	0.42	0.60	0.54	1.00
NO_2	D2	1.00	0.48	0.63	−0.14
	QT	0.48	1.00	0.31	—
	Zoo	0.63	0.31	1.00	0.35
	TSH	−0.14	—	0.35	1.00
SO_2	D2	1.00	0.19	—	0.27
	QT	0.19	1.00	—	0.23
	Zoo	—	—	—	—
	TSH	0.27	0.23	—	1.00

Table 15. Distribution of Estimated Mean Daily Pollutant Concentrations (μg/m^3) Citywide, by Year, 2003–2005

Pollutant	Year	Mean	SD	*N*[a]	Median	Minimum	Maximum
Overall							
PM_{10}	2003	66.3	27.7	364	57.1	19.3	155.8
	2004	76.6	29.6	361	69.3	27.6	195.7
	2005	77.2	27.8	315	71.3	26.3	159.9
	Overall	73.2	28.8	1040	65.7	19.3	195.7
O_3	2003	75.0	28.5	365	72.5	17.0	157.4
	2004	75.8	31.7	365	74.8	21.7	162.3
	2005	74.2	30.7	327	68.2	25.6	184.8
	Overall	75.0	30.3	1057	70.9	17.0	184.8
NO_2	2003	22.4	6.3	359	21.1	10.2	43.5
	2004	21.3	8.3	361	20.0	7.1	50.6
	2005	22.7	8.3	302	21.9	5.0	55.2
	Overall	22.1	7.7	1022	20.9	5.0	55.2
SO_2	2003	20.5	9.5	325	20.6	2.8	57.7
	2004	18.3	8.1	305	18.0	2.7	52.3
	2005	36.5	13.2	90	35.2	12.5	80.4
	Overall	21.6	11.1	720	20.1	2.7	80.4
Dry Season							
PM_{10}	2003	78.5	31.5	181	67.8	34.3	155.8
	2004	82.8	31.6	177	76.8	32.2	195.7
	2005	90.7	27.3	153	88.1	36.6	159.9
	Overall	83.6	30.7	511	78.5	32.2	195.7
O_3	2003	91.9	24.9	181	89.7	22.8	157.4
	2004	93.5	25.1	181	90.1	41.8	162.3
	2005	89.8	32.4	154	82.9	27.9	184.8
	Overall	91.8	27.4	516	88.0	22.8	184.8
NO_2	2003	22.5	7.1	179	20.6	12.3	43.5
	2004	21.9	9.0	178	19.3	8.4	50.6
	2005	25.3	7.7	141	25.6	9.6	44.8
	Overall	23.1	8.1	498	21.0	8.4	50.6
SO_2	2003	26.0	7.8	164	25.0	6.3	57.7
	2004	21.1	7.4	162	20.7	6.0	52.3
	2005	36.5	13.2	90	35.2	12.5	80.4
	Overall	26.4	10.8	416	24.6	6.0	80.4
Rainy Season							
PM_{10}	2003	54.4	15.9	183	52.1	19.3	113.0
	2004	70.6	26.1	184	66.6	27.6	185.4
	2005	64.5	21.6	162	60.6	26.3	137.9
	Overall	63.1	22.6	529	59.1	19.3	185.4
O_3	2003	58.4	21.1	184	53.4	17.0	125.9
	2004	58.5	27.7	184	50.1	21.7	143.2
	2005	60.2	20.8	173	56.7	25.6	125.4
	Overall	59.0	23.4	541	53.9	17.0	143.2
NO_2	2003	22.2	5.4	180	21.4	10.2	37.6
	2004	20.8	7.5	183	20.8	7.1	40.2
	2005	20.5	8.3	161	19.5	5.0	55.2
	Overall	21.2	7.1	524	20.8	5.0	55.2
SO_2	2003	14.9	7.5	161	14.1	2.8	36.7
	2004	15.1	7.7	143	13.8	2.7	37.5
	2005	—	—	—	—	—	—
	Overall	15.0	7.6	304	14.0	2.7	37.4

[a] *N* is the number of days with available data.

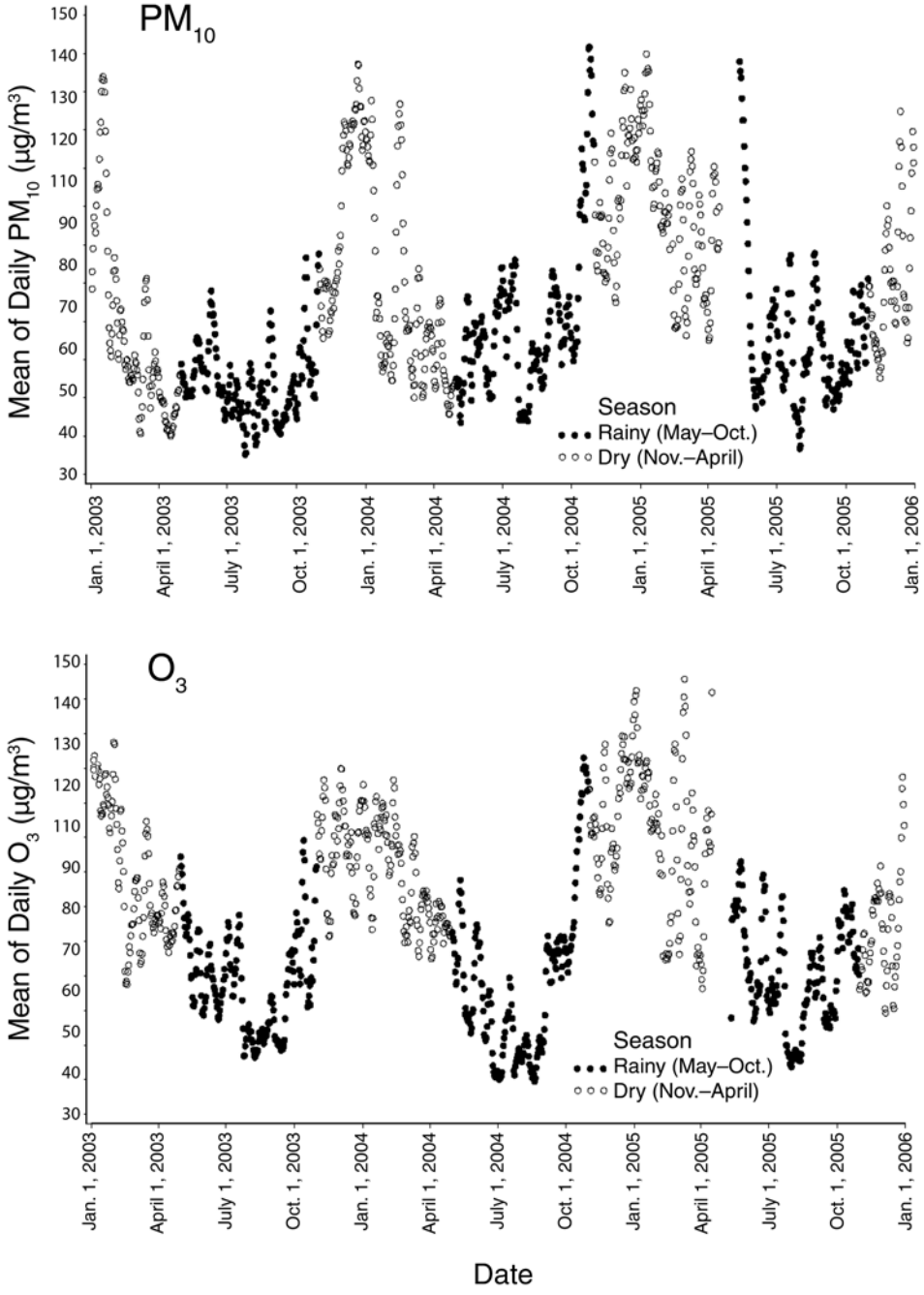

Figure 7. Mean of daily average pollutant concentrations for average lag (1–6 days), citywide estimate, 2003–2005. (*Figure continues on next page*)

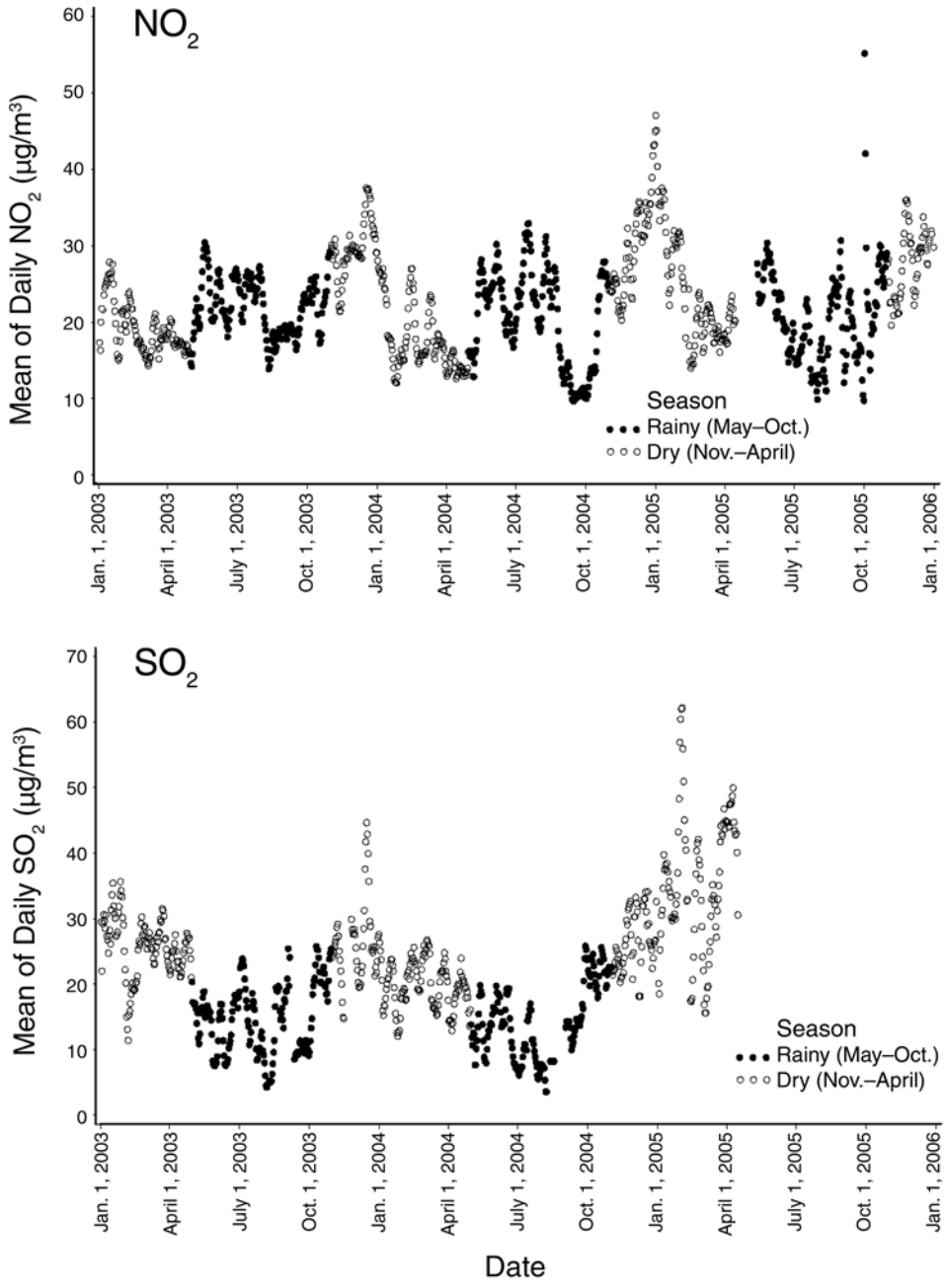

Figure 7 (*Continue*d).

PM_{10} and O_3 ($r = 0.66$), and fair for PM_{10} and SO_2 ($r = 0.32$) (Table 16). Figure 7 shows the time-series plots of daily average concentrations for 2003, 2004, and 2005. During the rainy season, correlations between values for the pollutants were considerable for PM_{10} and O_3 ($r = 0.60$) and for O_3 and SO_2 (0.65), fair for PM_{10} and SO_2 (0.36), but limited between other pollutants.

The time-series plots indicate that the dry season arrived slightly earlier than expected in October 2004, and that it lasted longer than expected, through May 2005. The impact of reclassifying these periods in October 2004 and May 2005 from the rainy season to the dry season was addressed in the sensitivity analyses.

Table 16. Interpollutant Correlations, by Season, 2003–2005

Pollutant	PM_{10}	O_3	NO_2	SO_2
Dry Season				
PM_{10}	1.00	0.66	0.78	0.32
O_3	0.66	1.00	0.44	0.19
NO_2	0.78	0.44	1.00	0.29
SO_2	0.32	0.19	0.29	1.00
Rainy Season				
PM_{10}	1.00	0.60	0.18	0.36
O_3	0.60	1.00	0.17	0.65
NO_2	0.18	0.17	1.00	0.01
SO_2	0.36	0.65	0.01	1.00

Meteorologic Data

Overall distributions indicate symmetry in the meteorologic data, so we report only the mean (i.e., not the median) of yearly, monthly, and seasonal distributions. Table 17 summarizes the distribution of temperature, relative humidity, and rainfall by year, month, and season. The seasonal definition used is consistent with the rainfall experienced during the study period. The average daily temperature in HCMC ranges from 23°C to 32°C, and the average daily relative humidity is consistently high, ranging from 51% to 93%. Figures 8 and 9 show time-series plots of daily temperature and relative humidity in HCMC throughout the study period. The observed seasonal variation corresponds to the dry and rainy seasons.

Figure 10 shows the correlation between mean daily temperature and relative humidity. The two are negatively correlated, with average daily relative humidity declining alongside increases in average daily temperature (Table 18).

SOCIOECONOMIC DATA

Individual-Level Indicator of SEP

More than 93% of the clinical records of patients admitted for ALRI were linked with financial records, as described in Figure 4. From the information on payment status in the patients' financial records, summarized in Table 6, only approximately 1% of case subjects were classified as poor, which is much lower than the reported poverty prevalence in the city as a whole (discussed below under "District-Level Indicator of SEP"). According to the hospital administrators, the low percentage was most likely due to the fact that many people believe they will receive better health care with payment and find ways to pay in full even when they may be eligible for free care or reduced fees.

The ratio of males to females remained relatively constant for the poor versus other patients. The age distribution was somewhat different, however, with 44% of the poor children admitted in the age group less than 1 year, compared with 32% of the nonpoor children (see Table 9).

Duration of Stay The mean duration of stay for the poor was longer in both hospitals. This may indicate that the poor children were admitted with more severe forms of illness. Data on length of stay are generally quite positively skewed, however, so the median is likely a more appropriate summary measure to consider. The median length of stay was 8 and 9 days for poor children admitted to CH1 and CH2, respectively, compared with 7 days for the children who were not poor (see Table 10).

Validation of Individual Poverty Status The information we used to classify a patient as poor would certainly misclassify a large proportion of the poor as nonpoor; however, those that we classified as poor are likely to be among the poorest of the poor.

As insurance cards were presented for only 67 of the ALRI case subjects at the pediatric hospitals during the study period, we attempted to validate the SEP classification system by manually linking cases to the DOLISA database, which contains information on all families officially classified as poor by the government. A list including information on all ALRI case subjects classified as poor from the hospital financial records and 50 ALRI case subjects per year from each hospital was provided to DOLISA for cross-checking. DOLISA was only able to identify 22 cases within its database, however, all of whom were already classified as poor according to the hospital financial records.

Table 17. Average Temperature, Relative Humidity, and Rainfall, by Year, Month, and Season, 2003–2005

Variable / Time Period	*N*	Mean	SD	Minimum	Maximum
Temperature (°C)					
2003	365	28.3	1.4	24.6	31.7
2004	366	28.2	1.3	25.4	32.0
2005	365	28.1	1.5	23.1	31.8
January	93	26.9	0.9	24.6	28.7
February	85	27.7	0.9	25.9	29.8
March	93	28.9	0.8	25.4	30.9
April	90	30.2	0.6	28.6	31.7
May	93	29.4	1.3	26.5	32.0
June	89	28.9	1.3	26.0	31.2
July	93	27.9	1.1	25.4	30.4
August	93	28.2	1.2	24.8	30.5
September	90	28.0	1.1	24.7	29.9
October	93	27.7	1.0	25.4	29.7
November	90	27.9	0.9	24.8	29.7
December	93	26.7	1.1	23.1	28.7
Dry season	544	28.1	1.5	23.1	31.7
Rainy season	551	28.3	1.3	24.7	32.0
Relative Humidity (%)					
2003	365	72.9	7.7	53.7	90.6
2004	366	74.2	7.4	51.1	93.4
2005	365	74.0	7.4	90.7	90.7
January	93	67.7	4.1	58.0	77.3
February	85	66.6	5.5	54.0	77.5
March	93	66.4	6.4	51.0	80.0
April	90	68.6	3.7	59.3	77.3
May	93	74.7	5.9	60.0	91.0
June	90	76.7	4.9	65.4	88.5
July	93	79.2	5.1	66.8	92.1
August	93	78.4	5.8	65.0	93.4
September	90	79.5	6.4	65.5	91.0
October	93	79.7	5.5	67.1	90.9
November	90	75.1	6.0	61.4	88.0
December	93	71.5	6.5	56.0	87.8
Dry season	544	69.3	6.3	51.0	88.0
Rainy season	552	78.0	5.9	60.0	93.4
Rainfall (cm)					
2003	365	4.9	12.4	3.2	91.7
2004	366	4.9	12.7	2.6	112.3
2005	365	4.8	11.7	4.6	114.4
January	93	0.0	0.4	0.0	3.5
February	85	0.0	0.0	0.0	0.0
March	93	0.0	0.1	0.0	0.5
April	90	0.3	1.6	0.0	11.6
May	93	7.6	15.9	0.0	112.3
June	90	9.4	19.8	0.0	114.4
July	93	8.4	13.8	0.0	73.8
August	93	5.9	9.6	0.0	59.8
September	90	8.5	16.7	0.0	91.7
October	93	11.2	16.4	0.0	72.7
November	90	5.1	11.1	0.0	64.4
December	93	1.3	3.7	0.0	22.5
Dry season	544	1.1	5.2	0.0	64.4
Rainy season	552	8.5	15.7	0.0	114.4

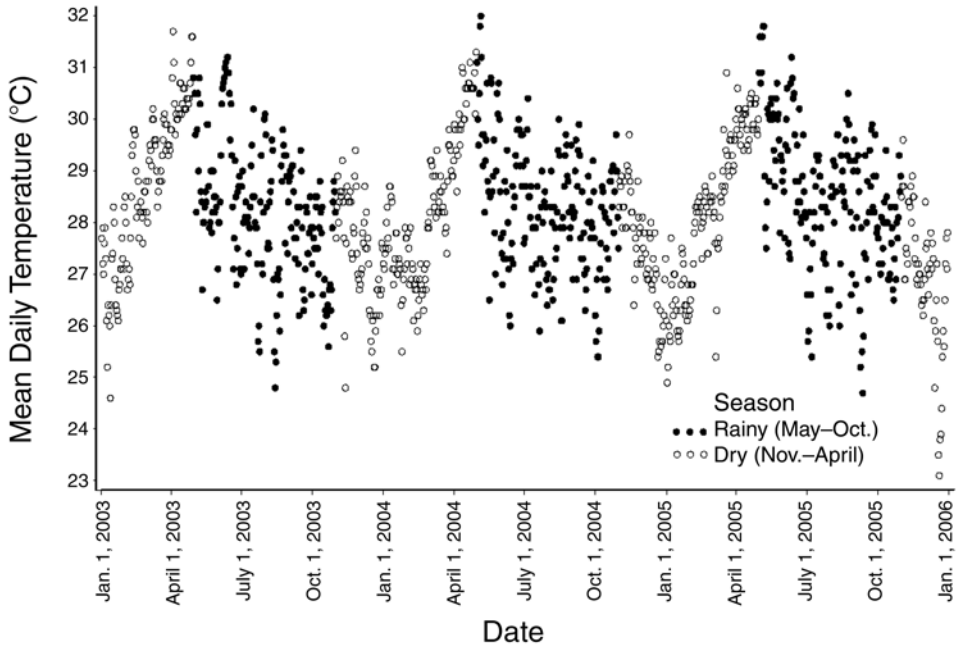

Figure 8. Mean daily temperature, 2003–2005.

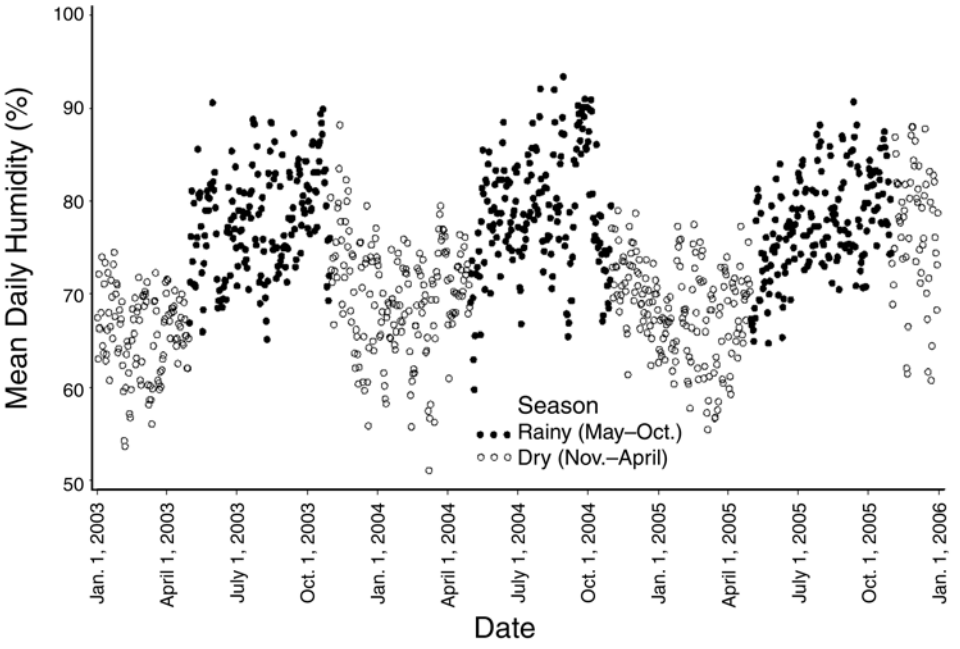

Figure 9. Mean daily relative humidity, 2003–2005.

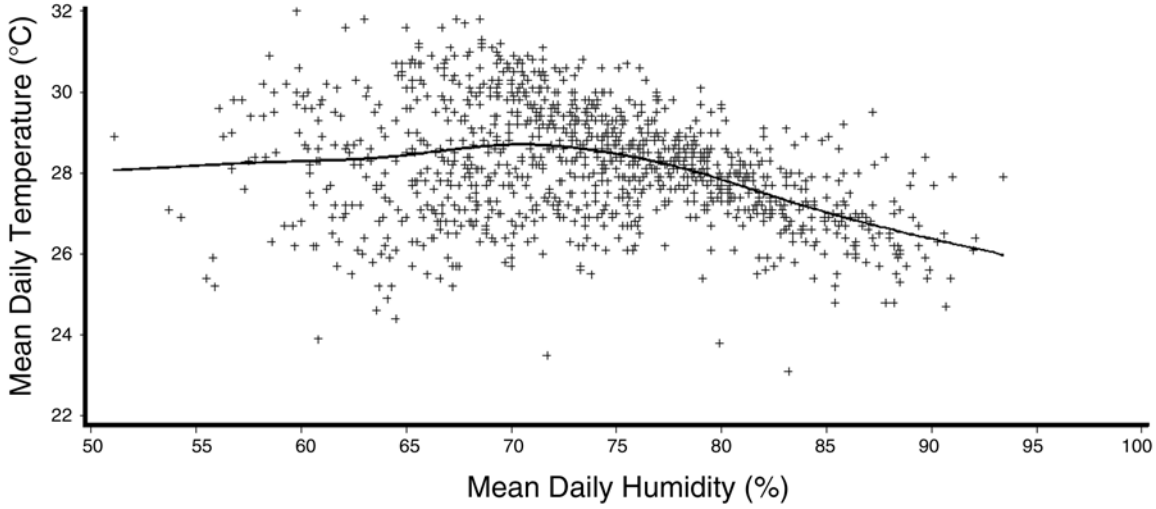

Figure 10. Mean daily temperature versus relative humidity, 2003–2005.

Table 18. Correlation Between Mean Daily Temperature and Relative Humidity, 2003–2005

Variable	*N*	Mean	SD	Minimum	Maximum
Temperature (°C)	1095	28.2	1.4	23.1	32.0
Relative humidity (%)	1096	73.7	7.5	51.0	93.4

Pearson correlation coefficient for temperature and relative humidity: −0.31.
Probability > |*r*| under H0 (ρ = 0): $P < 0.0001$.[a]

[a] Probability of observing this correlation coefficient or one more extreme under the null hypothesis (H0) that the correlation (ρ) is 0.

District-Level Indicator of SEP

Poverty prevalence in the districts of HCMC, with poverty defined on the basis of annual income limits of 4 million VND (a measure in use at the beginning of the study period) or 6 million VND (set by People's Committee Decision 145/2004/QD-UB on May 25, 2004, as part of a poverty reduction strategy for HCMC) are shown in Table 19. The 2004 poverty rate of HCMC (all districts) was 2.6% when based on the 4 million VND poverty line and 10.2% when based on the 6 million VND poverty line. District 1 had the lowest poverty level, and many districts had poverty prevalence greater than 10% according to the 6 million VND limit.

Quartiles of district-level poverty prevalence were created from the poverty prevalence estimates after removal of the five rural districts. The central districts of HCMC are in SEP quartiles 1 and 2, the two highest quartiles; in other words, they have the lowest district-level poverty prevalence. The districts on the periphery are in SEP quartiles 3 and 4, the two lowest quartiles as defined by district-level poverty prevalence (Table 20 and Figure 11). Yearly distributions of ALRI hospital admissions by quartile of SEP are provided in Table 21.

The mean age of case subjects was slightly lower in the poorest quartile, although the standard deviations overlap. Few differences in distribution by sex, mean age, or length of stay were observed (see Tables 9 and 10).

Table 19. District-Level Poverty Prevalence in 2004[a]

District	Poverty Line of 4 Million VND		Poverty Line of 6 Million VND	
	Poverty Prevalence (%)	SE	Poverty Prevalence (%)	SE
All Districts	2.56	0.65	10.22	1.96
Urban Districts				
District 1	0.91	0.45	4.56	1.54
District 2	2.83	1.10	11.06	3.00
District 3	1.33	0.60	5.26	1.66
District 4	3.03	1.22	11.37	3.12
District 5	1.14	0.56	5.52	1.80
District 6	2.33	0.88	9.40	2.54
District 7	2.49	0.95	9.87	2.78
District 8	3.46	1.15	12.29	2.94
District 9	1.96	0.82	9.11	2.64
District 10	1.45	0.61	6.32	1.92
District 11	2.06	0.81	8.96	2.47
District 12	2.69	0.99	11.66	3.01
Go Vap	1.89	0.74	8.31	2.30
Tan Binh	1.48	0.62	6.77	1.98
Tan Phu	1.75	0.74	7.81	2.26
Binh Thanh	1.98	0.77	7.78	2.14
Phu Nhuan	1.35	0.58	6.01	1.77
Thu Duc	2.25	0.85	9.76	2.59
Binh Tan	2.69	1.01	11.45	3.03
Rural Districts				
Huyen Cu Chi	5.31	1.70	19.32	4.20
Huyen Hoc Mon	3.75	1.32	14.00	3.34
Huyen Binh Chanh	4.29	1.41	16.12	3.62
Huyen Nha Be	6.36	1.72	20.56	3.68
Huyen Can Gio	10.53	2.82	30.57	5.15

[a] Based on small area estimation (HCMC Bureau of Statistics 2005).

Table 20. Quartiles of SEP, Based on 2004 District-Level Poverty Prevalence[a]

SEP Quartile	District	Poverty Prevalence[a] (%)	SE
1	District 1	4.56	1.54
1	District 3	5.26	1.66
1	District 5	5.52	1.80
1	Phu Nhuan	6.01	1.77
1	District 10	6.32	1.92
2	Tan Binh	6.77	1.98
2	Binh Thanh	7.78	2.14
2	Tan Phu	7.81	2.26
2	Go Vap	8.31	2.30
3	District 11	8.96	2.47
3	District 9	9.11	2.64
3	District 6	9.40	2.54
3	Thu Duc	9.76	2.59
3	District 7	9.87	2.78
4	District 2	11.06	3.00
4	District 4	11.37	3.12
4	Binh Tan	11.45	3.03
4	District 12	11.66	3.01
4	District 8	12.29	2.94

[a] Based on poverty line = 6 million VND.

STATISTICAL ANALYSES

PRESENTATION OF RESULTS

All excess risk estimates and confidence intervals are reported per increase of 10 μg/m^3 in pollutant concentrations.

As the time between onset of illness and hospital admission was thought to range from 1 to 6 days, it was not possible to specify a priori a single-day lag. On the basis of typical referral patterns and pathways to hospital admission, the relevant window of exposure was thought to be within the week before hospital admission, in other words, 1 to 6 days before the date of admission. We assessed results for single-day lags from lag 0 through lag 10 days (Tables 22 and 23; Figures 12 and 13), but emphasize results for the average lag (1–6 days), since this best reflects the case reference period. These results take into account pollution levels in the 1 to 6 days leading up to admission. All results were calculated using lag 0 for temperature; the sensitivity of results to this assumption is explored in the section on sensitivity analyses.

To facilitate comparison with the preponderance of published time-series and case–crossover studies, we present time-series results based on R analyses and case–crossover results based on SAS analyses in the main body of the text.

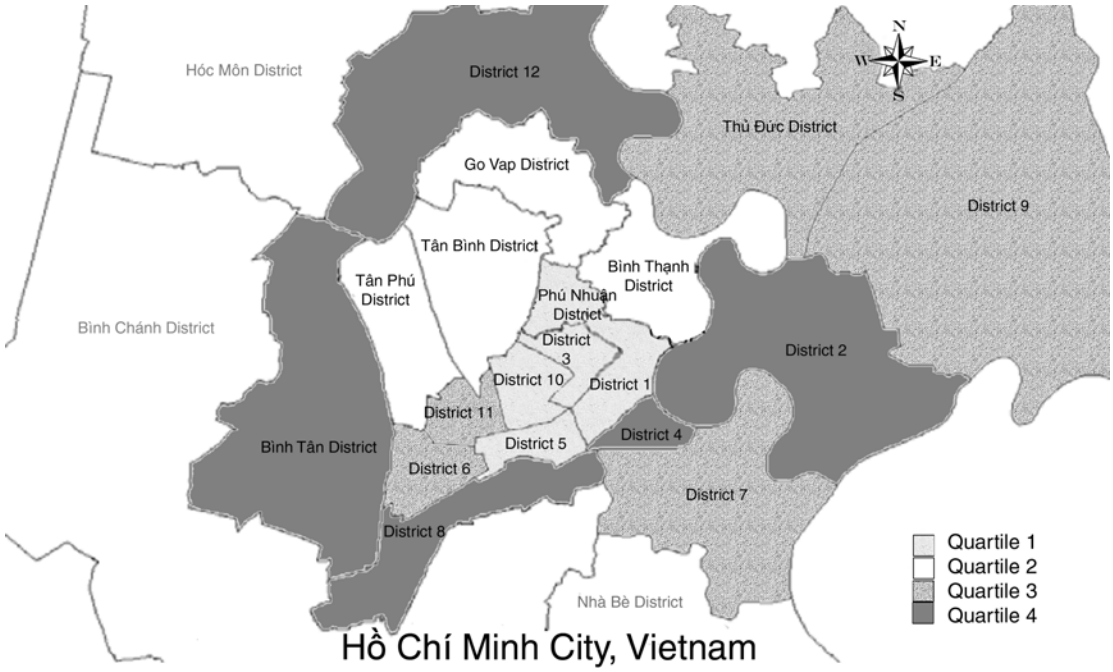

Figure 11. Map of HCMC districts showing quartiles of SEP, based on 2004 district-level poverty prevalence. Five districts are in SEP quartile 1, four in quartile 2, five in quartile 3, and five in quartile 4.

Table 21. Annual ALRI Admissions, Sex, and Age Distribution by District-Level SEP Quartile, 2003–2005[a]

Annual ALRI Admissions by SEP Quartile, 2003–2005

Quartile	*N*	2003, % (*N*)	2004, % (*N*)	2005, % (*N*)
1	4,618	37.22 (1719)	31.20 (1441)	31.57 (1458)
2	5,474	35.18 (1926)	27.79 (1521)	37.03 (2027)
3	4,976	32.36 (1610)	29.90 (1488)	37.74 (1878)
4	640	35.78 (229)	31.25 (200)	32.97 (211)
Overall	15,708	34.91 (5484)	29.60 (4650)	35.49 (5574)

ALRI Patients by Sex and SEP Quartile, 2003–2005

Quartile	*N*	Male, % (*N*)	Female, % (*N*)
1	4,618	67.04 (3096)	32.96 (1522)
2	5,474	62.97 (3447)	37.03 (2027)
3	4,976	64.39 (3204)	35.61 (1772)
4	640	67.19 (430)	32.81 (210)
Overall	15,708	64.79 (10,177)	35.21 (5531)

Age Distribution of Patients Within SEP Quartiles, 2003–2005

Quartile	*N*	Mean	SD	Median	Minimum	Maximum
1	4618	1.07	1.04	1	0	5
2	5474	1.09	1.05	1	0	5
3	4976	1.09	1.03	1	0	5
4	640	0.82	0.93	1	0	5

[a] Quartile 1 is the highest quartile of SEP.

Table 22. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, for Multiple Lags of 0–10 Days and Average Lag (1–6 Days), Based on Case–Crossover Analyses

Pollutant / Lag Days	Overall	Dry Season	Rainy Season
PM_{10}			
Lag 0	0.40 (−0.51 to 1.32)	1.57 (0.21 to 2.94)	−0.57 (−1.83 to 0.72)
Lag 1	−0.11 (−1.02 to 0.80)	0.97 (−0.37 to 2.32)	−1.02 (−2.28 to 0.25)
Lag 2	−0.28 (−1.16 to 0.62)	1.36 (0.06 to 2.68)	−1.74 (−2.96 to −0.49)
Lag 3	−1.21 (−2.07 to −0.34)	0.66 (−0.59 to 1.94)	−2.90 (−4.09 to −1.70)
Lag 4	−1.12 (−1.97 to −0.26)	0.39 (−0.85 to 1.64)	−2.52 (−3.71 to −1.32)
Lag 5	−0.93 (−1.80 to −0.05)	−0.42 (−1.65 to 0.83)	−1.43 (−2.67 to −0.17)
Lag 6	0.63 (−0.26 to 1.53)	1.15 (−0.08 to 2.39)	0.12 (−1.19 to 1.44)
Lag 7	0.77 (−0.12 to 1.67)	1.33 (0.10 to 2.59)	0.21 (−1.08 to 1.51)
Lag 8	−0.29 (−1.18 to 0.60)	0.30 (−0.93 to 1.54)	−0.94 (−2.23 to 0.37)
Lag 9	0.10 (−0.80 to 1.00)	1.26 (0.03 to 2.51)	−1.22 (−2.54 to 0.11)
Lag 10	−0.08 (−0.99 to 0.85)	0.82 (−0.42 to 2.07)	−1.15 (−2.52 to 0.23)
Average lag 1–6	−1.10 (−2.31 to 0.12)	1.25 (−0.55 to 3.09)	−3.11 (−4.76 to −1.42)
O_3			
Lag 0	−0.16 (−1.03 to 0.71)	1.06 (−0.16 to 2.29)	−1.41 (−2.65 to −0.16)
Lag 1	−0.51 (−1.37 to 0.36)	0.08 (−1.13 to 1.30)	−1.07 (−2.31 to 0.17)
Lag 2	−1.37 (−2.21 to −0.52)	−0.78 (−1.97 to 0.42)	−1.94 (−3.15 to −0.72)
Lag 3	−1.15 (−1.98 to −0.31)	−0.28 (−1.45 to 0.90)	−2.04 (−3.24 to −0.83)
Lag 4	−0.72 (−1.56 to 0.13)	0.25 (−0.90 to 1.42)	−1.80 (−3.03 to −0.56)
Lag 5	−0.73 (−1.57 to 0.12)	−0.29 (−1.45 to 0.88)	−1.20 (−2.43 to 0.05)
Lag 6	−0.40 (−1.24 to 0.45)	−0.50 (−1.66 to 0.67)	−0.26 (−1.47 to 0.97)
Lag 7	−0.36 (−1.20 to 0.50)	−0.61 (−1.77 to 0.56)	−0.06 (−1.30 to 1.21)
Lag 8	−1.09 (−1.95 to −0.23)	−0.69 (−1.85 to 0.48)	−1.60 (−2.88 to −0.30)
Lag 9	−0.79 (−1.66 to 0.08)	0.27 (−0.91 to 1.46)	−2.16 (−3.46 to −0.85)
Lag 10	−1.06 (−1.92 to −0.19)	−0.75 (−1.91 to 0.43)	−1.49 (−2.78 to −0.17)
Average lag 1–6	−1.96 (−3.25 to −0.64)	−0.79 (−2.67 to 1.13)	−2.98 (−4.78 to −1.14)
NO_2			
Lag 0	−1.64 (−4.83 to 1.66)	5.15 (−0.96 to 11.64)	−4.47 (−8.19 to −0.60)
Lag 1	−1.11 (−4.25 to 2.14)	3.18 (−2.53 to 9.22)	−3.04 (−6.78 to 0.86)
Lag 2	−0.04 (−3.14 to 3.16)	6.21 (0.40 to 12.37)	−2.64 (−6.28 to 1.15)
Lag 3	−0.83 (−3.85 to 2.30)	8.49 (2.60 to 14.71)	−4.61 (−8.12 to −0.97)
Lag 4	−0.64 (−3.62 to 2.44)	4.98 (−0.60 to 10.87)	−2.92 (−6.45 to 0.74)
Lag 5	−1.10 (−4.08 to 1.97)	2.64 (−2.75 to 8.32)	−2.70 (−6.29 to 1.02)
Lag 6	1.74 (−1.29 to 4.86)	4.40 (−0.99 to 10.08)	0.70 (−3.02 to 4.55)
Lag 7	2.47 (−0.58 to 5.61)	5.25 (−0.12 to 10.92)	1.42 (−2.35 to 5.33)
Lag 8	−0.21 (−3.20 to 2.88)	3.26 (−2.03 to 8.83)	−1.77 (−5.41 to 2.02)
Lag 9	−1.81 (−4.77 to 1.23)	2.05 (−3.26 to 7.65)	−3.55 (−7.10 to 0.14)
Lag 10	0.51 (−2.52 to 3.64)	2.49 (−2.94 to 8.21)	−0.36 (−4.00 to 3.41)
Average lag 1–6	−1.08 (−5.14 to 3.17)	8.50 (0.80 to 16.79)	−5.15 (−9.94 to −0.10)
SO_2			
Lag 0	−1.36 (−4.25 to 1.62)	0.40 (−3.47 to 4.43)	−4.00 (−8.39 to 0.61)
Lag 1	0.11 (−2.88 to 3.19)	1.39 (−2.62 to 5.56)	−1.71 (−6.19 to 2.97)
Lag 2	−0.57 (−3.48 to 2.43)	1.67 (−2.29 to 5.79)	−3.44 (−7.69 to 1.01)
Lag 3	1.19 (−1.75 to 4.22)	2.22 (−1.76 to 6.37)	−0.12 (−4.43 to 4.39)
Lag 4	1.74 (−1.26 to 4.82)	4.00 (−0.08 to 8.24)	−1.12 (−5.47 to 3.43)
Lag 5	0.71 (−2.25 to 3.77)	3.04 (−1.00 to 7.26)	−2.07 (−6.38 to 2.43)
Lag 6	1.67 (−1.39 to 4.83)	4.41 (0.21 to 8.78)	−1.42 (−5.90 to 3.28)
Lag 7	1.70 (−1.37 to 4.86)	4.02 (−0.18 to 8.41)	−0.88 (−5.36 to 3.81)
Lag 8	−1.14 (−4.17 to 1.98)	2.57 (−1.60 to 6.92)	−5.50 (−9.89 to −0.91)
Lag 9	−2.60 (−5.62 to 0.51)	−0.86 (−4.91 to 3.36)	−4.57 (−9.09 to 0.18)
Lag 10	−4.79 (−7.73 to −1.77)	−4.02 (−7.93 to 0.07)	−5.51 (−9.97 to −0.83)
Average lag 1–6	2.61 (−1.49 to 6.87)	5.85 (0.44 to 11.55)	−2.13 (−8.25 to 4.41)

Table 23. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, for Multiple Lags of 0–10 Days and Average Lag (1–6 Days), Based on Time-Series Analyses

Pollutant / Lag Days	Overall	Dry Season	Rainy Season
PM_{10}			
Lag 0	0.53 (−0.31 to 1.38)	0.33 (−0.96 to 1.64)	−0.14 (−1.34 to 1.08)
Lag 1	0.22 (−0.61 to 1.07)	0.48 (−0.80 to 1.77)	−0.82 (−2.02 to 0.40)
Lag 2	0.60 (−0.23 to 1.43)	1.07 (−0.17 to 2.33)	−0.79 (−1.99 to 0.44)
Lag 3	−0.39 (−1.21 to 0.43)	0.31 (−0.92 to 1.56)	−2.30 (−3.48 to −1.10)
Lag 4	−0.25 (−1.06 to 0.57)	−0.28 (−1.50 to 0.95)	−1.46 (−2.65 to −0.25)
Lag 5	−0.33 (−1.14 to 0.49)	−1.14 (−2.34 to 0.08)	−0.73 (−1.94 to 0.50)
Lag 6	0.83 (0.01 to 1.65)	0.23 (−0.97 to 1.43)	0.70 (−0.56 to 1.97)
Lag 7	0.90 (0.09 to 1.72)	0.62 (−0.56 to 1.82)	0.89 (−0.38 to 2.17)
Lag 8	−0.12 (−0.93 to 0.70)	−0.28 (−1.47 to 0.93)	−0.85 (−2.09 to 0.41)
Lag 9	0.50 (−0.32 to 1.32)	0.91 (−0.30 to 2.13)	−0.78 (−2.02 to 0.47)
Lag 10	−0.17 (−0.99 to 0.66)	0.13 (−1.07 to 1.34)	−1.35 (−2.59 to −0.09)
Average lag 1–6	0.26 (−0.94 to 1.47)	0.53 (−1.46 to 2.56)	−2.58 (−4.44 to −0.68)
O_3			
Lag 0	0.18 (−0.63 to 0.99)	0.93 (−0.21 to 2.08)	−0.49 (−1.71 to 0.74)
Lag 1	0.03 (−0.75 to 0.82)	0.64 (−0.48 to 1.77)	−0.52 (−1.70 to 0.67)
Lag 2	−0.43 (−1.21 to 0.35)	−0.03 (−1.14 to 1.09)	−0.92 (−2.08 to 0.26)
Lag 3	−0.18 (−0.97 to 0.61)	0.61 (−0.52 to 1.74)	−1.13 (−2.30 to 0.04)
Lag 4	−0.21 (−0.99 to 0.58)	0.70 (−0.42 to 1.84)	−1.24 (−2.41 to −0.06)
Lag 5	−0.64 (−1.41 to 0.15)	−0.18 (−1.28 to 0.93)	−1.07 (−2.23 to 0.10)
Lag 6	−0.44 (−1.22 to 0.35)	−0.44 (−1.54 to 0.68)	−0.31 (−1.48 to 0.87)
Lag 7	−0.24 (−1.03 to 0.55)	−0.36 (−1.45 to 0.75)	0.28 (−0.92 to 1.48)
Lag 8	−0.95 (−1.73 to −0.16)	−0.24 (−1.33 to 0.86)	−1.59 (−2.78 to −0.39)
Lag 9	−0.80 (−1.58 to −0.01)	0.27 (−0.83 to 1.38)	−1.74 (−2.95 to −0.52)
Lag 10	−0.97 (−1.75 to −0.18)	−0.52 (−1.61 to 0.59)	−1.07 (−2.28 to 0.15)
Average lag 1–6	−0.98 (−2.30 to 0.35)	0.47 (−1.56 to 2.54)	−2.33 (−4.26 to −0.36)
NO_2			
Lag 0	0.01 (−3.03 to 3.14)	0.33 (−5.25 to 6.24)	−2.02 (−5.69 to 1.79)
Lag 1	1.00 (−1.98 to 4.08)	2.63 (−2.81 to 8.38)	−1.52 (−5.18 to 2.29)
Lag 2	3.87 (0.87 to 6.96)	6.19 (0.59 to 12.09)	0.98 (−2.67 to 4.77)
Lag 3	1.55 (−1.41 to 4.60)	7.48 (1.85 to 13.43)	−3.43 (−6.98 to 0.25)
Lag 4	1.53 (−1.40 to 4.54)	4.36 (−1.11 to 10.13)	−1.81 (−5.40 to 1.91)
Lag 5	0.74 (−2.17 to 3.74)	1.91 (−3.42 to 7.54)	−2.36 (−5.95 to 1.37)
Lag 6	2.75 (−0.20 to 5.79)	2.98 (−2.37 to 8.63)	0.44 (−3.26 to 4.28)
Lag 7	2.55 (−0.41 to 5.59)	1.98 (−3.30 to 7.54)	0.83 (−2.92 to 4.73)
Lag 8	0.11 (−2.80 to 3.12)	0.81 (−4.40 to 6.30)	−3.02 (−6.67 to 0.77)
Lag 9	−0.40 (−3.29 to 2.57)	0.04 (−5.14 to 5.50)	−3.53 (−7.13 to 0.21)
Lag 10	1.24 (−1.72 to 4.28)	−1.24 (−6.33 to 4.12)	−0.25 (−4.00 to 3.66)
Average lag 1–6	4.32 (0.04 to 8.79)	12.62 (3.91 to 22.05)	−3.29 (−8.51 to 2.23)
SO_2			
Lag 0	−0.06 (−2.87 to 2.84)	−2.67 (−6.28 to 1.08)	2.04 (−2.81 to 7.14)
Lag 1	1.30 (−1.49 to 4.18)	0.15 (−3.57 to 4.01)	0.43 (−4.16 to 5.24)
Lag 2	0.44 (−2.30 to 3.26)	−0.37 (−4.02 to 3.42)	−0.61 (−5.16 to 4.15)
Lag 3	2.67 (−0.13 to 5.55)	1.18 (−2.53 to 5.04)	1.92 (−2.74 to 6.81)
Lag 4	2.90 (0.12 to 5.76)	2.79 (−0.94 to 6.66)	2.26 (−2.42 to 7.18)
Lag 5	1.75 (−1.01 to 4.58)	2.64 (−1.12 to 6.55)	−0.68 (−5.20 to 4.04)
Lag 6	1.82 (−0.97 to 4.68)	2.64 (−1.12 to 6.55)	−0.77 (−5.04 to 3.69)
Lag 7	1.50 (−1.31 to 4.39)	2.19 (−1.64 to 6.18)	−0.66 (−4.98 to 3.85)
Lag 8	0.16 (−2.61 to 3.01)	1.99 (−1.81 to 5.95)	−4.36 (−8.61 to 0.10)
Lag 9	−1.58 (−4.30 to 1.22)	−1.36 (−5.01 to 2.43)	−3.92 (−8.24 to 0.60)
Lag 10	−2.26 (−4.99 to 0.55)	−1.93 (−5.63 to 1.92)	−3.00 (−7.22 to 1.42)
Average lag 1–6	4.98 (0.83 to 9.31)	4.21 (−1.37 to 10.10)	2.70 (−4.88 to 10.88)

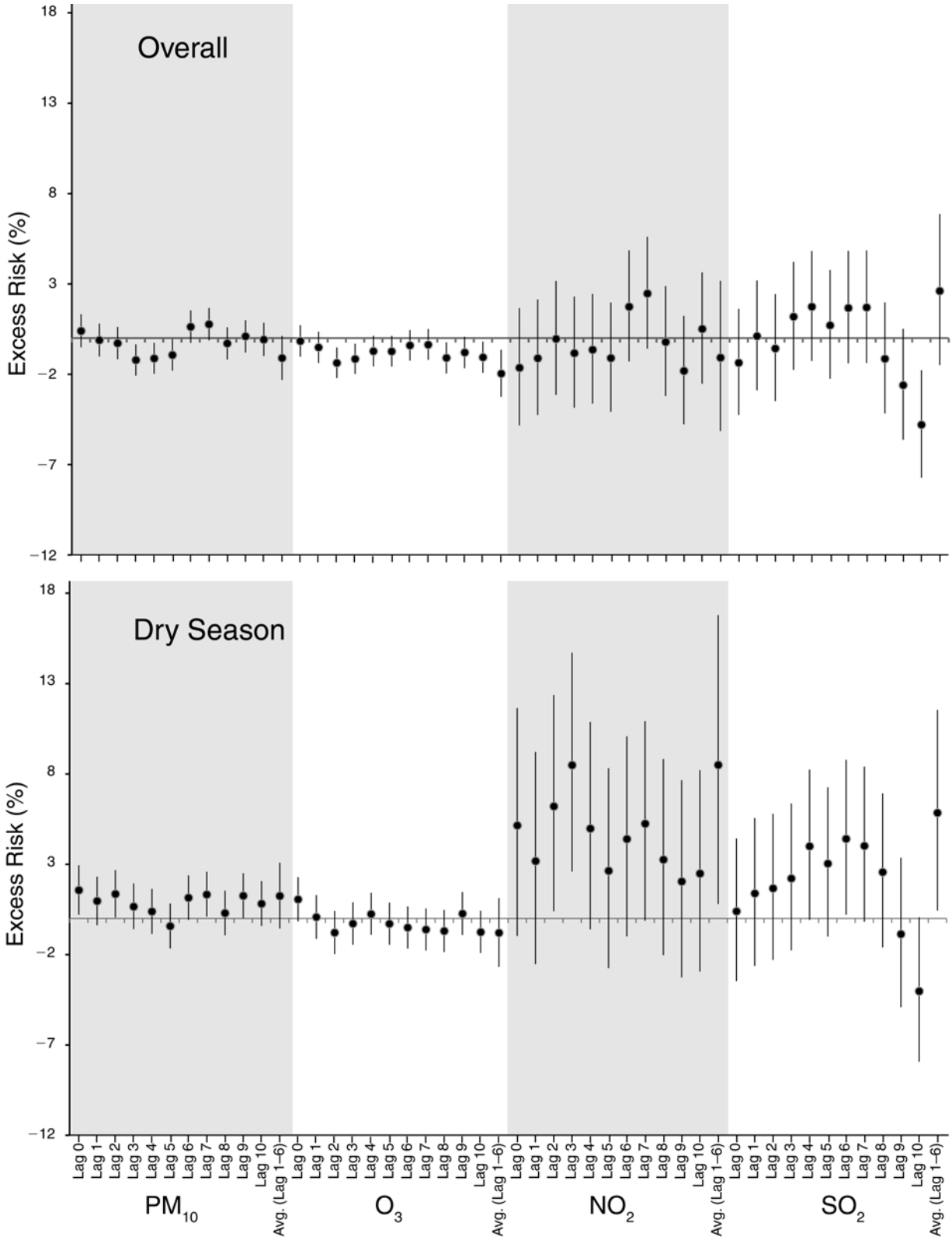

Figure 12. Excess risk of ALRI hospital admission (%) per 10-μg/m³ increase in pollutant concentrations, overall and by season, at multiple lags (0–10 days) and average lag (1–6 days), based on case–crossover analyses. (*Figure continues on next page*)

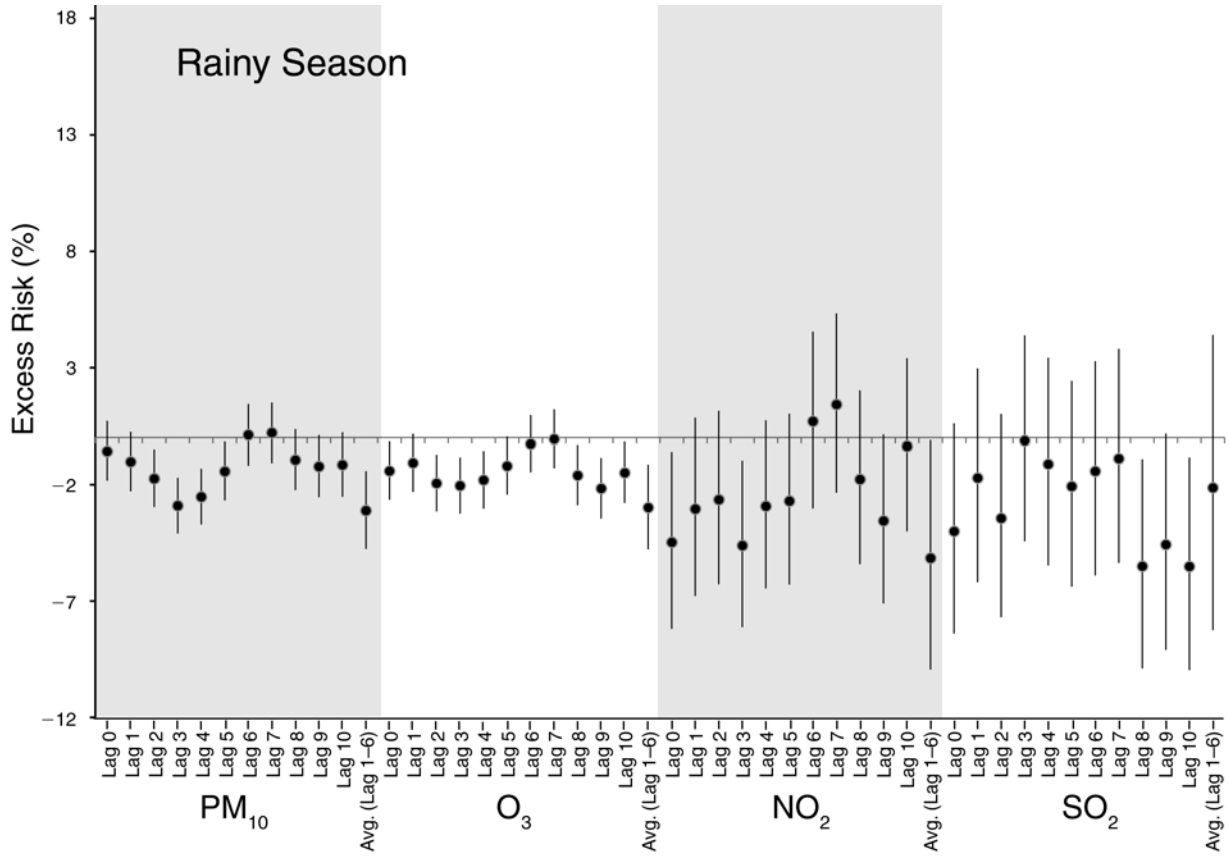

Figure 12 (*Continued*).

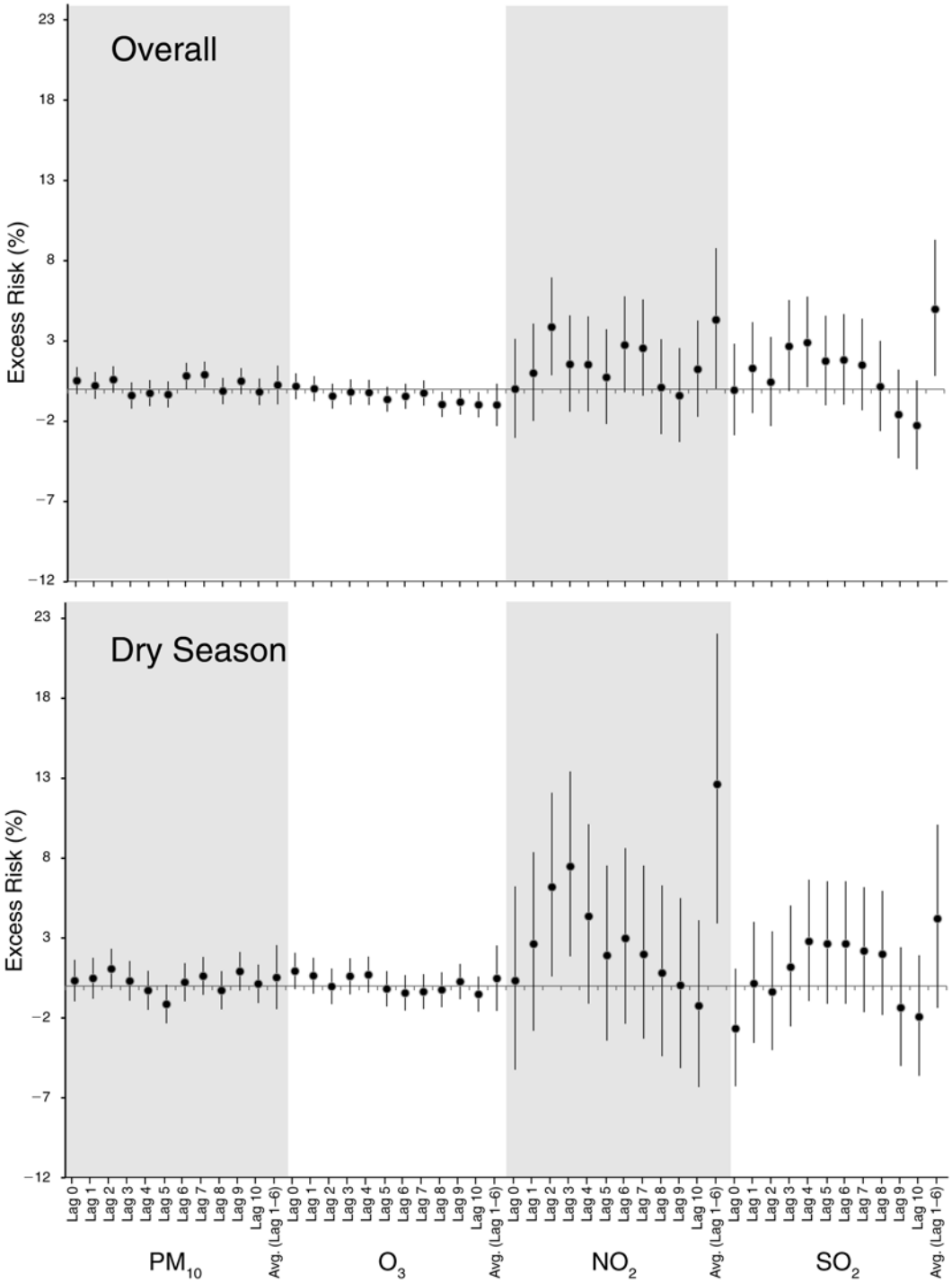

Figure 13. Excess risk of ALRI hospital admission (%) per 10-µg/m³ increase in pollutant concentrations, overall and by season, at multiple lags (0–10 days) and average lag (1–6 days), based on time-series (Poisson regression) analyses. (*Figure continues on next page*)

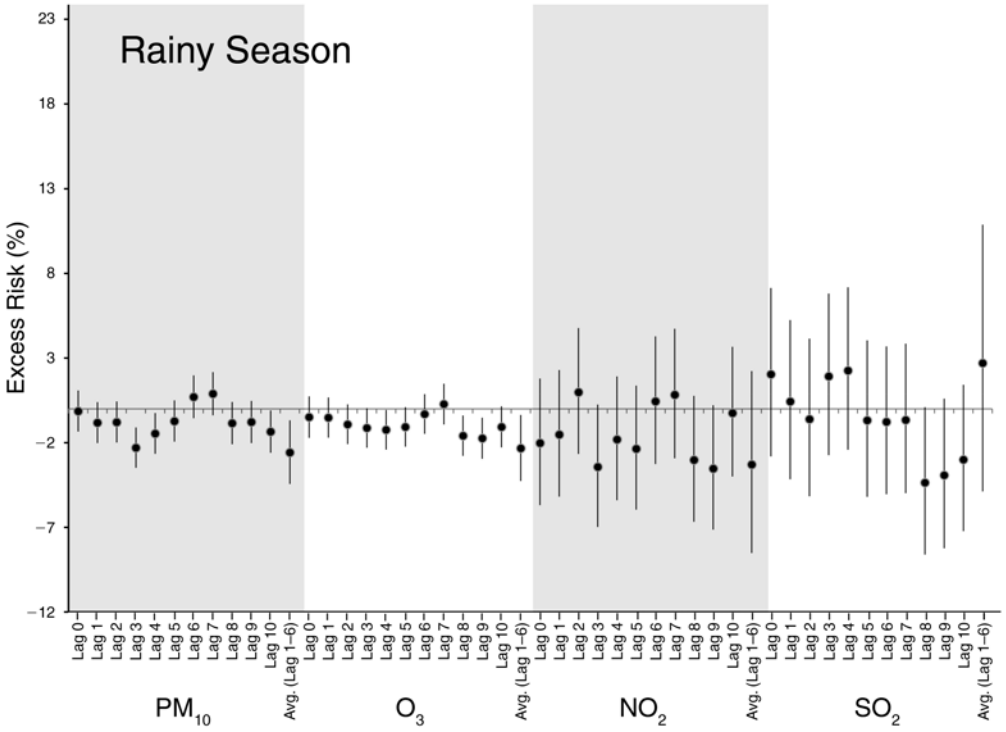

Figure 13 (*Continued*).

The time-series results based on SAS software are presented in Appendix C. (A comparison of results by software type is provided in Appendix G, available on the HEI Web site.) As only 1.34% of the case subjects were classified as poor using the information from the individual financial records, we lacked the statistical power to conduct a time-series analysis stratified by individual SEP. Case–crossover results stratified by SEP are presented in the text. Time-series results for analyses of effect modification by SEP are presented in Appendix D.

ALRI ADMISSIONS AND POLLUTANT LEVELS

Large seasonal differences in admission patterns and pollution levels were observed: 60% of ALRI admissions occurred during the rainy season, while the highest pollutant concentrations were in the dry season. We initially adjusted to control for seasonal differences in ALRI admissions and pollution levels and checked for seasonal interaction in the single-pollutant time-series (Poisson regression) models (Table 24). The significance of the seasonal interaction term for NO_2 ($P < 0.0008$) provided us with further indication that we should conduct stratified analyses to reduce the potential for confounding by season. We also conducted sensitivity analyses to assess the adequacy of our binary classification of season.

Overall and season-specific results of case–crossover and time-series analyses for the single-pollutant and two-pollutant models are summarized in Table 25 and Figure 14. Results differed markedly when analyses were stratified by (rather than simply adjusted for) season. ALRI admissions were generally positively associated with ambient levels of PM_{10}, NO_2, and SO_2 during the dry season, but not during the rainy season.

PM_{10} Results

In the dry season, increased exposure to PM_{10} was associated with a 1.25% (95% CI, −0.55 to 3.09) excess risk of ALRI admissions in the single-pollutant case–crossover model. This weak association remained similar after adjusting for SO_2 and O_3, but was no longer observed after adjusting for NO_2. Issues related to the confounding of PM_{10} results by NO_2 are discussed below. Negative associations between PM_{10} and ALRI admissions were observed in the rainy season.

Table 24. *P* Values for Seasonal Interaction Terms, Based on Time-Series Analysis

Pollutant	*P* Value
PM_{10}	0.289
O_3	0.411
NO_2	0.0008
SO_2	0.747

O_3 Results

Positive associations between O_3 and ALRI admissions were not observed in either season. In the dry season, associations between exposure to O_3 and ALRI admissions were not observed in the single-pollutant model or after adjustment for other pollutants in the two-pollutant model. In the rainy season, no association was observed in the single-pollutant model, but O_3 exposure was negatively associated with ALRI admissions in the two-pollutant model.

NO_2 Results

There was strong evidence of an NO_2 effect on ALRI admissions in the dry season, with excess risk estimates ranging from 7% to 18%. The highest increase in risk of ALRI admissions was associated with exposure to NO_2, with an excess risk of 12.62% (95% CI, 3.91–22.05) observed in the single-pollutant time-series model for average lag 1–6 days. These effects were robust to adjustment for other pollutants and became even more pronounced after adjustment for PM_{10}.

There was little evidence of an association between NO_2 and ALRI admissions in the rainy season. The single-pollutant estimate from the case–crossover analysis suggested a negative association between NO_2 and ALRI admissions, but this effect was no longer apparent after adjustment for other pollutants.

The magnitude of the effects observed for NO_2, along with the wide confidence intervals, can be partially explained by the fact that excess risks were calculated for every 10-μg/m^3 increase in pollutant concentrations, which is a larger increment than the standard deviation for this pollutant during the study period (Table 15).

SO_2 Results

There was limited evidence that SO_2 had an effect on ALRI admissions in the dry season, with excess risk ranging from 2% to 6%. In the single-pollutant model, SO_2 was associated with an increased risk of ALRI admissions of 5.85% (95% CI, 0.44–11.55). This association was relatively robust to adjustment for PM_{10} and O_3, but the two-pollutant model adjusted for NO_2 indicated confounding of effects by NO_2.

Table 25. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, Average Lag (1–6 Days), Single and Bipollutant Results, Case–Crossover and Time-Series Analyses

Pollutant / Analysis	Overall	Dry Season	Rainy Season
PM_{10}			
Case–crossover			
Single	−1.10 (−2.31 to 0.12)	1.25 (−0.55 to 3.09)	−3.11 (−4.76 to −1.42)
Adj. SO_2	−0.57 (−2.08 to 0.95)	1.88 (−0.15 to 3.95)	−3.62 (−5.90 to −1.28)
Adj. O_3	−0.19 (−1.60 to 1.25)	2.03 (−0.01 to 4.11)	−2.18 (−4.14 to −0.19)
Adj. NO_2	−1.20 (−2.60 to 0.22)	−0.36 (−3.02 to 2.37)	−2.90 (−4.67 to −1.10)
Time series			
Single	0.26 (−0.94 to 1.47)	0.53 (−1.46 to 2.56)	−2.58 (−4.44 to −0.68)
Adj. SO_2	0.16 (−1.45 to 1.79)	0.78 (−1.46 to 3.07)	−3.07 (−6.29 to 0.27)
Adj. O_3	0.92 (−0.45 to 2.31)	0.42 (−1.81 to 2.72)	−1.85 (−3.97 to 0.32)
Adj. NO_2	−0.31 (−1.65 to 1.04)	−1.96 (−4.49 to 0.64)	−2.40 (−4.32 to −0.43)
O_3			
Case–crossover			
Single	−1.96 (−3.25 to −0.64)	−0.79 (−2.67 to 1.13)	−2.98 (−4.78 to −1.14)
Adj. SO_2	−1.18 (−2.75 to 0.42)	−0.63 (−2.78 to 1.56)	−1.01 (−3.51 to 1.56)
Adj. PM_{10}	−1.98 (−3.48 to −0.45)	−1.78 (−3.87 to 0.36)	−1.96 (−4.13 to 0.25)
Adj. NO_2	−2.07 (−3.46 to −0.67)	−1.28 (−3.27 to 0.74)	−2.91 (−4.85 to −0.92)
Time series			
Single	−0.98 (−2.30 to 0.35)	0.47 (−1.56 to 2.54)	−2.33 (−4.26 to −0.36)
Adj. SO_2	0.41 (−1.26 to 2.11)	−0.16 (−2.47 to 2.22)	1.13 (−2.28 to 4.65)
Adj. PM_{10}	−1.51 (−3.01 to 0.00)	0.22 (−2.06 to 2.55)	−1.60 (−3.86 to 0.72)
Adj. NO_2	−1.37 (−2.76 to 0.03)	0.09 (−2.03 to 2.26)	−2.46 (−4.51 to −0.37)
NO_2			
Case–crossover			
Single	−1.08 (−5.14 to 3.17)	8.50 (0.80 to 16.79)	−5.15 (−9.94 to −0.10)
Adj. SO_2	3.40 (−2.39 to 9.53)	12.07 (2.76 to 22.22)	−2.71 (−9.98 to 5.16)
Adj. PM_{10}	0.95 (−3.81 to 5.94)	9.70 (−1.80 to 22.55)	−2.42 (−7.61 to 3.07)
Adj. O_3	1.11 (−3.30 to 5.72)	10.12 (1.93 to 18.97)	−2.48 (−7.73 to 3.06)
Time series			
Single	4.32 (0.04 to 8.79)	12.62 (3.91 to 22.05)	−3.29 (−8.51 to 2.23)
Adj. SO_2	2.96 (−3.30 to 9.62)	13.23 (2.83 to 24.68)	−6.10 (−15.04 to 3.80)
Adj. PM_{10}	4.81 (0.04 to 9.80)	18.45 (6.23 to 32.07)	−1.70 (−7.10 to 4.02)
Adj. O_3	5.63 (1.10 to 10.35)	12.49 (3.43 to 22.33)	−1.37 (−6.82 to 4.41)
SO_2			
Case–crossover			
Single	2.61 (−1.49 to 6.87)	5.85 (0.44 to 11.55)	−2.13 (−8.25 to 4.41)
Adj. PM_{10}	2.77 (−1.35 to 7.06)	5.44 (0.01 to 11.15)	−0.81 (−7.05 to 5.86)
Adj. O_3	2.95 (−1.18 to 7.25)	5.72 (0.31 to 11.43)	−1.16 (−7.76 to 5.92)
Adj. NO_2	1.84 (−2.31 to 6.16)	3.70 (−1.76 to 9.47)	−1.78 (−7.99 to 4.85)
Time series			
Single	4.98 (0.83 to 9.31)	4.21 (−1.37 to 10.10)	2.70 (−4.88 to 10.88)
Adj. PM_{10}	4.94 (0.77 to 9.29)	4.03 (−1.56 to 9.94)	4.46 (−3.81 to 13.44)
Adj. O_3	4.89 (0.73 to 9.23)	4.23 (−1.37 to 10.15)	1.43 (−6.56 to 10.11)
Adj. NO_2	4.17 (−0.07 to 8.59)	2.11 (−3.38 to 7.91)	4.11 (−3.83 to 12.71)

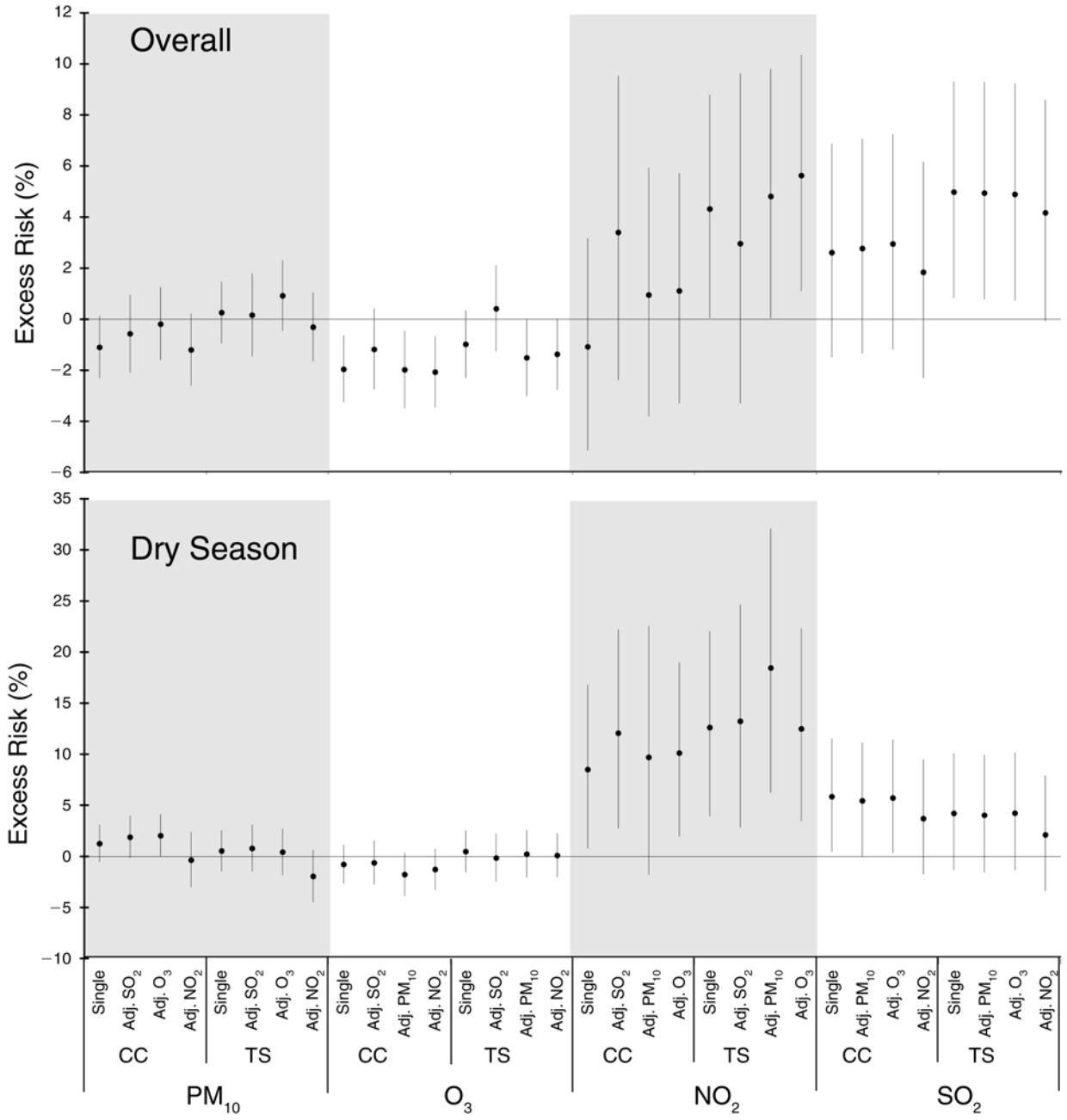

Figure 14. Excess risk of ALRI hospital admission (%) per 10-μg/m³ increase in pollutant concentrations, overall and by season, average lag (1–6 days), single- and two-pollutant results, case–crossover (CC) and time-series (TS) analyses. Note that the scales on the *y* axes differ. (*Figure continues on next page*)

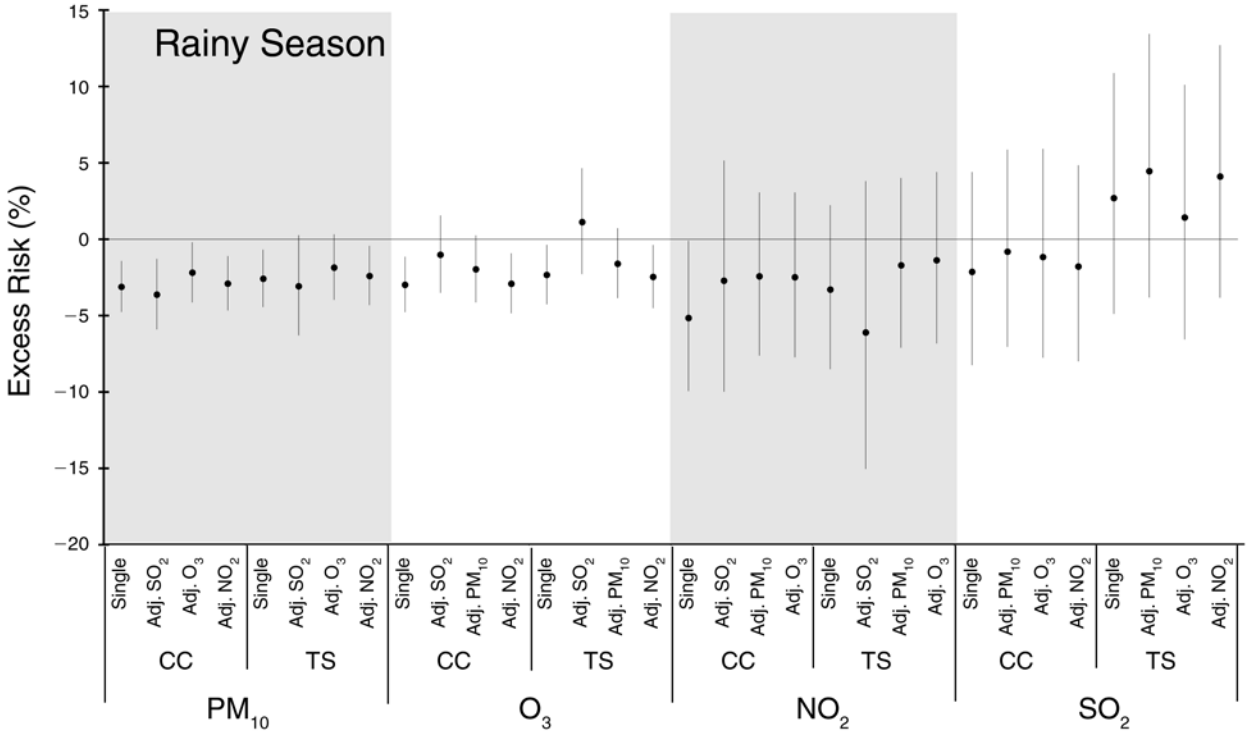

Figure 14 (*Continued*).

Associations between SO_2 and ALRI admissions were not observed in the rainy season. Point estimates for the case–crossover analyses suggested negative associations, while time-series analyses suggested positive associations.

Sensitivity Analyses

Sensitivity analyses were conducted to examine the potential impact of temperature lag choice on observed results and to explore seasonal effects (inclusion of rainfall as a continuous variable and reclassification of selected time periods), differential effects by age, and station-specific effects.

Temperature Lags To assess the effect of different temperature lags, we compared results for temperature with lag 0 and average lag (1–6 days). Very little difference in the results was observed, suggesting that the results are robust to differences in temperature lags (Table 26).

Seasonal Effects Although visual inspection of the time-series analysis of rainfall data suggested that the classifications used were appropriate and consistent from year to year, we conducted sensitivity analyses to explore the validity of the seasonal classifications used. The inclusion of rainfall as a continuous variable did not have much effect on the results. Table 27 and Figure 15 compare results of analyses that include rainfall as a continuous variable with results of the core analyses, which do not (Table 23).

In addition, after looking carefully at the time-series data, it appeared that there was a longer dry season that extended from October 2004 through May 2005. This was most evident in the PM_{10} time series, so we assessed the impact of reclassifying PM_{10} data from October 2004 and May 2005 on study results using average lag (1–6 days). Reclassification slightly dampened the PM_{10} effects in the dry season, from 1.25% excess risk of ALRI (95% CI, −0.55 to 3.09) to 0.56% excess risk (95% CI, −1.14 to 2.29), but

Table 26. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m³ Increase in Pollutant Concentrations, Using Lag 0 and Average Lag (1–6 Days) for Temperature, Based on Case–Crossover Analyses

Pollutant / Lag Days	Dry Season	Rainy Season
PM_{10}		
Lag 0	1.25 (−0.55 to 3.09)	−3.11 (−1.42 to −4.76)
Lag 1–6	1.63 (−0.3 to 3.59)	−2.43 (−0.69 to −4.13)
O_3		
Lag 0	−0.79 (−2.67 to 1.13)	−2.98 (−1.14 to −4.78)
Lag 1–6	−0.65 (−2.61 to 1.35)	−2.49 (−0.5 to −4.43)
NO_2		
Lag 0	8.50 (0.8 to 16.79)	−5.15 (−0.1 to −9.94)
Lag 1–6	12.69 (4.07 to 22.02)	−4.34 (0.81 to −9.23)
SO_2		
Lag 0	5.85 (0.44 to 11.55)	−2.13 (4.41 to −8.25)
Lag 1–6	5.90 (0.42 to 11.68)	−2.95 (3.6 to −9.09)

Table 27. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m³ Increase in Pollutant Concentrations, Including Rainfall as a Continuous Variable, Average Lag (1–6 Days), Based on Single-Pollutant Time-Series Analyses

	Dry Season		Rainy Season	
Pollutant	Core Analyses	Analyses with Rainfall	Core Analyses	Analyses with Rainfall
PM_{10}	0.53 (−1.46 to 2.56)	1.2 (−0.6 to 3.04)	−2.58 (−4.44 to −0.68)	−3.06 (−4.71 to −1.38)
O_3	0.47 (−1.56 to 2.54)	−0.87 (−2.76 to 1.06)	−2.33 (−4.26 to −0.36)	−2.91 (−4.72 to −1.07)
NO_2	12.62 (3.91 to 22.05)	8.24 (0.53 to 16.53)	−3.29 (−8.51 to 2.23)	−4.99 (−9.79 to 0.07)
SO_2	4.21 (−1.37 to 10.10)	5.87 (0.45 to 11.57)	2.70 (−4.88 to 10.88)	−1.72 (−7.87 to 4.84)

confidence intervals from the two sets of analyses largely overlap. In the rainy season, the PM_{10} effect was −3.11% (95% CI, −4.76 to −1.42) in the original analysis and −4.7% (95% CI, −6.97 to −2.38) after reclassification.

Age To explore whether very young children were more susceptible to the effects of air pollution, we conducted stratified analyses by age category (under 1 year of age and from 1 to 5 years of age) (Table 28 and Figure 16). Indeed, patterns were relatively consistent overall. With the exception of SO_2 in the dry season, which showed wide, overlapping confidence intervals, stronger effects were suggested among children under 1 year of age across both seasons. In some cases, clear effects observed in the younger age group were only suggestive or of borderline significance in the older age group.

Station-Specific Effects We conducted analyses to assess whether there may be station-specific effects impacting our results (Table 29 and Figure 17). Results were relatively consistent across monitoring stations, with citywide results closely following results from the D2 and Zoo monitoring stations.

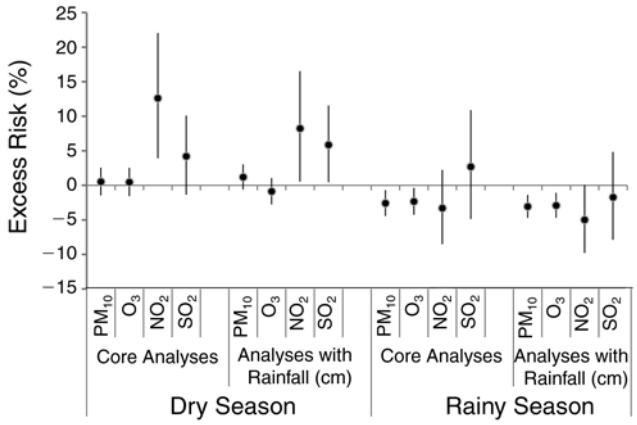

Figure 15. Excess risk of ALRI hospital admission (%) per 10-µg/m³ increase in pollutant concentrations, including rainfall as a continuous variable, average lag (1–6 days), based on single-pollutant time-series analyses.

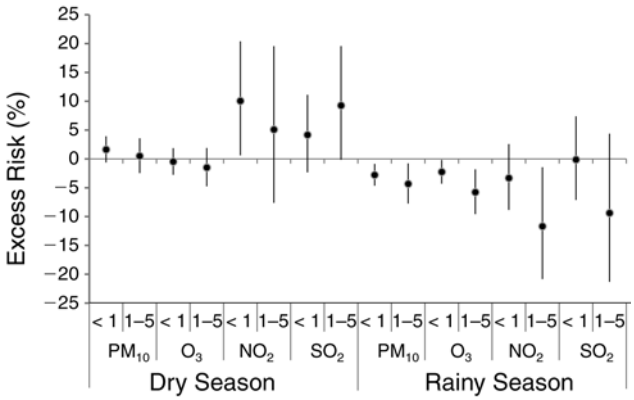

Figure 16. Excess risk of ALRI hospital admission (%) per 10-µg/m³ increase in pollutant concentrations, by age, average lag (1–6 days), based on single-pollutant case–crossover analyses.

Table 28. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-µg/m³ Increase in Pollutant Concentrations, by Age, Average Lag (1–6 Days), Based on Single-Pollutant Case–Crossover Analyses

Pollutant / Age (yr)	Dry Season	Rainy Season
PM_{10}		
< 1	1.63 (−0.62 to 3.94)	−2.78 (−4.66 to −0.86)
1–5	0.51 (−2.46 to 3.58)	−4.32 (−7.74 to −0.77)
O_3		
< 1	−0.47 (−2.76 to 1.87)	−2.25 (−4.3 to −0.17)
1–5	−1.49 (−4.76 to 1.9)	−5.77 (−9.58 to −1.81)
NO_2		
< 1	10.06 (0.61 to 20.4)	−3.31 (−8.85 to 2.57)
1–5	5.09 (−7.63 to 19.55)	−11.68 (−20.85 to −1.44)
SO_2		
< 1	4.17 (−2.35 to 11.12)	−0.12 (−7.13 to 7.41)
1–5	9.27 (−0.15 to 19.57)	−9.38 (−21.32 to 4.38)

Table 29. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, by Monitoring Station, Average Lag (1–6 Days), Based on Case–Crossover Analyses

Pollutant / Station	Dry Season	Rainy Season
PM_{10}		
Citywide estimate	1.25 (−0.55 to 3.09)	−3.11 (−4.76 to −1.42)
D2	0.82 (−0.76 to 2.43)	−2.98 (−1.15 to −4.79)
QT	−0.22 (−3.64 to 3.31)	−1.17 (1.44 to −3.71)
TSH	2.55 (0.44 to 4.70)	−1.59 (3.16 to −6.12)
Zoo	0.92 (−1.19 to 3.08)	−2.47 (−0.39 to −4.50)
O_3		
Citywide estimate	−0.79 (−2.67 to 1.13)	−2.98 (−4.78 to −1.14)
D2	−1.33 (−2.96 to 0.32)	−1.74 (−0.03 to −3.43)
QT	−0.83 (−2.68 to 1.06)	−1.30 (0.74 to −3.30)
TSH	−0.63 (−2.33 to 1.11)	−1.02 (0.68 to −2.69)
Zoo	0.15 (−1.61 to 1.95)	−2.16 (−0.56 to −3.74)
NO_2		
Citywide estimate	8.50 (0.80 to 16.79)	−5.15 (−9.94 to −0.10)
D2	7.81 (0.09 to 16.12)	−8.47 (−2.62 to −13.96)
Zoo	3.32 (−5.84 to 13.37)	−3.11 (2.77 to −8.65)
SO_2		
Citywide estimate	5.85 (0.44 to 11.55)	−2.13 (−8.25 to 4.41)
D2	3.00 (−2.54 to 8.87)	−3.17 (5.91 to −11.47)
Zoo	2.12 (−3.65 to 8.25)	−2.74 (2.85 to −8.03)

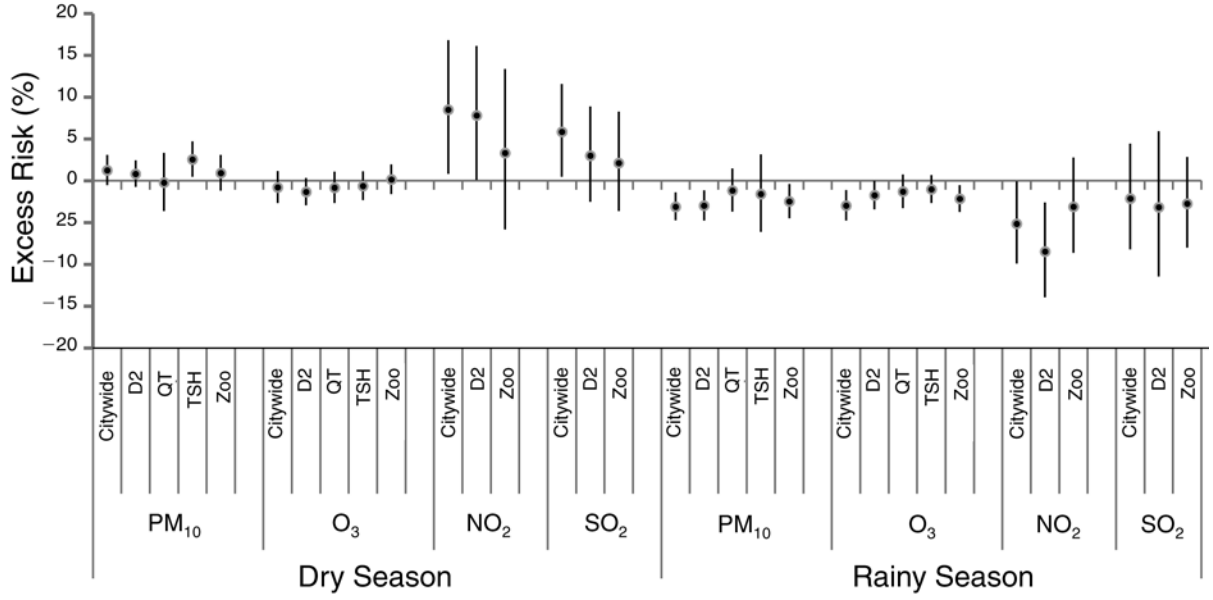

Figure 17. Excess risk of ALRI hospital admission (%) per 10-μg/m^3 increase in pollutant concentrations, by monitoring station, average lag (1–6 days), based on case–crossover analyses.

EFFECT MODIFICATION BY SEP

Individual-Level Indicator of SEP

Results of the case–crossover analysis for the individual-level indicator of SEP based on payment exemption at the hospital are provided in Table 30 and Figure 18. Because only 210 case subjects were classified as poor on the basis of their financial records, results exploring differential effects by this individual-level indicator of SEP were inconclusive, and no meaningful patterns of risk by SEP could be detected.

District-Level Indicator of SEP

Analyses assessing differences in effect by district-level indicator of SEP, namely SEP quartile based on district-level poverty prevalence, did not indicate a clear trend in risk across SEP (Table 30 and Figure 18); however, a slightly higher risk was observed among the residents of districts with the highest quartile of SEP. In the dry season, increased concentrations of NO_2 and SO_2 were associated with increased risk of hospital admissions in the highest quartile. NO_2 was associated with an excess risk of 20.92% (95% CI, 5.39–38.74). Excess risk associated with SO_2 was similar, but slightly lower, at 14.52% (95% CI, 4.00–26.11). There was no clear evidence of a monotonic increase in risk across quartiles of SEP.

Table 30. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, by SEP, Average Lag (1–6 Days), Based on Case–Crossover Analyses

Pollutant / SEP	Dry Season	Rainy Season
Individual-Level Indicator of SEP		
PM_{10}		
Nonpoor	1.69 (−0.25 to 3.67)	−3.21 (−4.94 to −1.46)
Poor	3.43 (−11.88 to 21.41)	−0.94 (−14.54 to 14.82)
O_3		
Nonpoor	−1.22 (−3.22 to 0.82)	−2.98 (−4.88 to −1.06)
Poor	−0.74 (−14.62 to 15.39)	6.63 (−10.43 to 26.94)
NO_2		
Nonpoor	10.47 (2.15 to 19.47)	−4.13 (−9.35 to 1.39)
Poor	17.17 (−39.64 to 127.45)	−21.78 (−52.69 to 29.34)
SO_2		
Nonpoor	5.56 (0.08 to 11.35)	−1.99 (−8.25 to 4.7)
Poor	0.79 (−34.74 to 55.67)	−5.71 (−42.36 to 54.25)
District-Level Indicator of SEP[a]		
PM_{10}		
Quartile 1	2.96 (−0.40 to 6.45)	2.24 (−0.96 to −4.06)
Quartile 2	0.31 (−2.71 to 3.42)	−2.11 (−4.90 to −7.60)
Quartile 3	1.30 (−1.84 to 4.56)	−0.34 (−3.37 to −6.31)
Quartile 4	−2.41 (−11.18 to 7.22)	8.66 (−0.24 to −8.41)
O_3		
Quartile 1	0.09 (−3.41 to 3.71)	2.53 (−0.96 to −4.33)
Quartile 2	−0.31 (−3.49 to 2.97)	−0.54 (−3.65 to −6.66)
Quartile 3	−1.21 (−4.46 to 2.16)	−0.21 (−3.50 to −6.69)
Quartile 4	−9.00 (−18.22 to 1.25)	1.71 (−7.32 to −15.54)
NO_2		
Quartile 1	20.92 (5.39 to 38.74)	2.65 (−6.81 to −15.39)
Quartile 2	1.09 (−10.59 to 14.29)	4.80 (−4.08 to −12.21)
Quartile 3	7.98 (−5.30 to 23.13)	7.09 (−2.16 to −10.61)
Quartile 4	−4.76 (−35.75 to 41.17)	−1.28 (−23.89 to −41.31)
SO_2		
Quartile 1	14.52 (4.00 to 26.11)	12.30 (−0.01 to −10.98)
Quartile 2	4.66 (−4.26 to 14.42)	15.84 (3.89 to −6.83)
Quartile 3	1.03 (−7.98 to 10.93)	2.78 (−8.71 to −18.92)
Quartile 4	−12.33 (−33.11 to 14.89)	16.68 (−15.86 to −39.33)

[a] Quartile 1 is the highest quartile of SEP.

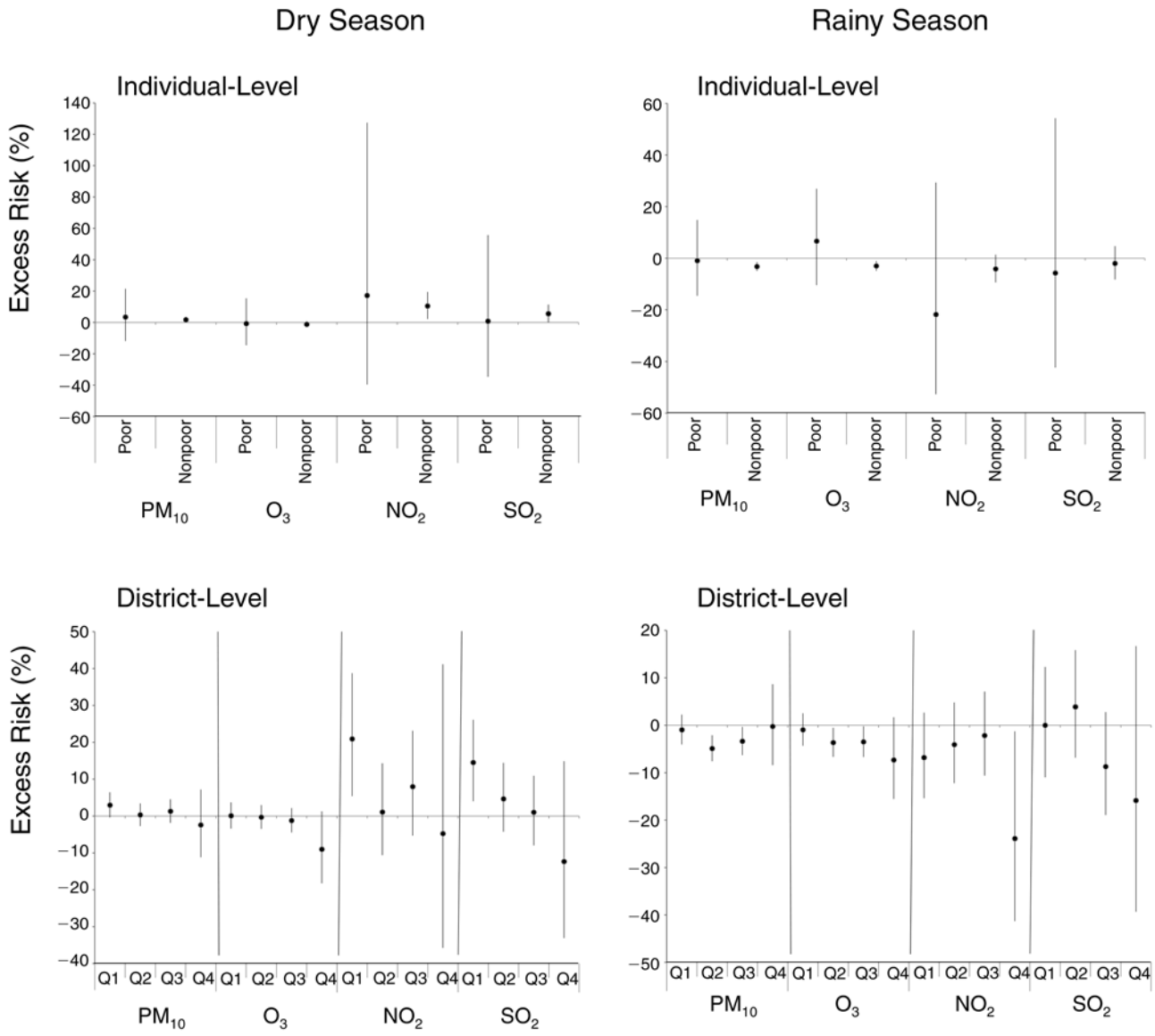

Figure 18. Excess risk of ALRI hospital admission (%) per 10-µg/m³ increase in pollutant concentrations, by SEP and season, average lag (1–6 days), based on case–crossover analyses. Note that the scales on the *y* axes differ.

DISCUSSION

ALRI ADMISSIONS AND POLLUTANT LEVELS

Exposure to air pollutants was generally positively associated with hospital admissions for ALRI during the dry season (November–April) and was inversely associated during the rainy season (May–October). Results of this study suggest that increased concentrations of NO_2, SO_2, and PM_{10} were associated with increased hospital admissions for ALRI in young children of HCMC in the dry season, although SO_2 and NO_2 displayed the most robust relationships. PM_{10} could also be associated with increased hospital admissions in the dry season, but the high correlation between PM_{10} and NO_2 ($r = 0.78$) limited our ability to distinguish between PM_{10} and NO_2 effects.

We know of no reason to think that exposure to air pollution could reduce the risk of ALRI in the rainy season, and we infer that these results could be driven by residual confounding or other bias present within the rainy season data. Although we could not specifically identify such sources of bias, factors influencing the results in the rainy season could potentially affect results in the dry season as well. Respiratory illness is more prevalent during the rainy season, when there are likely to be other competing risk factors that play a stronger role than air pollution. Pollutant levels are at their lowest during the rainy season. Thus, in HCMC the rainy season is associated with increased disease incidence, but decreased pollution levels, which increases the potential for negative confounding within the rainy season.

In sensitivity analyses, results were not affected by differences in seasonal classification. Inclusion of rainfall as a continuous variable and the seasonal reclassification of selected series of data did not influence results. No clear evidence of station-specific effects could be observed, since differences across monitoring stations had overlapping confidence intervals.

Seasonal differences in the prevalence of viral ALRI could be driving the observed differences in effects by season. If ALRI of bacterial etiology is more strongly associated with air pollution exposures than ALRI caused by viruses such as RSV, it is possible that our models, which did not take RSV into account, may have induced a spurious negative association between ALRI and air pollution.

Exploratory analyses using limited historical and regional data on monthly RSV prevalence offer suggestive evidence that an unmeasured, time-varying confounder such as RSV could have, in an observational study like this one, created enough bias to reverse the observed effect estimates of pollutants in the rainy season (Appendix B). In addition, with virtually no RSV incidence in the dry season, these findings also lend some credibility to the notion that RSV could influence results primarily in the rainy season.

EFFECT MODIFICATION BY SEP

Analyses were not able to identify differential effects by the individual-level indicator of SEP because of the small number of children classified as poor on the basis of information in the hospital financial records. Results of the analysis by district-level indicator of SEP were similarly inconclusive, though there appeared to be a slightly higher risk among the residents of districts with the highest quartile of SEP. As these are the districts within the urban center of HCMC, results could be indicative of increased exposures for residents living within the city center. It remains possible that poorer children systematically experience higher exposures to air pollution per unit of reported air quality on any given day compared with other children, regardless of district of residence. Since in these analyses a single daily measurement of pollution was assigned to all children for a particular day, however, we were not able to estimate daily differences in individual exposures across districts or socioeconomic groups.

CASE–CROSSOVER VS. TIME-SERIES ANALYSES

In the absence of measurement error, confounding, and other sources of bias, time-series and case–crossover approaches should provide estimates that differ only with regard to precision. The impact of residual temporal confounding is likely to be stronger in the time-series analyses, however. With the exception of single-pollutant results for SO_2 in the rainy season, results were consistent between time-series (Poisson regression) and case–crossover approaches. In addition, although theory suggests that the case–crossover estimates should be less efficient, the widths of the confidence intervals were surprisingly similar for the two approaches. Our results suggest that with 9 *df* per year, the time-series approach achieved temporal control that was similar to the control achieved in the case–crossover approach.

COMPARISON WITH OTHER STUDIES

The diversity in disease classifications, averaging times, and seasonal definitions used limits the ability to make direct comparisons between this study and similar studies conducted elsewhere. We explored how these differences in studies may impact their results.

Disease Classifications

As discussed earlier, the two pediatric hospitals in HCMC did not use objective clinical measures to distinguish between pneumonia and bronchiolitis, so we created a single outcome category including both classifications. Studies that have found the strongest PM effects have focused specifically on bronchiolitis (Karr et al. 2006; Segala et al. 2008), while most of the studies that used a more broadly grouped disease classification found similarly inconclusive results for PM_{10} (Gouveia and Fletcher 2000; Barnett et al. 2005; Hernández-Cadena et al. 2007).

Averaging Times

Recent publications that focus on the effects of subchronic exposures to air pollution have used averaging times on the order of weeks or months, and they seem to suggest stronger effects (Karr et al. 2009). Consistent with other studies in the literature on short-term exposure to air pollution, however, this study used averaging times on the order of days, with a focus on an average lag of 1 to 6 days.

Seasonal Definitions

Although other studies have looked for potential effect modification by season, how the seasons are defined has varied from study to study. Seasonal differences in effects are location-dependent in that different seasonal patterns translate into different trends in temperature, precipitation, and disease incidence. Studies conducted in North America and Western Europe have found effects in the winter season, when both pollution levels and disease incidence are likely to be high (Karr et al. 2006; Segala et al. 2008). A study conducted in Australia and New Zealand (Barnett et al. 2005), with different seasonal patterns of temperature and disease, found stronger effects in the warm season.

To the best of our knowledge, this is the first study to focus specifically on assessing differences by rainy and dry seasons. HCMC has a tropical climate with little variation in temperature, but distinct seasonal patterns of rainfall that are correlated with distributions of respiratory infection. Thus, although the seasonal definition we used is appropriate for this particular study, it may not be directly comparable with definitions in other studies.

Differentiating PM_{10} and NO_2 Effects

PM_{10} could also be associated with increased hospital admissions in the dry season, but the results of the two-pollutant model indicate strong confounding by NO_2. While effects in this study appear to be driven by exposure to NO_2, given the high correlation between PM_{10} and NO_2 (0.78), the statistical constraints of adequately addressing collinearity limited our ability to clearly distinguish PM_{10} and NO_2 effects. Other studies focused on the association between air pollution and ALRI in young children also have noted the challenges of adequately distinguishing between PM_{10} and NO_2 effects (Gouveia and Fletcher 2000; Braga et al. 2001; Barnett et al. 2005). One study (Saldiva et al. 1994) that found a strong positive association between nitrogen oxide and respiratory mortality in children did not find PM_{10} effects.

PM_{10} is a complex mixture of components that, like NO_2, serves as an imperfect indicator of combustion-related pollutants, but also represents noncombustion or crustal sources of air pollution that are prominent in HCMC, such as construction. The much lower correlation between NO_2 and PM_{10} during the rainy season provides further evidence that these indicator pollutants may not be accurately characterizing exposures to air pollution from combustion processes in the rainy season. $PM_{2.5}$ data, which would serve as a better indicator of combustion processes, are not routinely available in HCMC, and differences in PM composition by season also remain unknown. Nevertheless, taken as a whole, results suggest that increased risks of ALRI admissions in young children are associated with increases in combustion-related pollution (including, but not exclusive to, traffic pollution).

To the best of our knowledge, this is the first study of ALRI admissions in young children to be conducted in an Asian city, and it is the first study of the health effects of air pollution to be conducted in Ho Chi Minh City, Vietnam. Ambient pollution levels in HCMC are certainly much higher than those reported in the existing literature on air pollution and ALRI morbidity, but remain somewhat lower than levels in other Asian megacities. The results of this study may inform global health impact assessments at the mid-range of the exposure–response curve. In addition, the study contributes to the growing literature on the health effects of air pollution in Asia, particularly given the lack of studies in Southeast Asia (HEI International Scientific Oversight Committee 2010).

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Group on Air Pollution, Poverty, and Health in Ho Chi Minh City (see "About the Authors"). The Working Group is especially grateful to the Clean Air Initiative for Asian Cities (CAI-Asia), for initiating communications between HEI, the Asian Development Bank, and the government of Vietnam. The Working Group is also grateful to the Local Steering Committee for the project (see "About the Authors"). We thank the PAPA Program's International Scientific Oversight Committee, especially Drs. Michael Brauer, Ross Anderson, Kirk Smith, and Frank Speizer, for providing technical guidance and suggestions throughout the process, and we are also most grateful for the useful comments provided to us by HEI's Review Committee, as well as David Bush, external quality assurance consultant.

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APPENDIX A. HEI Quality Assurance Statement

The conduct of this study was subjected to independent audit by Mr. David Bush of T&B Systems, Inc. Mr. Bush is an expert in quality assurance for air quality monitoring studies and data management. The audit included reviews of study activities for conformance to the study protocol and reviews of the overall data quality. The audit activities are described below.

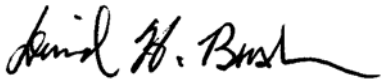
October 28–29, 2009

The auditor conducted an on-site audit at HEI, with both HEI and Harvard Medical School personnel present for the audit. The audit consisted of a review of the draft final report and the project data set utilized in the final report. This included a review of procedures for data collection, processing, and analysis. No problems were noted with the hospital data, though significant issues were noted with the air quality data. The issues centered on the investigators' attempts to generate an improved hourly data set using available 5-minute air quality data, which was found to be problematic. The auditor recommended that the hourly data set supplied by HEPA be reviewed and used instead for the analyses.

February 2010

The auditor reviewed the responses to the audit report, as well as a resubmitted data set. All recommendations from the initial audit had been addressed, including use of the HEPA data set. Some additional recommendations were made for further validating the data set.

Written reports of the audit were provided to the HEI project manager, who transmitted the findings to the Principal Investigators. The quality assurance audit demonstrated that the study was conducted by an experienced team with a high concern for data quality.



David H. Bush

Quality Assurance Officer

APPENDIX B. Exploring the Potential Influence of RSV as an Unmeasured, Time-Varying Confounder

In this study, excess risk of ALRI hospital admissions was generally positively associated with air pollution during the dry season from November through April and inversely associated with air pollution in the rainy season from May through October (Table B.1).

As we know of no reason to think that the increased exposure to air pollution could reduce the risk of ALRI in the rainy season, we inferred that the ALRI results could be driven by residual confounding or other bias present within the rainy season. Moreover, although we could not specifically identify any sources of such bias, we acknowledge that factors influencing the results in the rainy season could potentially influence results observed in the dry season as well.

In Vietnam's tropical climate, respiratory illness is more prevalent during the rainy season, when pollutant levels are lowest. In sensitivity analyses we conducted as part of this study, results were not affected by differences in seasonal classification. Moreover, inclusion of rainfall as a continuous variable and the reclassification of selected series of data did not influence results. Thus, we were interested in identifying time-varying confounders, in particular, confounders with seasonal differences. The limited (and somewhat conflicting) evidence described below motivated us to focus on RSV.

RSV EPIDEMICS

RSV is the most common cause of childhood ALRI on a global scale, with an estimated 33.8 million new cases of ALRI occurring in children under age 5 each year, of which at least 3.4 million are severe enough to necessitate hospitalization (Nair et al. 2010). What triggers the annual RSV epidemics is not well understood, however. It has been suggested that environmental factors such as temperature, daylight, and humidity may initiate epidemics (Bhatt and Everard 2004), but the potential influence of environmental factors, as well as environmental pollutants, on RSV remains unclear (Bhatt and Everard 2004).

RSV IN EAST AND SOUTHEAST ASIA

The prevalence of RSV has been shown to be negatively associated with temperature and positively associated with rainfall (De Silva and Hanlon 1986). Studies in Asian countries bordering or near Vietnam that have tropical weather and rainy and dry seasons (Thailand, Singapore, and Hong Kong, China) showed that RSV was prevalent during the rainy season (May–October) (Sung et al. 1987). The Hong Kong study reported that the monthly percentage of RSV cases was highly correlated with rainfall ($r = 0.78$), temperature ($r = 0.66$), and humidity ($r = 0.74$) (Sung et al. 1987) and suggested that a possible explanation for the high prevalence of RSV during the rainy season is that the rain, high temperatures, and humidity keep people indoors and thereby facilitate RSV transmission.

Le et al. (1999) published a monthly distribution of RSV data in HCMC, including data on 349 children admitted to CH1 (one of the two pediatric hospitals in our study) from June 1996 to May 1997. The prevalence of RSV was indeed higher in the rainy season (May–October), with few cases identified in April, at the end of the dry season. This monthly pattern is markedly different from the seasonal distribution of influenza B cases. Figure B.1 shows the monthly detection rates of RSV and influenza B among residents of HCMC from June 1996 to May 1997. It should be noted that Figure B.1 reflects the population from 0 to 60 years of age, in which RSV is less prevalent than among young children; RSV was detected in 13.5% of children under 5 over the study period, compared with only 6.1% of adults ages 25 to 60 (Le et al. 1999).

Although these data are somewhat dated, seasonal patterns in rainfall and infectious disease transmission are unlikely to change drastically over a short time period; thus, these data support the notion that RSV prevalence closely follows the pattern of rainfall in HCMC, with considerably fewer cases observed in the dry season. As such, if estimated RSV prevalence can be used as a rough indicator of the elusive time-varying confounder for which we have been searching, it would support the notion that the confounder is only influencing results in the rainy season.

Data on RSV in children with lower respiratory illness in Hong Kong (Sung et al. 1987) show a remarkably similar pattern, with a higher frequency of infection during the rainy season, as expected. Figure B.2 also reflects the very similar distributions of RSV cases and rainfall.

Our evaluation is based on the following assumptions:

- ALRI of bacterial etiology is more strongly associated with air pollution than ALRI of viral (RSV) etiology, which is supported by weak, somewhat inconclusive evidence from the available epidemiology.
- In the rainy season in Southeast Asian and East Asian regions, including HCMC, all (or nearly all) ALRI is due to RSV, which is supported by Figures B.1 and B.2.
- RSV prevalence is negatively associated with ALRI of bacterial etiology.
- RSV is negatively associated with air pollution, which is supported by the descriptive statistics in this study. Rainfall is positively correlated with RSV prevalence, which is supported in the literature, and it is negatively correlated with PM_{10}, which is supported by our data; therefore, we assume that RSV prevalence is negatively correlated with PM_{10} levels.

Table B.1. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, Average Lag (1–6 Days), Single and Bipollutant Results, Case–Crossover and Time-Series Analyses

Pollutant / Analysis	Overall	Dry Season	Rainy Season
PM_{10}			
Case–crossover			
Single	−1.10 (−2.31 to 0.12)	1.25 (−0.55 to 3.09)	−3.11 (−4.76 to −1.42)
Adjusted for SO_2	−0.57 (−2.08 to 0.95)	1.88 (−0.15 to 3.95)	−3.62 (−5.90 to −1.28)
Adjusted for O_3	−0.19 (−1.60 to 1.25)	2.03 (−0.01 to 4.11)	−2.18 (−4.14 to −0.19)
Adjusted for NO_2	−1.20 (−2.60 to 0.22)	−0.36 (−3.02 to 2.37)	−2.90 (−4.67 to −1.10)
Time series			
Single	0.26 (−0.94 to 1.47)	0.53 (−1.46 to 2.56)	−2.58 (−4.44 to −0.68)
Adjusted for SO_2	0.16 (−1.45 to 1.79)	0.78 (−1.46 to 3.07)	−3.07 (−6.29 to 0.27)
Adjusted for O_3	0.92 (−0.45 to 2.31)	0.42 (−1.81 to 2.72)	−1.85 (−3.97 to 0.32)
Adjusted for NO_2	−0.31 (−1.65 to 1.04)	−1.96 (−4.49 to 0.64)	−2.40 (−4.32 to −0.43)
O_3			
Case–crossover			
Single	−1.96 (−3.25 to −0.64)	−0.79 (−2.67 to 1.13)	−2.98 (−4.78 to −1.14)
Adjusted for SO_2	−1.18 (−2.75 to 0.42)	−0.63 (−2.78 to 1.56)	−1.01 (−3.51 to 1.56)
Adjusted for PM_{10}	−1.98 (−3.48 to −0.45)	−1.78 (−3.87 to 0.36)	−1.96 (−4.13 to 0.25)
Adjusted for NO_2	−2.07 (−3.46 to −0.67)	−1.28 (−3.27 to 0.74)	−2.91 (−4.85 to −0.92)
Time series			
Single	−0.98 (−2.30 to 0.35)	0.47 (−1.56 to 2.54)	−2.33 (−4.26 to −0.36)
Adjusted for SO_2	0.41 (−1.26 to 2.11)	−0.16 (−2.47 to 2.22)	1.13 (−2.28 to 4.65)
Adjusted for PM_{10}	−1.51 (−3.01 to 0.00)	0.22 (−2.06 to 2.55)	−1.60 (−3.86 to 0.72)
Adjusted for NO_2	−1.37 (−2.76 to 0.03)	0.09 (−2.03 to 2.26)	−2.46 (−4.51 to −0.37)
NO_2			
Case–crossover			
Single	−1.08 (−5.14 to 3.17)	8.50 (0.80 to 16.79)	−5.15 (−9.94 to −0.10)
Adjusted for SO_2	3.40 (−2.39 to 9.53)	12.07 (2.76 to 22.22)	−2.71 (−9.98 to 5.16)
Adjusted for PM_{10}	0.95 (−3.81 to 5.94)	9.70 (−1.80 to 22.55)	−2.42 (−7.61 to 3.07)
Adjusted for O_3	1.11 (−3.30 to 5.72)	10.12 (1.93 to 18.97)	−2.48 (−7.73 to 3.06)
Time series			
Single	4.32 (0.04 to 8.79)	12.62 (3.91 to 22.05)	−3.29 (−8.51 to 2.23)
Adjusted for SO_2	2.96 (−3.30 to 9.62)	13.23 (2.83 to 24.68)	−6.10 (−15.04 to 3.80)
Adjusted for PM_{10}	4.81 (0.04 to 9.80)	18.45 (6.23 to 32.07)	−1.70 (−7.10 to 4.02)
Adjusted for O_3	5.63 (1.10 to 10.35)	12.49 (3.43 to 22.33)	−1.37 (−6.82 to 4.41)
SO_2			
Case–crossover			
Single	2.61 (−1.49 to 6.87)	5.85 (0.44 to 11.55)	−2.13 (−8.25 to 4.41)
Adjusted for PM_{10}	2.77 (−1.35 to 7.06)	5.44 (0.01 to 11.15)	−0.81 (−7.05 to 5.86)
Adjusted for O_3	2.95 (−1.18 to 7.25)	5.72 (0.31 to 11.43)	−1.16 (−7.76 to 5.92)
Adjusted for NO_2	1.84 (−2.31 to 6.16)	3.70 (−1.76 to 9.47)	−1.78 (−7.99 to 4.85)
Time series			
Single	4.98 (0.83 to 9.31)	4.21 (−1.37 to 10.10)	2.70 (−4.88 to 10.88)
Adjusted for PM_{10}	4.94 (0.77 to 9.29)	4.03 (−1.56 to 9.94)	4.46 (−3.81 to 13.44)
Adjusted for O_3	4.89 (0.73 to 9.23)	4.23 (−1.37 to 10.15)	1.43 (−6.56 to 10.11)
Adjusted for NO_2	4.17 (−0.07 to 8.59)	2.11 (−3.38 to 7.91)	4.11 (−3.83 to 12.71)

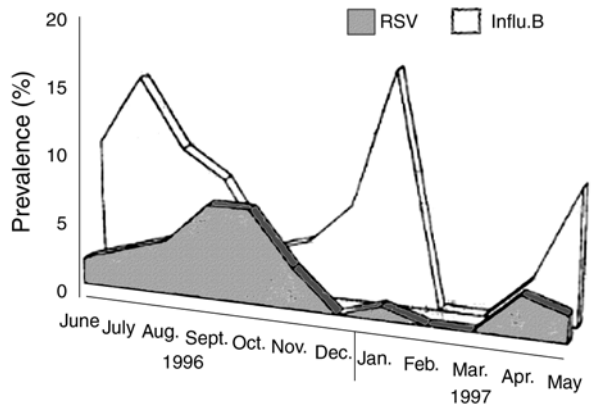


Figure B.1. Detection rates of RSV and influenza B among HCMC residents, June 1996–May 1997. Adapted from Le et al. 1999.

INFLUENCE OF ENVIRONMENTAL POLLUTANTS

One toxicologic study has demonstrated that exposure to carbon black can exacerbate RSV-induced airway hyperresponsiveness, pulmonary inflammation, and chemokine expression in mice (Lambert et al. 2003). The available evidence from published studies on the association between human exposure to air pollution and RSV is conflicting, however, and indicates the need for further investigation.

A systematic review of the epidemiology of ALRI and indoor air pollution from household use of solid fuels identified studies that addressed RSV (Dherani et al. 2008). One study exploring potential risk factors for RSV found a negative association between exposure to smoke from cooking fires and ALRI admissions among RSV-positive children under 5 years of age in The Gambia (Weber et al. 1999). In contrast, another study in South Africa observed a positive association between exposure to household air pollution (defined as indoor exposure to products of combustion of cooking fuels, but suggesting the inclusion of gases and kerosene within the exposed category) and RSV-positive hospital admissions (Jeena et al. 2003). A study conducted in Yemen observed increased risk of severe hypoxemic acute respiratory infection among patients positive for RSV (OR, 10.3; 95% CI, 2.2–48.0) and human metapneumovirus (HMPV) (OR, 13.1; 95% CI, 2.2–78.0) (Al-Sonboli et al. 2006). Finally, preliminary evidence from a randomized

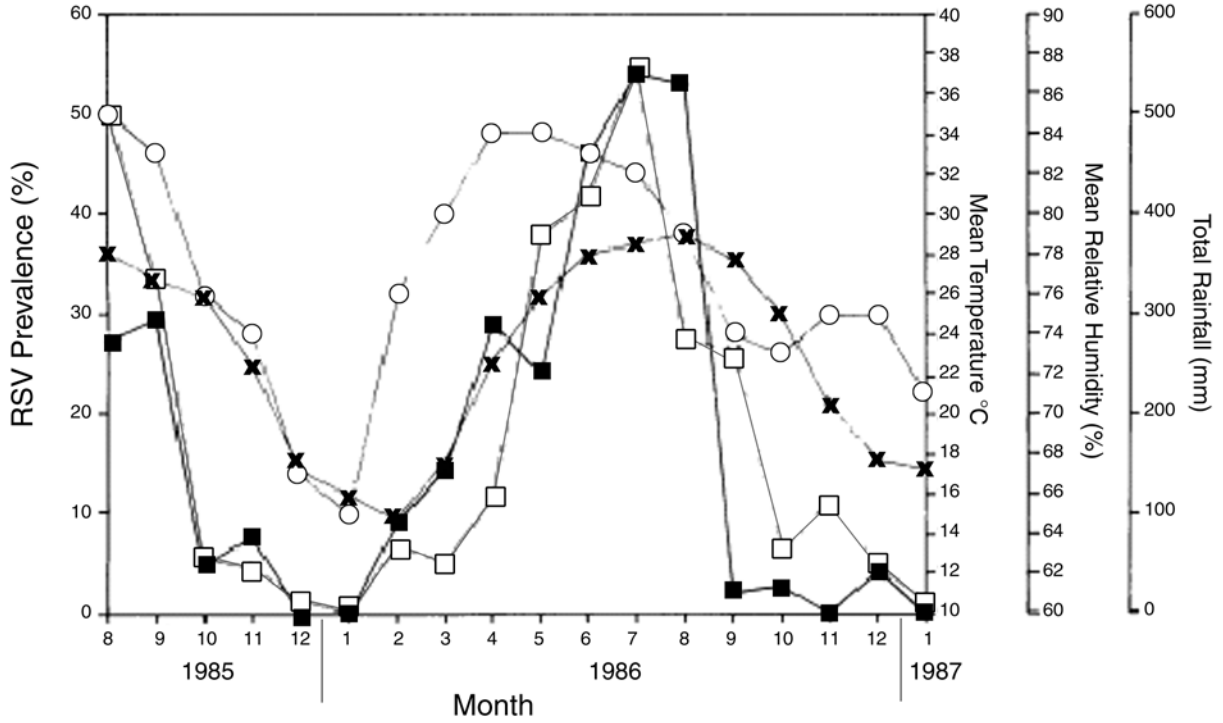


Figure B.2. Detection rates of RSV (■) in children with ALRIs in relation to temperature (x), relative humidity (○), and rainfall (□) in Hong Kong, August 1985–January 1987. Adapted from Sung et al. 1987, with permission from the Infectious Diseases Society of America.

trial involving the use of improved cookstoves in Guatemala suggested an increased risk of severe (hypoxemic) ALRI among RSV-negative children, and no increase in risk among RSV-positive children (Smith et al. 2006), although more recent evidence from the trial suggests a positive, but lower risk among RSV-positive children (Smith et al. 2011).

Limited evidence from epidemiologic studies on the effects of ambient air pollution is equally conflicting. A Chilean study that assessed risk factors for acute bronchiolitis among RSV-positive and RSV-negative patients in Santiago found no association with exposure to PM_{10} or $PM_{2.5}$ during the winter rainy season, between May and September 2001 (Zamorano et al. 2003). Another study of air pollution and hospital admissions of infants for RSV conducted in Sheffield, England, failed to find an association between outdoor air pollutants and RSV (Bhatt and Everard 2004). A study conducted in the Puget Sound region of Washington reported stronger effects for RSV-positive bronchiolitis than nonspecified bronchiolitis (Karr et al. 2009), but cases were defined solely on the basis of ICD coding, without confirmation from laboratory results. The investigators hypothesize that this increased risk may be due to better classification of outcomes, but it may also reflect a reporting bias in the peak RSV season (winter, in this case), rather than a true increase in risk among RSV-positive cases.

RSV AS AN UNMEASURED CONFOUNDER

It is indeed possible that an unmeasured confounder such as RSV in an observational study such as this one could cause a bias large enough to reverse estimates of effect, depending on the association between the unmeasured confounder, the covariate of interest, and the outcome. Lin et al. (1998) proposed a number of algorithms for the adjustment of the effect of interest in classical regression models, such as logistic regression, and survival time. In the case of logistic regression with a binary outcome, the adjusted β coefficient is expressed as follows:

$$\beta = \beta^* - \log \frac{e^{\alpha_1} P_1 + \left(1 - P_1\right)}{e^{\alpha_0} P_0 + \left(1 - P_0\right)}$$

β^* is the regression estimate when the unmeasured confounder (e.g., RSV) is not taken into account. P_1 is the prevalence of the unmeasured confounder in the exposed group (the algorithm assumes that the exposure variable is binary, so in our case PM_{10} for this exercise would have to be dichotomized into low-exposure and high-exposure groups). P_0 is the prevalence of the unmeasured confounder in the unexposed group. α_1 and α_0 represent the log odds of an RSV effect on ALRI incidence in the exposed group and the unexposed group, respectively.

We explored the sensitivity of the case–crossover estimate of PM_{10} (mean of lag 1 to lag 6 days) in the rainy season (excess risk, −3.11%; Table B.1) to the prevalence of RSV as estimated from data on known RSV prevalence in the region. Although we used a conditional logistic regression model, and not exactly the classical model from which the adjustment formula above was derived, the adjustment would still be appropriate. We dichotomized PM_{10} levels at 50 μg/m^3, so that above 50 μg/m^3 the patient is considered "exposed" and at or below 50 μg/m^3 the patient is considered "unexposed."

Since the estimated excess risk of −3.11% in our study was based on a model with continuous PM_{10}, the model was rerun with PM_{10} dichotomized at 50 μg/m^3, resulting in a coefficient of −0.09247, which corresponds to an excess risk of −8.8%, from $[1 - \exp(-0.09247)] \times 100$. We wanted to know whether accounting for RSV in the model, assuming it was distributed under conditions similar to those reported in the studies from Hong Kong, Thailand, Singapore, and Vietnam, would reverse the negative effect of PM_{10} (−0.09247) on ALRI incidence observed in the rainy season.

We assumed RSV prevalence of 10% for the exposed group P_1 and RSV prevalence from 10% to 30% for the unexposed group P_0, so that on average the RSV prevalence in the population would be approximately 20%, comparable to estimates from the Asian studies mentioned above (Table B.2). In our study, the level of rainfall was slightly inversely correlated with the level of PM_{10} (correlation coefficient, −0.1; P value = 0.04), so when PM_{10} was high (exposed group), rainfall was low. Therefore, we would expect lower prevalence of RSV when PM_{10} is high (exposed group, P_1), and higher prevalence of RSV when PM_{10} is low (unexposed group, P_0).

In this exercise, we assume that the association between RSV and ALRI incidence has an odds ratio of 1.1 in the exposed group, and ranges from 1.1 to 1.3 in the unexposed group. We assume that the odds ratio for an association between RSV and ALRI is higher in the unexposed group because RSV prevalence is higher in the unexposed group than in the exposed group. In Table B.2, the first row presents a case where RSV is not a confounder ($P_1 = P_0$) and thus the adjusted regression coefficient (β) is the same as the unadjusted regression coefficient (β^*). This would be the case during the dry season in HCMC, when RSV incidence is very low and thus the temporal distribution of RSV cases (e.g., monthly or daily) varies little across the

Table B.2. Sensitivity Analysis of Effect of PM_{10} Due to the Distribution of RSV: Eight Observations

Obs.	OR of RSV on ALRI for PM_{10} > 50 μg/m³	Log OR of RSV on ALRI for PM_{10} > 50 μg/m³	OR of RSV on ALRI for PM_{10} ≤ 50 μg/m³	Log OR of RSV on ALRI for PM_{10} ≤ 50 μg/m³	% RSV for PM_{10} > 50 μg/m³	% RSV for PM_{10} ≤ 50 μg/m³	PM_{10} Regression Coefficient Without RSV Adjustment	PM_{10} Regression Coefficient With RSV Adjustment
1	1.1	0.095310	1.1	0.09531	0.1	0.1	−0.09247	−0.09247
2	1.1	0.095310	1.1	0.09531	0.1	0.2	−0.09247	0.06193
3	1.1	0.095310	1.1	0.09531	0.1	0.3	−0.09247	0.19565
4	1.1	0.095310	1.2	0.18232	0.1	0.1	−0.09247	−0.06649
5	1.1	0.095310	1.2	0.18232	0.1	0.1	−0.09247	−0.06649
6	1.1	0.095310	1.3	0.26236	0.1	0.1	−0.09247	−0.03854
7	1.1	0.095310	1.2	0.18232	0.1	0.2	−0.09247	0.10605
8	1.1	0.095310	1.3	0.26236	0.1	0.3	−0.09247	0.31309

distribution of pollutant levels, so there is no association between RSV incidence and the level of pollution. In rows 2 and 3 of Table B.2, we see negative unadjusted coefficient estimates (−0.09247) become positive adjusted coefficient estimates (0.06193 and 0.19565) when $P_1 > P_0$, even though the odds ratios for the association between RSV on ALRI are equal ($\alpha_1 = \alpha_0$) at 1.1. In rows 4, 5, and 6 of Table B.2, the adjusted coefficient estimate is not positive because RSV prevalence is the same for both exposed and unexposed groups ($P_1 = P_0$) and thus, by definition, is not a confounder, even though $\alpha_1 \leq \alpha_0$. In rows 7 and 8, the adjusted coefficient estimate is positive when both $P_0 > P_1$ and $\alpha_1 < \alpha_0$. The cases of rows 7 and 8 are more likely to occur in the rainy season than the cases of rows 2 and 3 and yield an even stronger adjustment due to the presence of RSV (i.e., higher positive adjusted estimates).

These are all plausible descriptions of how, if RSV data were accurately measured and available, the observed negative results in the rainy season could be reversed. This appears to be possible even for the relatively strong negative estimate of PM_{10} excess risk in our results.

We acknowledge the assumptions made in this quantitative exercise, particularly with respect to the applicability of RSV prevalence data; however, we believe this suggests that it is plausible for an unmeasured, time-varying confounder such as RSV, in an observational study like this one, to create enough bias to reverse the observed effect estimates in the rainy season. If ALRI of bacterial etiology is more strongly associated with air pollution exposures than lower respiratory infection caused by viruses such as RSV, our analytic methods may have induced a spurious negative association between ALRI and air pollution. In addition, with virtually no RSV incidence in the dry season, these findings also lend credibility to the notion that there may indeed be a confounder that acts mainly in the rainy season.

APPENDIX C. Time-Series Results Based on SAS Analyses

Table C.1. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, for Multiple Lags, Based on Time-Series Analyses

Pollutant / Lag Days		Overall	Dry Season	Rainy Season
PM_{10}	Lag 0	0.63 (−0.04 to 1.31)	0.33 (−0.68 to 1.34)	−0.03 (−0.99 to 0.94)
	Lag 1	0.33 (−0.33 to 1)	0.55 (−0.43 to 1.54)	−0.84 (−1.8 to 0.13)
	Lag 2	0.7 (0.04 to 1.36)	1.21 (0.25 to 2.19)	−0.69 (−1.65 to 0.28)
	Lag 3	−0.29 (−0.94 to 0.37)	0.55 (−0.4 to 1.52)	−2.4 (−3.35 to −1.44)
	Lag 4	−0.17 (−0.82 to 0.5)	−0.08 (−1.03 to 0.89)	−1.39 (−2.34 to −0.43)
	Lag 5	−0.27 (−0.93 to 0.4)	−1.07 (−2.03 to −0.11)	−0.48 (−1.45 to 0.51)
	Lag 6	0.87 (0.2 to 1.54)	0.36 (−0.59 to 1.32)	0.94 (−0.06 to 1.96)
	Lag 7	0.94 (0.27 to 1.62)	0.75 (−0.21 to 1.71)	1.18 (0.16 to 2.2)
	Lag 8	−0.06 (−0.74 to 0.62)	−0.21 (−1.15 to 0.74)	−0.54 (−1.56 to 0.48)
	Lag 9	0.56 (−0.12 to 1.24)	0.97 (0.02 to 1.93)	−0.61 (−1.62 to 0.42)
	Lag 10	−0.12 (−0.8 to 0.57)	0.08 (−0.86 to 1.02)	−1.2 (−2.25 to −0.15)
	Average lag 1–6	0.38 (−0.43 to 1.2)	0.79 (−0.45 to 2.04)	−2.67 (−3.81 to −1.51)
O_3	Lag 0	0.31 (−0.37 to 0.98)	0.96 (−0.06 to 1.99)	−0.41 (−1.32 to 0.51)
	Lag 1	0.15 (−0.51 to 0.81)	0.66 (−0.34 to 1.66)	−0.41 (−1.31 to 0.49)
	Lag 2	−0.31 (−0.96 to 0.34)	0.03 (−0.95 to 1.02)	−0.77 (−1.67 to 0.13)
	Lag 3	−0.04 (−0.69 to 0.62)	0.7 (−0.29 to 1.69)	−0.94 (−1.84 to −0.04)
	Lag 4	−0.07 (−0.72 to 0.59)	0.78 (−0.2 to 1.78)	−0.95 (−1.86 to −0.03)
	Lag 5	−0.49 (−1.15 to 0.17)	−0.16 (−1.14 to 0.82)	−0.76 (−1.69 to 0.17)
	Lag 6	−0.31 (−0.97 to 0.36)	−0.4 (−1.38 to 0.58)	0.1 (−0.82 to 1.03)
	Lag 7	−0.09 (−0.75 to 0.59)	−0.24 (−1.21 to 0.74)	0.76 (−0.18 to 1.71)
	Lag 8	−0.79 (−1.45 to −0.12)	−0.09 (−1.05 to 0.89)	−1.28 (−2.21 to −0.33)
	Lag 9	−0.62 (−1.28 to 0.05)	0.4 (−0.56 to 1.37)	−1.48 (−2.43 to −0.53)
	Lag 10	−0.78 (−1.45 to −0.12)	−0.45 (−1.4 to 0.52)	−0.8 (−1.75 to 0.16)
	Average lag 1–6	−0.6 (−1.49 to 0.29)	0.68 (−0.79 to 2.16)	−2 (−3.15 to −0.83)
NO_2	Lag 0	−0.12 (−2.42 to 2.23)	−0.59 (−4.57 to 3.56)	−2.18 (−5.11 to 0.85)
	Lag 1	0.82 (−1.47 to 3.15)	1.87 (−2.08 to 5.97)	−1.45 (−4.43 to 1.62)
	Lag 2	3.74 (1.43 to 6.1)	5.74 (1.65 to 9.98)	1.28 (−1.76 to 4.41)
	Lag 3	1.51 (−0.76 to 3.83)	7.37 (3.2 to 11.7)	−3.46 (−6.39 to −0.45)
	Lag 4	1.4 (−0.86 to 3.72)	3.98 (−0.09 to 8.22)	−1.72 (−4.68 to 1.32)
	Lag 5	0.52 (−1.73 to 2.83)	2.13 (−1.91 to 6.34)	−2.1 (−5.07 to 0.97)
	Lag 6	2.49 (0.19 to 4.83)	2.8 (−1.27 to 7.04)	1.01 (−2.05 to 4.16)
	Lag 7	2.23 (−0.07 to 4.58)	1.81 (−2.19 to 5.97)	1.31 (−1.79 to 4.5)
	Lag 8	−0.11 (−2.39 to 2.21)	0.59 (−3.32 to 4.66)	−2.85 (−5.85 to 0.25)
	Lag 9	−0.64 (−2.9 to 1.66)	−0.19 (−4.08 to 3.86)	−3.16 (−6.12 to −0.1)
	Lag 10	1.05 (−1.25 to 3.41)	−1.6 (−5.46 to 2.42)	0.57 (−2.48 to 3.72)
	Average lag 1–6	3.81 (1.04 to 6.66)	11.08 (5.91 to 16.49)	−3.19 (−6.84 to 0.6)
SO_2	Lag 0	−0.05 (−2.35 to 2.29)	−2.82 (−5.67 to 0.12)	1.84 (−1.96 to 5.79)
	Lag 1	1.23 (−1.06 to 3.57)	0.01 (−2.9 to 3)	0.15 (−3.53 to 3.96)
	Lag 2	0.14 (−2.11 to 2.44)	−0.56 (−3.43 to 2.39)	−0.88 (−4.51 to 2.88)
	Lag 3	2.43 (0.13 to 4.78)	0.98 (−1.93 to 3.98)	2.01 (−1.7 to 5.87)
	Lag 4	2.47 (0.18 to 4.81)	2.45 (−0.48 to 5.47)	2.56 (−1.14 to 6.4)
	Lag 5	1.42 (−0.86 to 3.76)	2.65 (−0.32 to 5.71)	−0.66 (−4.27 to 3.07)
	Lag 6	1.32 (−0.99 to 3.68)	2.71 (−0.28 to 5.8)	−0.19 (−3.88 to 3.64)
	Lag 7	1.01 (−1.31 to 3.38)	2.06 (−0.96 to 5.18)	0.1 (−3.58 to 3.93)
	Lag 8	−0.4 (−2.69 to 1.95)	1.74 (−1.28 to 4.86)	−4.54 (−8.08 to −0.87)
	Lag 9	−2.09 (−4.34 to 0.21)	−1.67 (−4.58 to 1.33)	−3.61 (−7.15 to 0.08)
	Lag 10	−2.65 (−4.91 to −0.33)	−2.44 (−5.38 to 0.6)	−3.28 (−6.86 to 0.44)
	Average lag 1–6	4.62 (1.69 to 7.63)	4.13 (0.46 to 7.94)	4.67 (−0.19 to 9.76)

Table C.2. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, Overall and by Season, Average Lag (1–6 Days), Based on Two-Pollutant Time-Series Analyses

Pollutant	Overall	Dry Season	Rainy Season
PM_{10}	0.38 (−0.43 to 1.2)	0.79 (−0.45 to 2.04)	−2.67 (−3.81 to −1.51)
Adjusted for SO_2	0.38 (−0.69 to 1.47)	0.79 (−0.73 to 2.33)	−3.42 (−5.33 to −1.46)
Adjusted for O_3	0.86 (−0.18 to 1.92)	0.62 (−0.93 to 2.18)	−2.12 (−3.61 to −0.6)
Adjusted for NO_2	−0.05 (−0.96 to 0.86)	−1.57 (−3.19 to 0.08)	−2.51 (−3.69 to −1.31)
O_3	−0.6 (−1.49 to 0.29)	0.68 (−0.79 to 2.16)	−2 (−3.15 to −0.83)
Adjusted for SO_2	0.39 (−0.78 to 1.57)	−0.11 (−1.95 to 1.77)	0.98 (−0.99 to 3)
Adjusted for PM_{10}	−1.1 (−2.23 to 0.05)	0.36 (−1.46 to 2.22)	−1.09 (−2.6 to 0.45)
Adjusted for NO_2	−0.89 (−1.81 to 0.04)	0.28 (−1.28 to 1.87)	−2.04 (−3.22 to −0.84)
NO_2	3.81 (1.04 to 6.66)	11.08 (5.91 to 16.49)	−3.19 (−6.84 to 0.6)
Adjusted for SO_2	4.37 (0.88 to 7.98)	10.4 (4.7 to 16.4)	−7.63 (−12.47 to −2.52)
Adjusted for PM_{10}	3.89 (0.81 to 7.07)	16.13 (8.99 to 23.74)	−1.37 (−5.14 to 2.55)
Adjusted for NO_2	4.65 (1.76 to 7.62)	10.72 (5.27 to 16.45)	−1.51 (−5.31 to 2.43)
SO_2	4.62 (1.69 to 7.63)	4.13 (0.46 to 7.94)	4.67 (−0.19 to 9.76)
Adjusted for PM_{10}	4.51 (1.49 to 7.61)	3.98 (0.2 to 7.89)	5.82 (0.46 to 11.46)
Adjusted for O_3	4.48 (1.39 to 7.67)	4.17 (0.46 to 8)	3.61 (−2.75 to 10.39)
Adjusted for NO_2	3.52 (0.59 to 6.54)	2.28 (−1.42 to 6.11)	6.82 (1.86 to 12.03)

APPENDIX D. Effect Modification by Indicators of SEP in Time-Series Analyses

Table D.1. Percentage of Excess Risk of ALRI Admission (95% CI) per 10-μg/m^3 Increase in Pollutant Concentrations, by SEP, Average Lag (1–6 Days), Based on Time-Series Analysis Using SAS

Pollutant / SEP	Dry Season	Rainy Season
Individual-Level Indicator of SEP		
PM_{10}		
Nonpoor	1.54 (0.19 to 2.91)	−2.83 (−4.02 to −1.62)
Poor	1.29 (−10.51 to 14.65)	−5.79 (−14.01 to 3.22)
O_3		
Nonpoor	0.68 (−0.91 to 2.3)	−2.11 (−3.31 to −0.89)
Poor	−3.12 (−15.75 to 11.41)	0.4 (−9.68 to 11.6)
NO_2		
Nonpoor	13.81 (8.31 to 19.58)	−2.2 (−6.12 to 1.89)
Poor	3.53 (−33.24 to 60.56)	−20.13 (−46.8 to 19.92)
SO_2		
Nonpoor	4.45 (0.68 to 8.36)	4.76 (−0.21 to 9.97)
Poor	0.42 (−30.88 to 45.89)	18.1 (−23.86 to 83.17)
District-Level Indicator of SEP[a]		
PM_{10}		
Quartile 1	2.21 (−0.09 to 4.56)	−0.09 (−2.21 to 2.07)
Quartile 2	0.14 (−1.96 to 2.29)	−4.32 (−6.22 to −2.38)
Quartile 3	0.63 (−1.55 to 2.86)	−3.54 (−5.58 to −1.45)
Quartile 4	−2.59 (−8.56 to 3.78)	8.08 (1.88 to 14.67)
O_3		
Quartile 1	2.96 (0.21 to 5.78)	1.21 (−0.92 to 3.39)
Quartile 2	0.7 (−1.78 to 3.25)	−3.83 (−5.75 to −1.86)
Quartile 3	−0.26 (−2.75 to 2.3)	−1.86 (−3.93 to 0.27)
Quartile 4	−0.09 (−8.62 to 9.24)	6.77 (0.65 to 13.25)
NO_2		
Quartile 1	18.89 (8.74 to 29.99)	−3.44 (−10.09 to 3.71)
Quartile 2	5.98 (−2.22 to 14.87)	−5.91 (−11.89 to 0.47)
Quartile 3	7.02 (−1.63 to 16.45)	2.65 (−4.02 to 9.77)
Quartile 4	−8.51 (−28.67 to 17.35)	−4.74 (−20.94 to 14.78)
SO_2		
Quartile 1	11.14 (4.06 to 18.7)	14.09 (4.92 to 24.07)
Quartile 2	1.03 (−5.02 to 7.46)	6.81 (−1.48 to 15.8)
Quartile 3	−2.04 (−8.04 to 4.35)	−1.19 (−9.53 to 7.93)
Quartile 4	6.04 (−13.63 to 30.19)	2.66 (−18.78 to 29.76)

[a] Quartile 1 is the highest quartile of SEP.

APPENDICES AVAILABLE ON THE WEB

Appendices E, F, and G contain supplemental material not included in the printed report. They are available on the HEI Web site *http://pubs.healtheffects.org*.

Appendix E. SOP for Construction of the Clinical Database from Children's Hospitals 1 and 2

Appendix F. SOP for Derivation of Daily Pollutant Data

Appendix G. Comparison of Results Generated Using R vs. SAS Software

ABOUT THE AUTHORS

The HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City (HCMC) includes collaborators from the HCMC Department of Public Health, HCMC Environmental Protection Agency (HEPA), Department of Labor, Invalids and Social Affairs (DOLISA), People's Committee, University of Medicine and Pharmacy, Center for Environmental and Occupational Health, University of Science, Bureau of Statistics, Preventive Medicine Center, and Children's Hospitals 1 and 2 in Ho Chi Minh City, Vietnam; the Health Effects Institute and Beth Israel Deaconess Medical Center in Boston, Massachusetts; and the University of Hong Kong in Hong Kong, China.

Authors listed below prepared this report on behalf of all members. Lists of all members of the Working Group and the Local Steering Committee follow.

Le Truong Giang is vice-director of the HCMC Department of Public Health and served as co–Principal Investigator for the Collaborative Working Group for this study. He served as the local leader in HCMC, assuming overall responsibility for the project on behalf of the government of Vietnam.

Long Ngo is a faculty member of Beth Israel Deaconess Medical Center and Harvard Medical School. He served as co–Principal Investigator, communicating with the HCMC team and providing statistical expertise, analysis, and training for the project. Together with Le Truong Giang, Sumi Mehta, and Do Van Dzung, he also helped lead the development of the study protocol and reports.

Sumi Mehta was a senior scientist at HEI at the time of the study. As co–Principal Investigator, she coordinated the activities of the Collaborative Working Group, playing a key capacity-building role. Dr. Mehta ensured that the HEI International Scientific Oversight Committee's input to the HCMC study was adequately addressed and led the development of all study proposals and reports. She is currently director of programs for the Global Alliance for Clean Cookstoves.

Do Van Dzung is a physician and statistician at the University of Medicine and Pharmacy in HCMC.

T.Q. Thach is a research officer in the Department of Community Medicine at the University of Hong Kong.

Vu Xuan Dan was the local coordinator for this project. He works for the Center for Occupational and Environmental Health in HCMC.

Nguyen Dinh Tuan is director of HEPA.

Aaron Cohen is a principal scientist at the Health Effects Institute.

HEI COLLABORATIVE WORKING GROUP ON AIR POLLUTION, POVERTY, AND HEALTH IN HO CHI MINH CITY

Le Truong Giang, *Department of Public Health*

Nguyen Dinh Tuan, *HEPA*

Sumi Mehta, *HEI*

Long Ngo, *Beth Israel Deaconess Medical Center and Harvard Medical School*

Vu Xuan Dan, *Center for Occupational and Environmental Health*

Do Van Dzung, *University of Medicine and Pharmacy*

T.Q. Thach, *University of Hong Kong*

Aaron Cohen, *HEI*

Hoang Thi Ngoc Ngan, *Preventive Medicine Center*

Tang Chi Thuong, *Children's Hospital 1*

Le Anh Tuan, *Children's Hospital 1*

Ha Manh Tuan, *Children's Hospital 2*

Vo Cong Dong, *University of Medicine and Pharmacy*

Vo Phuong Khanh, *Children's Hospital 2*

Nguyen Thanh Giang, *Children's Hospital 2*

Huynh Tan Son, *Department of Public Health*

Tran Thi Chau, *Department of Public Health*

Le Van Khoa, *HEPA*

Vo Thanh Dam, *HEPA*

Huynh Tan Tien, *Center for Occupational and Environmental Health*

Nguyen Dang Quoc Chan, *Center for Occupational and Environmental Health*

Nguyen Van Xe, *DOLISA*

Truong Van Luong, *DOLISA*

Tran Thu Dung, *DOLISA*

Le Thi Thanh Loan, *HCMC Bureau of Statistics*

Truong Thanh Canh, *HCMC University of Science*

Local Steering Committee

Nguyen Thanh Tai, *Deputy Chairman, HCMC People's Committee*

Le Truong Giang, *Vice-Director, HCMC Department of Public Health*

Tran The Ngoc, *Deputy Minister, Ministry of Natural Resources and Environment*

Nguyen Van Xe, *Vice-Director, DOLISA*

Le Thi Thanh Loan, *Deputy Head, HCMC Bureau of Statistics*

Hoang Thi Ngoc Ngan, *Preventive Medicine Center*

Vu Xuan Dan, *Center for Occupational and Environmental Health*

OTHER PUBLICATIONS RESULTING FROM THIS RESEARCH

Mehta S, Ngo LH, Do DV, Cohen A, Thach TQ, Vu DX, Nguyen TD, Le GT. Air pollution and admissions for acute lower respiratory infections in young children of Ho Chi Minh City [published online ahead of print September 2, 2011]. Air Qual Atmos Health. DOI: 10.1007/s11869-011-0158-z.

ABBREVIATIONS AND OTHER TERMS

ALRI	acute lower respiratory infection
CAI-Asia	Clean Air Initiative for Asian Cities
CH1	Children's Hospital 1
CH2	Children's Hospital 2
CRECER	Chronic Respiratory Effects of Early Childhood Exposure to Respirable Particulate Matter
D2	District 2 air quality monitoring station
DOLISA	HCMC Department of Labor, Invalids and Social Assistance
GAM	generalized additive model
GDP	gross domestic product
HCMC	Ho Chi Minh City
HEPA	HCMC Environmental Protection Agency
ICD-10	*International Classification of Diseases,* 10th revision
ID	identification
IMCI	Integrated Management of Childhood Illness
ISOC	International Scientific Oversight Committee
kWh	kilowatt-hours
NO_2	nitrogen dioxide
O_3	ozone
PAPA	Public Health and Air Pollution in Asia
PM	particulate matter
$PM_{2.5}$	particulate matter ≤ 2.5 μm in aerodynamic diameter
PM_{10}	particulate matter ≤ 10 μm in aerodynamic diameter
QT	Quang Trung air quality monitoring station
RSV	respiratory syncytial virus
RR	relative risk
SEP	socioeconomic position
SO_2	sulfur dioxide
TSH	Tan Son Hoa air quality monitoring station
UNICEF	United Nations Children's Fund
VHLSS	Vietnam Household Living Standards Survey
VND	Vietnamese dong (currency)
WHO	World Health Organization
Zoo	Zoo air quality monitoring station

Research Report 169, *Effects of Short-Term Exposure to Air Pollution on Hospital Admissions of Young Children for Acute Lower Respiratory Infections in Ho Chi Minh City, Vietnam*, HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City

INTRODUCTION

In the past decade HEI has made a substantial commitment to furthering air pollution science in Asia by funding studies that provide science for decision making as they develop the abilities of local scientists to conduct research on air pollution and public health. Research Report 169 describes a study of associations between hospital admissions of young children for acute lower respiratory infection (ALRI*) and air pollution levels in Ho Chi Minh City (HCMC), Vietnam. The study, led by Dr. Le Truong Giang, Dr. Long Ngo, and Dr. Sumi Mehta, is the first of two studies by the HEI Collaborative Working Group to enter the HEI review process. Results from a second study, in which children's exposures to air pollution and indicators of socioeconomic status were ascertained at the household level, will be reported in a forthcoming peer-reviewed journal article. These studies were financed by HEI, the Poverty Reduction Cooperation Fund of the Asian Development Bank (Technical Assistance 4714-VIE, approved by the South Asia Regional Department on October 3, 2006), and in-kind support from the government of Vietnam.

ROLE OF HEI

HEI directed this study under its Public Health and Air Pollution in Asia (PAPA) Program, dedicated to providing new science in understudied areas in the developing countries of Asia, along with technical capacity building for local investigators. This study was also based on the Asian Development Bank's model for providing technical assistance for collaborative research. Capacity-building projects help develop the abilities of new investigators and train local personnel to organize and conduct future studies in developing areas. Such projects are designed to answer scientific questions that are relevant to regional decisions about air quality, health, and related issues. Although the studies are designed to be achievable within the constraints of data and technical capacity often found in developing countries, they are subject to HEI's full peer-review procedures, which are intended to assess the quality and utility of the study. The current study by the Collaborative Working Group is the first study of health and air pollution conducted in Vietnam and one of the first in the region to focus on the important question of the relationship between air pollution and children's health.

The HEI International Scientific Oversight Committee (ISOC), a group of highly experienced academic researchers in various fields, was convened by HEI to provide technical expertise and supervision for its international capacity-building projects. ISOC members reviewed and approved the original proposal from the Collaborative Working Group and provided oversight for the study. In typical HEI-funded studies, investigators identify and propose projects that are carried out with supervision by the HEI Health Research Committee and HEI staff. The HCMC projects involved deeper participation by the ISOC members and HEI staff in the design and conduct of the research.

For this particular study, the Collaborative Working Group included the study's co–Principal Investigators, Le Truong Giang, vice-director of the HCMC Department of Public Health; Long Ngo, a biostatistician at Beth Israel Deaconess Medical Center in Boston, Massachusetts; and Sumi Mehta, who was at HEI at the time of the study and is currently director of programs at the Global Alliance for Clean Cookstoves. Le Truong Giang arranged access to the study data, supervised local staff in study activities, and participated in the study design. Long Ngo and Sumi Mehta advised the HCMC personnel, facilitated communication between Le Truong Giang and ISOC, analyzed the data, and wrote the report for the project. ISOC commenced the

The Collaborative Working Group's 2-year study, "The Effect of Short-Term Exposure on Hospital Admissions for ALRI in Young Children of HCMC," began in October 2006. Total expenditures were $216,000. The draft Investigators' Report from the Collaborative Working Group was received for review in April 2009. A revised report, received in May 2010, was accepted for publication in June 2010. During the review process, the HEI Health Review Committee and the investigators had the opportunity to exchange comments and to clarify issues in both the Investigators' Report and the Review Committee's Critique.

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

research project in September 2006, and work on the study was conducted in Vietnam between September 2006 and April 2008. The HEI Research Committee approved the final report on October 22, 2010.

This Critique is intended to aid the sponsors of HEI and the public by highlighting both the strengths and limitations of the study and by placing the Investigators' Report into scientific and regulatory perspective.

SCIENTIFIC CONTEXT

ALRI, a disease category that combines bronchiolitis (inflammation and mucus buildup in the smallest airways of the lungs) and pneumonia (fluid in the lungs) resulting from respiratory infection, is the chief cause of death among children under 5 years of age worldwide. In 2004 it was responsible for an estimated 17% of total deaths in this age group, killing nearly 2 million young children (Mathers et al. 2009). So many children under 2 years of age die from ALRI that it accounted for 6.3% of the global burden of disease in 2000, in terms of disability-adjusted life-years (World Health Organization 2001). Although the incidence of ALRI is similar in different countries worldwide, pediatric ALRI in developed countries is usually viral and mild. In developing countries, most serious cases of ALRI are believed to be bacterial, and without antibiotic therapy they progress rapidly, with serious and sometimes fatal consequences.

Poverty, including lack of access to adequate water, food, and housing, is associated with the incidence of and mortality from ALRI, as noted in the Investigators' Report by the Collaborative Working Group. The most important risk factor is malnutrition, according to the World Health Organization (WHO) Comparative Risk Assessment (World Health Organization 2002), which estimated that some 40% of ALRI cases are directly attributable to protein malnutrition. Exposure to indoor air pollution from burning solid fuel increases the risk of ALRI by 80% (Dherani et al. 2008).

The relationships between ALRI and outdoor air pollution have been studied in industrialized countries, but they have not been widely studied in the developing world, despite increasing emissions from industrial and vehicular sources in many developing countries (HEI International Scientific Oversight Committee 2010). The 2008 Integrated Science Assessment for Oxides of Nitrogen by the U.S. Environmental Protection Agency noted that in studies where animals were exposed to viable respiratory pathogens and either nitrogen dioxide (NO_2) or filtered air, infection rates were higher in the NO_2-exposed animals. Summarizing studies of personal NO_2 exposure and lung infections in children, the assessment concluded, "Together, the epidemiologic and experimental evidence show coherence for effects of NO_2 exposure on host defense or immune system effects. This group of outcomes also provides biological plausibility for other respiratory effects described subsequently, such as respiratory symptoms or [emergency department] visits for respiratory diseases" (U.S. Environmental Protection Agency 2008).

The current study attempted to explore some of the relationships among poverty, air pollution, and hospital admissions for ALRI in a developing Asian country, including how some aspects of low socioeconomic position (SEP) and air pollution may combine to contribute to high rates of ALRI in children less than 5 years of age.

STUDY DESIGN AND METHODS

The study focused on the short-term effects of daily average exposure to NO_2, particulate matter (PM) ≤ 10 µg/m^3 (PM_{10}), ozone (O_3), and sulfur dioxide (SO_2) in HCMC and had two specific aims. The first was to assess the effects of exposure to air pollution on hospitalization for ALRI of children under 5 years of age in HCMC from 2003 through 2005, using time-series and case–crossover analyses. The second aim was to compare the magnitude of the effect of air pollution in poor children with that in other children using individual-level and group-level indicators of SEP.

The willingness of the Asian Development Bank and ISOC to approve the study depended, in part, on the availability of reliable sources of data on air pollution and ALRI hospital admissions. The investigators took advantage of excellent record-keeping procedures in the two pediatric hospitals in HCMC to study hospital admissions for ALRI, instead of mortality statistics, which would have yielded an insufficient number of cases for study.

ALRI DATA

Because the investigators were not able to access or collect data on the incidence of ALRI in the HCMC population directly, they instead collected data from the two pediatric hospitals serving the city, Children's Hospital 1 and Children's Hospital 2. The study team was confident that nearly all hospitalizations of children for ALRI in HCMC would be at one or the other of these hospitals. The case data included all admissions of children who were between 28 days and 5 years of age, resided in an urban district of HCMC, and were hospitalized for ALRI (*International Classification of Diseases,* 10th revision [ICD-10], codes J13–J16, J18, or J21) at the two pediatric hospitals between January 1, 2003, and December 31, 2005.

Both Children's Hospital 1 and Children's Hospital 2 had participated in a United Nations Children's Fund

(UNICEF) research study that required adequate computer records and procedures to manage, extract, and tabulate data and in a WHO program that implemented standardized diagnostic and admissions criteria for ALRI. Both hospitals also used ICD-10 codes for reporting and classification of disease. Local collaborators noted, however, that hospital staff did not uniformly apply clinical criteria for distinguishing between bronchiolitis and pneumonia; as a result, the investigators created a single category for lower respiratory infections that included both diagnoses.

Once abstracted from hospital records, data on admissions for ALRI were uniquely identified by the child's hospital identification (ID) number and case ID number, admission date, discharge date, and ICD-10 codes noted at admission and discharge. The study database also included demographic information such as name, address, date of birth, and sex. As the investigators presumed a possible disease onset as much as 6 days preceding admission (and investigated associations with pollutant levels recorded as many as 10 days before admission), the exact time on the day of admission was not used.

AIR POLLUTION DATA

Air pollution data were obtained through the HCMC Environmental Protection Agency (HEPA), which has operated nine air quality monitoring stations throughout the city since 2001, with technical assistance from the Norwegian Institute for Air Research (NILU). NILU installed its proprietary AirQUIS system stations in HCMC for the purposes of conducting studies and planning related to environmental air quality and health. These stations are designed to collect data every 5 minutes on levels of O_3, NO_2, and SO_2 and 24-hour filter samples for PM_{10}. NILU trained local technicians to operate and maintain the network and report the data to their specifications (Norwegian Institute for Air Research 2011). An HEI-sponsored quality assurance audit found that the data were quality-checked in the field and that, when technicians computed hourly average concentrations, they used standard practices to remove erroneous data and excursions (extreme levels) commonly recorded when the equipment was switched on.

Because NILU and HEPA chose the locations of five of the nine AirQUIS stations specifically to measure traffic-related exposures in small areas of the city, the monitoring data used in this study were limited to the remaining four stations, which the investigators describe as measuring "background or residential" exposures. They averaged data from these four sites to calculate daily mean levels for PM_{10} and daily 8-hour maximum mean levels for O_3. Excessive numbers of missing and implausible readings for NO_2 and SO_2 restricted measurements of these pollutants to two monitoring sites each. Power outages and instrument downtime occasionally limited the data available for generating citywide average pollutant levels. The locations of the air pollution monitoring stations are shown in Figure 1 of the Investigators' Report.

For PM_{10} data, daily mean levels were calculated using gravimetric analysis of 24-hour samples. For NO_2 and SO_2 data, hourly averages of the 5-minute readings reported by HEPA were averaged to create 24-hour average pollutant concentrations for each day on which the data were available and met baseline quality requirements. For O_3, hourly averages were used to create 8-hour moving averages; the maximum 8-hour moving average concentration for a given day was used in the health effects analysis.

The investigators used hourly weather data from the Southern Regional Hydro-Meteorological Forecasting Center, located in District 1 of HCMC, to calculate mean daily temperature and humidity and to track rainfall as an indicator of rainy and dry seasons.

SOCIOECONOMIC INFORMATION

Socioeconomic information for the patients with ALRI in the study was obtained from two sources. Patient records included information on eligibility for free or reduced-cost medical care, as determined by a hospital social worker after admission. Also, some patients' families were eligible for free care because they were enrolled in a government-run health insurance program for low-income families. For the purposes of the study, payment information for patients was extracted from hospital financial records, and their payment status was categorized as "paid in full," "paid a reduced fee," "left without paying," "received free medical care," or "paid by insurance." The medical and financial records were difficult to link because they lacked a common unique identifier for each patient, and thus study staff had to review each record and connect it with others for the same patient. After June 2005 all children in HCMC who were less than 6 years of age became eligible for free medical care, so individual patient information was no longer noted after this time, and ALRI patients admitted after this date were not included in the SEP analysis.

A second source of information was a poverty mapping project by the Institute of Economic Research in HCMC, the General Statistics Office of Vietnam, and the World Bank (HCMC Bureau of Statistics 2005), which estimated poverty rates for each HCMC district in 2004. These were used to assign patients a district-level SEP indicator according to the location of their residence. As of the 2004 census, the inner districts of HCMC ranged from 125,000 to 450,000 in population (average, 270,542) and 4 to 53 km^2 in area (average, 26 km^2) (General Statistics Office of Vietnam 2004).

DATA ANALYSIS

The investigators used two different statistical methods to search for associations between cases of ALRI and pollution levels in HCMC: time-series (Poisson regression) analysis and case–crossover analysis. The time-series analyses used daily average pollutant levels to assess the impact of short-term changes in air pollution on daily counts of ALRI admissions. The time-series models were adjusted for potential time-varying confounders by modeling their expected values as smoothed functions. The case–crossover analyses estimated the excess risk of ALRI (expressed as a percentage) associated with exposure by comparing the exposure of a subject to pollution at the time of the hospital admission for ALRI with the same subject's exposure at a time not associated with the onset of disease. Reference exposure periods were selected according to the study protocol, which was designed in accordance with published methods and the known disease course for ALRI. By design, case–crossover studies control for short-term confounding by individual factors and for time-invariant confounders, but they are known to have lower precision than Poisson regression estimates (Fung et al. 2003).

For the time-series analyses in this study, the investigators modeled the daily count of ALRI admissions as a function of pollutant concentrations and meteorologic data for the day of admission, for each day up to 10 days before admission (lags 0–10), and over the range of days (lags 1–6) they considered to include the probable time of onset of ALRI. They included indicator variables for season (rainy or dry) and holidays and a variable for long-term time trend. They further specified natural spline smoothing functions for temperature (4 *df*), relative humidity (4 *df*), and day (27 *df*) and fixed effects for weekdays and holidays. The investigators also performed stratified analyses by season.

In the case–crossover analyses of the HCMC data, the investigators identified each ALRI admission by child and date of admission and linked that admission to daily average pollutant levels for the same date, for individual lag days, and for an average lag 1–6 days before admission. To select an appropriate, but not correlated, daily pollution level for comparison, the investigators used an established time-stratified design (Janes et al. 2005). Mean daily pollutant levels on every 7th day before and after the date of ALRI admission, within the same month as admission, were used as controls. The excess risk of ALRI in the case–crossover analysis was computed using conditional logistic regression with the statistical procedure PHREG in SAS/STAT version 9 (SAS Institute Inc. 2000).

The investigators explored SEP as a potential modifier of the effect of pollution exposure in separate time-series and case–crossover models. The number of case subjects identified as poor (about 1% of the total) was insufficient for time-series modeling of individual-level SEP as an effect modifier, but the team did attempt to stratify data by individual indicator of SEP in a case–crossover analysis. Using the district-level indicator of SEP, the authors created four quartiles of SEP, with quartile 1 being the wealthiest and quartile 4 the poorest. They performed both time-series and case–crossover analyses of the district-level data, with stratification by quartile and season.

SENSITIVITY ANALYSIS OF RESPIRATORY SYNCYTIAL VIRUS

In their final report the authors included some additional exploratory analyses aimed at assessing the effects of a possible confounding factor (see Appendix B of the Investigators' Report). Respiratory syncytial virus (RSV) is a common viral cause of ALRI that peaks in the rainy season in Vietnam and is believed to raise the incidence of ALRI at a time when air pollution levels are low.

The investigators reanalyzed their data while controlling for seasonal patterns of RSV infection in response to results that showed that exposure to some air pollutants in the rainy season had significantly protective effects against ALRI (excess risks < 0), despite significant associations between elevated pollutant levels and ALRI admissions in the dry season. Data on the presence or absence of RSV infection were not available for the case subjects hospitalized for ALRI in this study; therefore, the investigators conducted a sensitivity analysis of the case–crossover results for PM_{10} exposure and ALRI admissions based on seasonal patterns of RSV infection in the region. They dichotomized PM_{10} exposure as greater than 50 $\mu g/m^3$ ("exposed") or less than or equal to 50 $\mu g/m^3$ ("unexposed") and assigned and included imputed RSV status as a confounding variable in the analysis of the relationship between PM_{10} and hospital admissions for ALRI. Since RSV is more prevalent in the rainy season than the dry season, and since PM_{10} levels are lowest in the rainy season, the investigators explored the sensitivity of the results to the presence of RSV assuming a lower prevalence of RSV (10%) in the PM_{10}-exposed group of ALRI cases, as compared with the unexposed group (10% to 30% RSV prevalence), among other plausible scenarios.

SUMMARY OF RESULTS

Important results and findings are summarized in Critique Table 1. These include all statistically significant results from both dry and rainy seasons for exposure to PM_{10}, NO_2, SO_2, and O_3 on different lagged days before

Critique Table 1. Selected Results from the ALRI Hospitalization Study in HCMC[a]

Pollutant / Analysis Type	Lag (Days)	Dry Season % Excess Risk (95% CI)	Rainy Season % Excess Risk (95% CI)
PM_{10}			
Case–crossover	0	**1.57 (0.21 to 2.94)**	−0.57 (−1.83 to 0.72)
	2	**1.36 (0.06 to 2.68)**	**−1.74 (−2.96 to −0.49)**
	7	**1.33 (0.10 to 2.59)**	0.21 (−1.08 to 1.51)
	9	**1.26 (0.03 to 2.51)**	−1.22 (−2.54 to 0.11)
	Average 1–6	1.25 (−0.55 to 3.09)	**−3.11 (−4.76 to −1.42)**
Time series	3	0.31 (−0.92 to 1.56)	**−2.30 (−3.48 to −1.10)**
	10	0.13 (−1.07 to 1.34)	**−1.35 (−2.59 to −0.09)**
	Average 1–6	0.53 (−1.46 to 2.56)	**−2.58 (−4.44 to −0.68)**
NO_2			
Case–crossover	0	5.15 (−0.96 to 11.64)	**−4.47 (−8.19 to −0.60)**
	2	**6.21 (0.40 to 12.4)**	−2.64 (−6.28 to 1.15)
	3	**8.49 (2.60 to 14.7)**	**−4.61 (−8.12 to −0.97)**
	Average 1–6	**8.50 (0.80 to 16.8)**	**−5.15 (−9.94 to −0.10)**
Time series	2	**6.19 (0.59 to 12.1)**	0.98 (−2.67 to 4.77)
	3	**7.48 (1.85 to 13.4)**	−3.43 (−6.98 to 0.25)
	Average 1–6	**12.62 (3.91 to 22.1)**	−3.29 (−8.51 to 2.23)
SO_2			
Case–crossover	6	**4.41 (0.21 to 8.78)**	−1.42 (−5.90 to 3.28)
	8	2.57 (−1.60 to 6.92)	**−5.50 (−9.89 to −0.91)**
	10	−4.02 (−7.93 to 0.07)	**−5.51 (−9.97 to −0.83)**
	Average 1–6	**5.85 (0.44 to 11.6)**	−2.13 (−8.25 to 4.41)
O_3			
Case–crossover	3	−0.28 (−1.45 to 0.90)	**−2.04 (−3.24 to −0.83)**
	9	0.27 (−0.91 to 1.46)	**−2.16 (−3.46 to −0.85)**
	Average 1–6	−0.79 (−2.67 to 1.13)	**−2.98 (−4.78 to −1.14)**
Time series	4	0.70 (−0.42 to 1.84)	**−1.24 (−2.41 to −0.06)**
	9	0.27 (−0.83 to 1.38)	**−1.74 (−2.95 to −0.52)**
	Average 1–6	0.47 (−1.56 to 2.54)	**−2.33 (−4.26 to −0.36)**

Overall Results (Both Seasons)		% Excess Risk (95% CI)
PM_{10}		
Time series	6	**0.83 (0.01 to 1.65)**
	7	**0.90 (0.09 to 1.72)**
NO_2		
Time series	2	**3.87 (0.87 to 6.96)**
	Average 1–6	**4.32 (0.04 to 8.79)**
SO_2		
Time series	4	**2.90 (0.12 to 5.76)**
	Average 1–6	**4.98 (0.83 to 9.31)**
O_3		
Time series	8	**−0.95 (−1.73 to −0.16)**
	9	**−0.80 (−1.58 to −0.01)**
	10	**−0.97 (−1.75 to −0.18)**

[a] Statistically significant results shown in **boldface**.

hospitalization for ALRI, obtained using either case–crossover or time-series methods of statistical analysis. Complete results for all analyses appear in Tables 22–25 of the Investigators' Report.

PM_{10} RESULTS

For the PM_{10} analyses, the case–crossover analysis for the dry season noted positive associations between ALRI admissions and an increase of 10 μg/m^3 in the PM_{10} level on several different days before admission. ALRI was not positively associated with PM_{10} levels during the dry season in the time-series analysis. For the case–crossover analysis, PM_{10} exposure during the rainy season appeared to be protective against hospitalization for ALRI, a phenomenon also noted in the analogous time-series results. When data for both seasons were combined, the time-series analysis demonstrated significant positive associations between ALRI and PM_{10} level for lags of 6 and 7 days.

NO_2 RESULTS

Levels of NO_2 in HCMC demonstrated the most consistent relationships to ALRI hospital admissions, but the association was manifest only in the results of the dry season analyses. The case–crossover and time-series analyses found significant excess risk of ALRI hospitalization associated with a 10-μg/m^3 increase in the NO_2 concentration in the dry season, and in the two analyses the associations were of equivalent magnitude for the same lag days (2, 3, and average lag 1–6 days). ALRI hospitalizations were also significantly and positively associated with NO_2 levels in the overall time-series analyses for lag 2 and average lag 1–6 days. As with the PM_{10} analyses, the case–crossover results for NO_2 in the rainy season appeared to show significant "protective" effects of exposure for lags 0, 3, and average lag 1–6 days, but these effects do not appear in the time-series results. The consistency between the dry season NO_2 results for the two methods of analyses and the different lag times, along with the persistence of elevated effects when SO_2, O_3, and PM_{10} were included in the models (Investigators' Report Table 25; Critique Table 2), is notable.

SO_2 RESULTS

ALRI associations with SO_2 were largely null, save for two significant findings of excess risk in the dry season case–crossover analyses for lag 6 and average lag 1–6 days, and in the overall time-series analyses for lag 4 and average lag 1–6 days. As with the other pollutants studied, there were some significant negative associations between ALRI and SO_2 in the rainy season case–crossover analyses.

O_3 RESULTS

O_3 levels had no significant positive associations with ALRI hospital admissions in either type of analysis for any season, but they demonstrated multiple significant negative associations (increased O_3 levels associated with decreased ALRI admissions) in the rainy season case–crossover analyses (lags 3, 9, and average lag 1–6 days) and time-series analyses (lags 4, 9, and average lag 1–6 days), and in the overall time-series analyses (lags 8, 9, and 10 days). O_3 exposure was not associated with ALRI hospital admissions in the dry season in either the case–crossover or time-series analyses. These results suggest that O_3 exposure may be protective against ALRI during the rainy season, but seasonal confounders that have not been accounted for in the analysis may also be involved in this seasonal pattern.

TWO-POLLUTANT ANALYSES

The investigators also performed a number of two-pollutant analyses using both case–crossover and time-series methods. Critique Table 2 shows significant positive findings when pollutant levels averaged for lag days 1–6 were analyzed. Significant positive estimates of effect were found for NO_2 exposure in the dry season when the results were controlled for SO_2, O_3, and PM_{10} in the adjusted time-series analysis and for SO_2 and O_3 in the adjusted case–crossover analysis. Inclusion of PM_{10} in the analysis reduced the excess risk of ALRI associated with NO_2 exposure in the case–crossover analysis below the level of statistical significance, but it had little effect on the excess risk in the time-series analysis (Critique Table 2). Significant excess risks of ALRI hospitalization were associated with SO_2 when the overall time-series and dry season case–crossover analyses were adjusted for PM_{10} and O_3. When adjusted for NO_2, however, the excess risks associated with SO_2 were not significant. Rainy season results for multiple-pollutant analyses for NO_2 or SO_2 demonstrated no significantly elevated or reduced risks (data not shown). These results suggest possible interactions between NO_2 and SO_2, since the levels of these pollutants were not highly correlated (as shown in Investigators' Report Table 16).

SOCIOECONOMIC INDICATORS

The investigators attempted to conduct an analysis of poverty as a potential effect modifier by using an individual indicator of SEP to stratify case subjects as poor or nonpoor in a case–crossover analysis. This analysis was inconclusive because only 1% of the patients in the study were identified as poor, rendering the results unstable. The

Critique Table 2. Selected Results of Two-Pollutant Analyses For Average Lag (1–6 Days)[a]

Pollutant / Copollutant	Overall		Dry Season	
	Case–Crossover	Time Series	Case–Crossover	Time Series
NO_2				
None	−1.08 (−5.14 to 3.17)	**4.32 (0.04 to 8.79)**	**8.50 (0.80 to 16.8)**	**12.6 (3.91 to 22.1)**
PM_{10}	0.95 (−3.81 to 5.94)	**4.81 (0.04 to 9.80)**	9.70 (−1.80 to 22.6)	**18.5 (6.23 to 32.1)**
O_3	1.11 (−3.30 to 5.72)	**5.63 (1.10 to 10.4)**	**10.1 (1.93 to 19.0)**	**12.5 (3.43 to 22.3)**
SO_2	3.40 (−2.39 to 9.53)	2.96 (−3.30 to 9.62)	**12.1 (2.76 to 22.2)**	**13.2 (2.83 to 24.7)**
SO_2				
None	2.61 (−1.49 to 6.87)	**4.98 (0.83 to 9.31)**	**5.85 (0.44 to 11.6)**	4.21 (−1.37 to 10.1)
PM_{10}	2.77 (−1.35 to 7.06)	**4.94 (0.77 to 9.29)**	**5.44 (0.01 to 11.2)**	4.03 (−1.56 to 9.94)
O_3	2.95 (−1.18 to 7.25)	**4.89 (0.73 to 9.23)**	**5.72 (0.31 to 11.4)**	4.23 (−1.37 to 10.2)
NO_2	1.84 (−2.31 to 6.16)	4.17 (−0.07 to 8.59)	3.70 (−1.76 to 9.47)	2.11 (−3.38 to 7.91)

[a] Statistically significant results shown in **boldface**.

investigators were, however, able to divide the patient population into quartiles based on the percentage of residents in the patient's residential district who were living below the poverty line. This district-level indicator of SEP demonstrated an excess risk for ALRI of 20.9% (95% CI, 5.39–38.7) associated with increases in NO_2 levels in the dry season for patients living in the wealthiest districts (Investigators' Report Table 30), with similar findings for SO_2. Given the literature showing an association between poverty and increasing risk of ALRI, this inverse relationship is puzzling.

RSV CONFOUNDING OF ALRI RESULTS

Appendix B of the Investigators' Report describes a simulation analysis in which the authors use hypothetical but plausible seasonal patterns of prevalence of RSV infection as confounding variables in the analysis of PM_{10} effects on ALRI admissions. RSV is an independent, viral cause of ALRI. RSV infection is highly seasonal and is not likely to be influenced by air pollution levels. In South Asia, RSV incidence peaks during times of low air pollution exposures. This simulation was intended to investigate the confusing reversal of effects seen when the authors compared results for the rainy season and dry season. Their results, shown in Table B.2 of Appendix B, demonstrate that the study results for the effect of PM_{10} exposure on ALRI admissions in the rainy season could be reversed if accurate RSV data were available and were consistent with the known seasonal patterns for the region represented in this simulation. In other words, this sensitivity analysis demonstrates that the rainy season results from this study were possibly confounded by ALRI hospitalization due to RSV infection, which is most common during a time of seasonally low pollutant exposure in Vietnam.

HEI HEALTH REVIEW COMMITTEE EVALUATION

CONDUCT OF THE STUDY

The Review Committee determined that, overall, the study data were reasonably sound and the study was well conducted. They found that comparing and contrasting the results from the case–crossover and time-series methods of analysis for the same study data was informative and a strength of this study. Although time-series analysis using Poisson regression is typically more efficient and precise, use of the case–crossover design helped the investigators work around some limitations in the data, such as the possibility of unknown, unmeasured confounding variables. The ability to compare and contrast the results from the two methods strengthened confidence in the results for NO_2 in particular.

STUDY RESULTS

Recorded measurements of ambient air pollutants used for this study indicate that, overall, HCMC has low-to-moderate levels of PM_{10}, NO_2, and SO_2 compared with levels reported in other Asian cities. Overall mean levels of pollutants reported for the years 2003–2005 in this study indicate that HCMC's annual average PM_{10} concentration of 73.2 $\mu g/m^3$ is higher than annual average levels

in 20% of 230 other Asian cities, comparable with levels in 21%, and lower than levels in 59%, according to data compiled by the Clean Air Initiative for Asian Cities (CAI-Asia 2010). Similarly, HCMC's overall average NO_2 concentration of 22.1 μg/m^3 makes it one of the 73% of 234 Asian cities with annual average readings below 40 μg/m^3. SO_2 concentrations in HCMC are also in the middle range of levels in 213 Asian cities: the overall HCMC study average SO_2 concentration was 21.6 μg/m^3, which is similar to values for the middle 36% of Asian cities (levels in 40% of the cities were lower than HCMC levels; levels in 24% were higher). O_3 was not assessed by the CAI-Asia study (CAI-Asia 2010), since adequate monitoring data were not available for a sufficient number of cities. However, HCMC's overall mean O_3 level of 75.0 μg/m^3 is relatively high when compared with annual mean levels reported for time-series studies in three of the four cities in the PAPA studies in Thailand and China — 59.4 μg/m^3 for Bangkok, 36.7 μg/m^3 for Hong Kong, and 63.4 μg/m^3 for Shanghai — and lower only than the 85.7 μg/m^3 for Wuhan (Wong et al. 2008).

The most consistent ALRI and air pollution results from the study in HCMC are the NO_2 associations with ALRI in the overall analysis and the dry season analysis. These results remain significant across both analysis methods and with adjustment for other pollutants. The SO_2 findings are not as strong or consistent across analyses as those for NO_2, and the significant associations disappear in the two-pollutant models that include NO_2. The SO_2 results are, however, still potentially informative if SO_2 could be used to identify sources emitting both NO_2 and SO_2. Positive associations between ALRI hospitalization and estimated PM_{10} exposure appear only in the dry season case–crossover analysis and the overall time-series analysis.

Critique Table 3 details findings from four similar studies of ALRI and exposure to PM_{10} and NO_2 in children under the age of 5 (Gouveia and Fletcher 2000; Braga et al. 2001; Barnett et al. 2005; Segala et al. 2008), along with results from the present study in HCMC. The results of the current study, for PM_{10} in particular, are roughly consistent with prior findings for ALRI reported in the literature. The NO_2 results of the HCMC study are noteworthy for their somewhat larger risk estimate in the time-series analysis, null risk estimate in the case–crossover analysis, and wider conference intervals when compared with the four other studies. It is also important to note that the reported average concentration and concentration range for PM_{10} in HCMC are similar to those in the other referenced studies, while the NO_2 concentration in the HCMC study is markedly lower, despite being rather "typical" of levels measured in other Asian cities.

The Review Committee was concerned about the finding that pollution exposure had an association with excess risk for ALRI in the dry season that either vanished or appeared to become a protective effect in the rainy season, as well as the apparently protective effect of O_3 exposure in the rainy season. These counterintuitive shifts in the results according to season, which occurred for all pollutants in at least some of the analyses, point to the possible effect of an unmeasured seasonal confounder. The Committee noted that although the investigators' simulations to explore the role of RSV as a possible confounder are based on well-grounded assumptions, rather than data from patients in the study, the results provide a plausible mechanism of confounding in the rainy season results.

The Review Committee was not confident about the results of the authors' attempts to analyze the impact of socioeconomic status on ALRI hospitalizations with respect to pollutant exposure. The low rate of poverty recorded in the patient records is not plausible because it is not consistent with known poverty levels in HCMC. It may indicate a failure in record-keeping, or it may reflect parental choices not to indicate that they could not pay for the hospitalization because of concern that it would negatively affect how their child was treated. Whatever the reasons, the lack of data and lack of variability in the data made it impossible to conduct a conclusive analysis of individual-level SEP, pollutant exposure, and ALRI in this study.

The district-level indicator of SEP provided some information on its potential relationships to air pollution and ALRI hospitalization. The authors found that ALRI risk increased in wealthier districts, contrary to the known association between poverty and increased ALRI risk. The Committee noted that these elevated risks may indicate a correlation between increased income and exposure to household or local pollution sources that could affect ALRI hospitalization (for example, increasing proximity to roadways with increasing wealth has been noted in some areas of the world), and that the likelihood of a child's being taken to a hospital at all might also increase with neighborhood income level. However, the mixed-income nature of neighborhoods in HCMC noted by the investigators would tend to increase the potential for misclassification of patient risk based on neighborhood values, particularly given the high population and the large area covered by the districts themselves, resulting in an inconclusive analysis. Thus, the finding of increasing ALRI risk in the dry season for areas with the least poverty may be unreliable.

Critique Table 3. Comparison of Results from Short-Term Studies of ALRI and Air Pollution in Children Less Than Five Years of Age[a]

Reference	Country	Study Period	Study Design	Outcome	Season	Age (years)	PM_{10} (µg/m^3) Mean (range)	PM_{10} (µg/m^3) RR (CI) per 10 µg/m^3	NO_2 (µg/m^3) Mean (range)	NO_2 (µg/m^3) RR (CI) per 10 µg/m^3
Barnett et al. 2005	Australia and New Zealand	1998–2001	Case–crossover	Pneumonia and acute bronchitis hospital admissions	All year	1–4	11.4 (1.3–156.3)	1.064 (1.001–1.092)	— (0.0–162.2) 1 hr. average	1.016 (1.004–1.029)
Braga et al. 2001	Brazil	1993–1997	Time series	Respiratory hospital admissions	All year	< 3	66.5 (16.0–230.5)	1.026 (1.022–1.030)	141.4 (25.0–652)	1.012 (1.008–1.016)
						3–5		1.009 (1.001–1.018)		1.002 (0.992–1.012)
Gouveia and Fletcher 2000	Brazil	1992–1994	Time series	Pneumonia hospital admissions	All year	< 5	64.9 (18.4–231.8)	1.005 (0.998–1.012)	174.3 (26.0–693)	1.003 (1.001–1.006)
Segala et al. 2008	France	1997–2001	Case–crossover	Bronchiolitis hospital consultations and admissions	Winter	< 3	22.7 (6.3–99.1)	1.060 (1.030–1.100)	50.8 (13.0–170)	1.040 (1.020–1.070)
This study	Vietnam	2003–2005	Time series (average lag 1–6)	ALRI hospital admissions	All year	< 5	73.2 (19.3–195.7)	1.026 (0.906–1.147)	22.1 (5.03–55.2)	1.043 (1.000–1.088)
			Case–crossover (average lag 1–6)	ALRI hospital admissions	All year	< 5		0.989 (0.769–1.012)		0.989 (0.949–1.032)

[a] The presentation of risk estimates varied among these studies. For consistency, all risk estimates are presented here as relative risk per 10-µg/m^3 increase in pollutant exposure estimate.

CONCLUSIONS

This is the first study of air pollution and children's health conducted in Vietnam, and it provides useful information on associations between individual pollutants and ALRI in an Asian city that are somewhat consistent with findings for ALRI and air pollution from other regions. The air quality data and the hospitalization data were quite good, permitting a thorough exploration of patterns of hospital admission relative to pollution levels in HCMC. The associations between NO_2 exposure and ALRI hospitalization in the dry season, which were very similar for the case–crossover and the time-series analyses, suggest possible household sources and environmental sources such as traffic and industrial fuel use. Moreover, they point to a potential role of pollution exposure in the development of ALRI. Further work is needed to verify these findings in developing countries.

The Review Committee also notes that certain issues complicated the study of SEP, air pollution, and ALRI. The lack of information recorded in individual hospital records made it difficult to study the role of socioeconomic status in ALRI hospitalization in this environment, and the certainty of the results was not much improved by using district-level data. Furthermore, strongly seasonal and unmeasured confounding variables were likely to have resulted in contradictory results, as demonstrated by the analyses incorporating variations in RSV prevalence between the rainy season and the dry season. These difficulties underscore the need for capacity-building initiatives in developing countries, since investigators' familiarity with the environments that they study increases the likelihood that they will be able to design studies that consider local disease trends, social factors, and environmental conditions.

From a programmatic standpoint, this first study of air pollution and ALRI hospitalization in HCMC provided useful information about the complex relationships among specific pollutants and health and explored the additional role of poverty in that relationship. It also served to strengthen the capacity of local investigators to conduct future studies in this important area, a key rationale for support of this project by HEI, ISOC, and the Asian Development Bank. Although the second study from HCMC uses a different study design in that the exposures are measured at the individual level, the Collaborative Working Group has been building on what they have learned from conducting this study to strengthen that effort.

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INSTITUTE

101 Federal Street, Suite 500
Boston, MA 02110, USA
+1-617-488-2300
www.healtheffects.org

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