Journal of Local Global Health Science

A Qatar Foundation Academic Journal

OPEN ACCESS

Effect of air pollution on daily morbidity in Karachi, Pakistan

Haider A. Khwaja[1,2,*], Zafar Fatmi[3], Daniel Malashock[2], Zafar Aminov[2], Ambreen Kazi[3], Azhar Siddique[4,5], JahanZeb Qureshi[5], David O. Carpenter[6]

[1]Wadsworth Center, New York State Department of Health, Albany, NY, USA
[2]Department of Environmental Health Sciences, School of Public Health, University at Albany, Albany, NY, USA
[3]Department of Community Health Sciences, The Aga Khan University, Karachi, Pakistan
[4]Chemistry Department, University of Karachi, Karachi, Pakistan
[5]UAZRGR, King Abdulaziz University, Jeddah, 21589, Kingdom of Saudi Arabia
[6]Institute for the Health and the Environment, University at Albany, Albany, NY, USA

*Email: hkhwaja@albany.edu

ABSTRACT

Levels of daily particulates ($PM_{2.5}$) were monitored at two sites in Karachi, Pakistan. One site (Korangi) is an industrial and residential neighborhood, while the other (Tibet Center) is a commercial and residential area near a major highway. Monitoring was done daily for a period of six weeks during spring, summer, fall and winter. Particulate levels were extraordinarily high, with the great majority of days falling into the "unhealthy for sensitive groups" or "very unhealthy" categories. The mean $PM_{2.5}$ levels in Karachi exceeded the WHO's 24 h air quality guideline almost every day and often by a factor of greater than 5-fold. Daily emergency room (ER) visits and hospital admissions for cardiovascular diseases were obtained by review of medical records at three major tertiary and specialized hospitals. ER and hospitalizations were reported relative to days in which the concentration of $PM_{2.5}$ was less than 50 $\mu g/m^3$, and by 50 $\mu g/m^3$ increments up to 300 $\mu g/m^3$. There were statistically significant elevations in rates of hospital admissions at each of the $PM_{2.5}$ categories at the Korangi site, and at concentrations $>$150 $\mu g/m^3$ at the Tibet Center site. ER visits were significantly elevated only at $PM_{2.5}$ concentrations of between 151 and 200 $\mu g/m^3$ at both sites. These results show that the extremely elevated concentrations of $PM_{2.5}$ in Karachi, Pakistan are, as expected, associated with significantly elevated rates of hospital admission, and to a lesser extent, ER visits for cardiovascular disease.

Keywords: particulates, cardiovascular disease, respiratory disease, air monitoring, mega-city, developing country

http://dx.doi.org/10.5339/jlghs.2012.3

Accepted: 28 November 2012

Cite this article as: Khwaja HA, Fatmi Z, Malashock D, Aminov Z, Kazi A, Siddique A, Qureshi J, Carpenter DO. Effect of air pollution on daily morbidity in Karachi, Pakistan, *Journal of Local and Global Health Science* **2012:3** http://dx.doi.org/10.5339/jlghs.2012.3

BACKGROUND

Ambient air pollution is a significant factor shaping public health. Recent epidemiological studies in developed countries have highlighted an association between urban concentrations of air pollution and health effects.[1–26] Adverse health effects of air pollution primarily include pulmonary[27–32] and cardiovascular diseases.[33–45] Particulate matter with an aerodynamic diameter less than 10 μm (PM_{10}),[46–49] especially less than 2.5 μm ($PM_{2.5}$),[6,50–53] and total suspended particulate matter (TSP)[22,54] have been identified as major pollution factors affecting health. The focus of research on health effects of air pollution has shifted to smaller particles. Because of the smaller diameter, $PM_{2.5}$ can be deposited deeper in the lung alveoli where they cannot be removed by the ciliary action, a process that removes larger particulates, and consequently have negative effects on the lung.[55] Due to the large surface area of $PM_{2.5}$, toxins (e.g., organic compounds and heavy metals) can be absorbed onto the surface. Organs such as the lung and heart, cells, and DNA can be damaged by the toxins. The $PM_{2.5}$ particles are, therefore, regarded as being more toxic than PM_{10} and TSP.

Most studies investigating an association between levels of air pollution and rates of human disease have been conducted in developed countries where concentrations of air pollution, climatic conditions, and many other factors are significantly different from those in most developing countries. Air pollution is a critical problem in Asian cities with possibly serious health impact. The World Health Organization (WHO) estimates that urban air pollution contributes each year to about 800,000 deaths and 4.6 million healthy life-years lost worldwide, but the burden is not equally distributed: approximately 65% of the deaths and lost life-years occur in the developing countries of Asia.[56] This disparity demonstrates an urgent need for conducting and evaluating environmental studies on the health effects of air pollution in major cities of Asia.

The concurrent increase in the population, industrialization, energy use, and the number of automobiles on the roads every year is giving rise to a threateningly high rate of increase in air pollutants in the urban areas of Pakistan (population = 173 million in 2010). A study of air pollution levels in major urban centers found that two major cities in Pakistan have one of the highest TSP loading recorded so far in any mega city of the world (Fig. 1).[57] Karachi, located in the southeastern part of Pakistan on the Arabian Sea, has a population of 18 million and is one of the most heavily polluted mega cities in the world with serious human health risks.[57–59] The city is congested with a large number of motor vehicles (>1.3 million). It has a large industrial base in and around the city. Three major industrial areas, Landhi, Korangi, and Sindh Industrial Trading Estates (SITES), are shown on the map (Fig. 2). Air pollution health studies that incorporate emergency room visits and daily admissions to hospitals are advantageous, as they make it possible to examine the relationship

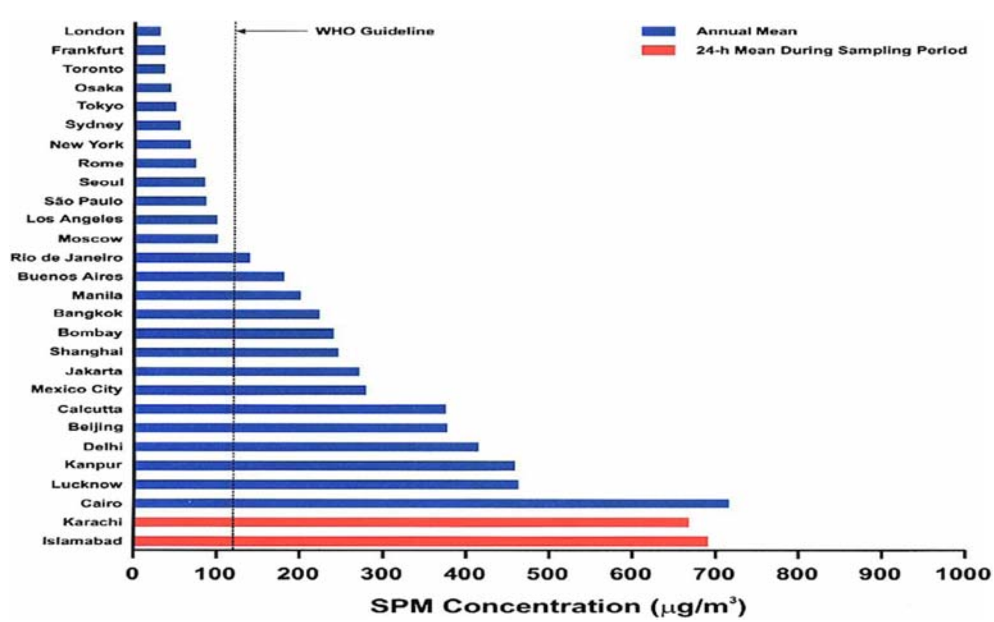

Figure 1. **Comparison of TSP concentrations at Karachi and Islamabad with those reported for the various megacities of the world. Reproduced with permission from Parekh et al.[57]**

between acute health outcomes and daily variations in air pollution.[19,28,34–36,39,40,60,61] However, not a single study of the health effects of air pollution has been performed in this developing mega city.

To respond to the call for an in-depth investigation of the health effects of ambient air pollution in one of the largest cities of the developing world,[62] we conducted a time-series study of the effects of short-term exposure to outdoor air pollution on daily morbidity for cardiovascular diseases. This research will provide the scientific community and policy makers as well as the public information about the health effects of poor ambient air quality and how it compares to other developing and developed countries of the world. The specific aim is to carry out a long-term environmental project to investigate the association between concentrations of $PM_{2.5}$ and hospital admissions and emergency room (ER) visits for cardiovascular diseases among residents of various communities in Karachi.

METHODS

Study location

This study covered a period of 12 months (August 2008 to August 2009) and was carried out in the city of Karachi. The study population consisted of all people who resided in various communities in Karachi and who visited ERs and/or were admitted to two major tertiary care hospitals serving the city [National Institute of Cardiovascular Diseases (NICVD) and Aga Khan University Hospital (AKUH with primary diagnoses of cardiovascular diseases.

The megacity Karachi (Fig. 2) is the most urbanized, industrialized, and affluent city in Pakistan. It is located in the southeastern part of Pakistan on the Arabian Sea (Latitude 24° 51′ N; Longitude 67° 02′ E). Most of the land consists largely of flat or rolling plains, with hills on the north and west and an undulating plain and long coastal area in the south-east. The hills in Karachi are the off-shoots of the Kirthar Range extending from north to south for about 300 km. The highest point of these hills is about 528 m in the extreme north of the city. The city is comprised of 18 urban/sub-urban towns (Baldia, Bin Qasim, Gadap, Gulberg, Gulshan, Jamshed, Kemari, Korangi, Landhi, Liaquatabad, Lyari, Malir, New Karachi, North Nazimabad, Orangi, Saddar, Shah Faisal, and Sindh Industrial Trading Estate) and 6 cantonments, with a population of 18 million, representing about 10% of Pakistan's total. About 40% of the city's population lives in low income, non-zoned settlements and squatter colonies or *"Kachi Abadis"*.

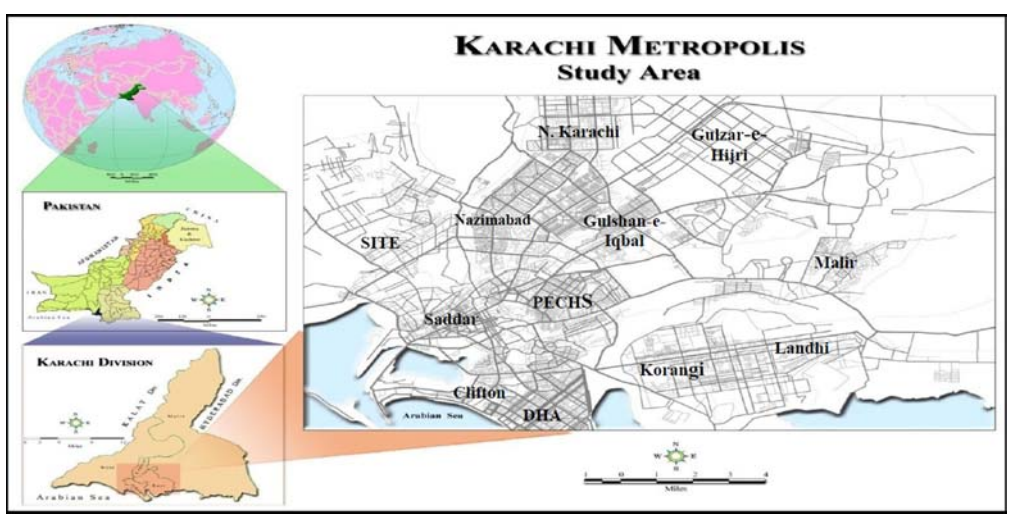

Figure 2. Map of Karachi, Pakistan.

Karachi's climate is subtropical, almost desert like with scanty rainfall (mean annual rainfall 256 mm), the bulk of which occurs during the July–August monsoon season. Pollutants are pushed towards the shore during the northeast monsoon season and inland during the southwest monsoons. The city is quite humid in the summer (85% humidity in August–the wettest month) and is relatively dry in the winter (58% humidity in December–the driest month). The average monthly temperature varies between 13°C and 34°C. During the summer (April–August), the temperatures are high, ranging from 30 to 44°C. Karachi has a large industrial base in and around the city including oil-fired power plants, cement factories, steel mills, scrap metal recycling plants, shipping, railroad yards, foundries, jute and textiles, oil refineries, heavy petrochemical industries, automobile assembly plants, pharmaceuticals, printing and publishing plants, food processing plants, paper mills, chemical, glass and ceramics, battery, tanneries, brick kilns, and several light industries. There is also solid waste incineration and open burning of municipal wastes.

Air pollution monitoring

Air pollution monitoring for $PM_{2.5}$ was conducted at two fixed stations located at Korangi (industrial/residential) and Tibet Center (commercial/residential), located on M.A. Jinnah road in Saddar town (Fig. 2).[63] The M. A. Jinnah road is located in the midst of a large central business district and is the main ring road in Karachi that is the busiest road throughout the day and late evening hours. Approximately 300,000 vehicles pass M. A. Jinnah road daily. The Korangi industrial area is the second largest industrial area of Karachi. Approximately 2000 industries of various types are located in this area, which include refineries, textile, chemical, and tanneries (>100 units). The criteria for site selection included: i) location of these stations should not be in the direct vicinity of vehicular traffic or industrial sources; ii) locations should not be influenced by local pollution sources and should avoid buildings, trees, or housing large emitters such as coal-, waste-, or oil-burning boilers, furnaces, flues, wood burning, and incinerators; iii) unrestricted airflow around the sampler; and iv) sampler should be placed at 4–7 m above the ground level so that the air is relatively well mixed and less likely to be strongly affected by sources in the immediate vicinity. Thus the $PM_{2.5}$ monitoring results reflect the general background urban air pollution level rather than local sources such as vehicular traffic or industrial emissions.

The sampler (Fig. 3) consisted of a housing, power supply, UPS as a backup, gooseneck, 5.72 cm inner diameter rubber stopper, 47 mm filter holder, data logger, mass flow meter, a pump with a flow controller, elapsed time indicator, and a Teflon coated aluminum cyclone separator (Model URG-2000-30EH) URG Corporation, Chapel Hill, NC, USA) with a cut size of 2.5 μm operated at a flow rate of 16.7 L/min. $PM_{2.5}$ samples for mass determination were collected on pre-weighed 47 mm 2.0 μm polytetrafluoroethylene (PTFE) membrane filters (Whatman Inc. Florham Park, NJ, USA) with a polypropylene support ring (sequentially numbered). Sampling duration was 24 h (7:00 a.m to 7:00 a.m) at each site for 6 weeks in each quarter (i.e., January–March; April–June; July–September; and October–December). The resulting total sampled air volume was $\sim$24 m^3. At the end of each 24 h period, filters were carefully removed from the sampling device and were placed inside the individual polyethylene petri-dishes. Graduate students under the expert supervision of faculty members operated the monitoring sites.

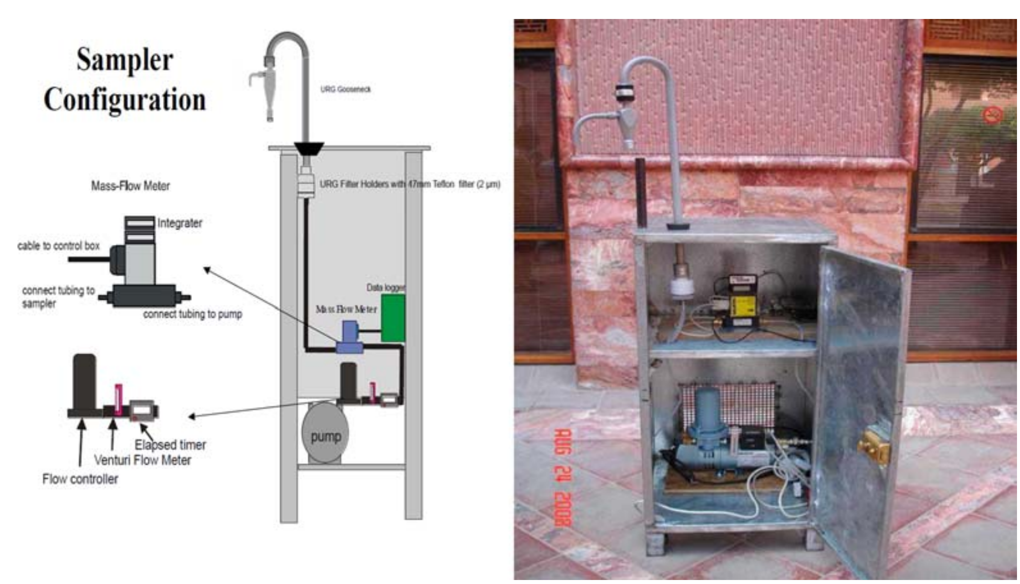

Figure 3. Schematic of the PM2.5 sampler (left) and image of sampler used in the study (right).

The laboratory for weighting $PM_{2.5}$ was maintained as a "*clean room*" conditions to minimize contamination, air flow interferences, and electrostatic charges. The filters, both before and after sampling, were visually inspected for pinhole, loose material, discoloration, and non-uniformity. They were conditioned for a minimum of 24 h in a controlled temperature/relative humidity (RH) room to minimize the effects of water artifact (if any). The filter weights were obtained on a microbalance (ATI CAHN, Model C-44). $PM_{2.5}$ mass concentration was calculated in $\mu g/m^3$ as the difference in filter weight before and after sampling divided by the total sampled air volume.

Hospital data acquisition

Daily records of patients who visited ERs and/or were admitted for cardiovascular diseases in NICVD and AKUH were collected. A protocol was developed for the collection of patient's information by trained team physicians. The data provided information on age, gender, date of ER visit and/or admission and discharge, and the principal diagnosis as well as demographic information. Data from AKUH was retrieved from a well-established hospital information management system (HIMS). Our analysis focused on finding the association between $PM_{2.5}$ and daily cardiovascular hospitalizations and ER visits. It was not able to address events that happened after admission. We reviewed the computerized records for the three hospitals for the study period to identify all cases that were seen in ERs and/or admitted to the hospitals for cardiovascular diseases. The causes of ER visits and/or hospital admissions were coded according to our Classification of Cardiovascular Diseases. Prior approvals from Ethical Review Committees of the participating hospitals (Aga Khan University) and the Institutional Review Boards of the New York State Department of Health and the University at Albany were obtained.

Meteorologic/weather variables

To allow adjustment for the effect of weather on ER visits and hospital admissions, meteorological data (temperature – mean, maximum, and minimum in °C, relative humidity – mean, maximum, and minimum expressed as percentages, barometric pressure, wind speed, and wind direction) were obtained as electronic files on a daily basis during the sampling period from: www.wunderground.com/global/stations. All the computerized data of $PM_{2.5}$ and meteorological conditions were reviewed.

Quality control

An extensive Quality Assurance/Quality Control Program was maintained throughout this investigation to ensure the integrity of data collected in the field. The QA/QC plan included: detailed description of field and laboratory methods used, equipment calibration procedures, procedures for field blanks, and storage conditions. One field filter blank check was analyzed per batch of 10 samples. The microbalance was regularly checked with NIST-traceable standard calibrated weights.

The PTFE filters used for $PM_{2.5}$ mass are comparatively small, each weighing ~150 milligrams. Because of the size and weight of particles that are collected on these filters, net weights were measured in micrograms. With the operational constraints of the microbalances, the introduction of water vapor on the filters, and the measurement of small particles and filter loadings, the weighing laboratory was designed to perform under strict operational criteria. Weights were considered valid if duplicate weights were within 10 μg of each other.

Throughout this study, careful consideration was given to all possibilities for the introduction of errors, either systematic or random, during each of the discrete steps that comprise the sequence of operations, ranging from sample and hospital data collection to data analysis. The computerized data for all the hospitals, $PM_{2.5}$ results, and meteorological conditions were reviewed thoroughly by at least two independent team members.

Statistical analysis

We created separated data records for each $PM_{2.5}$ monitoring site and hospital, including the number of ER visits per day and admissions per day, the daily concentrations of $PM_{2.5}$, and the daily mean temperature and relative humidity. Summary statistics were calculated for each variable including mean, standard deviation, minimum, maximum, and percentiles. We conducted analyses on hospital data, pollutant, and meteorological variables, stratified by location, hospital, ER visits and/or hospital admissions, age, and gender. A generalized linear model (GLM) using negative binomial regression[28,64] was used to conduct a time series analysis of daily counts of hospital data, daily concentrations of $PM_{2.5}$ ($\mu g/m^3$), and covariates in order to estimate the influence of air pollution on ER visits and hospital admissions due to cardiovascular diseases. In addition, data were modeled with generalized linear Poisson model with scaled variance estimates to account for Poisson overdispersion[61]; however, results yielded large ratio values between deviances to degree of freedom, possibly indicating the presence of model misspecification or over dispersion. Negative binomial regression yielded results with acceptable ratios, and consequently was chosen for final models. Deviance and Pearson residuals were used to assess goodness of fit.

Models were adjusted for the effects of temporal trends and meteorological variables by including the following: dummy variables for day of the week (DOW), holidays, season, cubic splines of day (study day) with knots at the first sampling of each month, and cubic splines of average temperature and relative humidity. Lag time between pollutant measurements and ER visits and/or hospital admissions were evaluated using 0-, 1-, 2-, and 3-day lags for cardiovascular diseases. Data were analyzed using the SAS statistical package (SAS Institute Inc., Cary, NC, USA; Version 9.2).

RESULTS AND DISCUSSION

No prior studies exist in Pakistan examining the association between levels of air pollution with daily morbidity due to cardiovascular diseases. These preliminary results will provide scientific community, public, and policy makers with estimates of current risks of cardiovascular ER visits and hospitalization as a result of poor air quality. A total of 24,124 (68.6%) ER visits and 11,023 (31.4%) hospital admissions (HAs) due to cardiovascular diseases among adults and children living in various communities in Karachi occurred in the study period. Table 1 gives the summary statistics for daily counts of ER visits and HAs at both sites, broken down into age groups and by gender. Variation among the hospitals is demonstrated by the fact that the most ER visits and hospitalizations were determined at the NICVD, which is the largest cardiac center in the country and receives only patients with cardiovascular diseases. Overall, there were more male hospitalizations than female. HAs were more common among males, which accounted for approximately 58% of the total number of patients from both AKUH and NICVD (63.2% and 57.2%, respectively). Female ER visits were somewhat higher than for males However, variations among hospitals were observed, with females comprising 39.4% and 56.6% at AKUH and NICVD, respectively. Men and women between the ages of 40 and 60 comprised the greatest percentage of all HAs and ER visits.

Table 1. Daily counts of ER visits and hospital admissions by sex and age groups due to cardiovascular diseases in Karachi, August 2008–August 2009.

	Percent of all patients n(%)			
	AKUH[a]		NICVD[b]	
	n	%	*n*	%
Hospital Admissions				
Male	644	63.2	5722	57.2
Female	375	36.8	4282	42.8
Age ≤ 40	191	18.7	2351	23.5
40 < Age ≤ 60	386	37.9	5181	51.8
60 < Age	442	43.4	2472	24.7
Emergency Room Visits				
Male	3261	60.6	8143	43.4
Female	2117	39.4	10603	56.6
Age ≤ 40	834	15.5	5078	27.1
40 < Age ≤ 60	2289	42.6	9747	52.0
60 < Age	2255	41.9	3921	20.9

[a] Aga Khan University Hospital.
[b] National Institute of Cardiovascular Disease.

Our hospital data indicated that the leading causes of cardiovascular disease are ischemic heart disease (IHD, 37%), hypertension (HTN, 25%), and myocardial infarction (MI, 12%). Cardiomyopathy (CMP, 3%) and mitral stenosis (MS, 3%) were the principal causes of ER visits and hospital admissions in the "All Other" category. Figure 4 shows the breakdown of ER visits and hospital admissions due to top three cardiovascular diseases by age. A persistent elevation in ER visits and hospital admissions with age is evident. Adults between 41 and 60 + years of age were the group seeking health care most

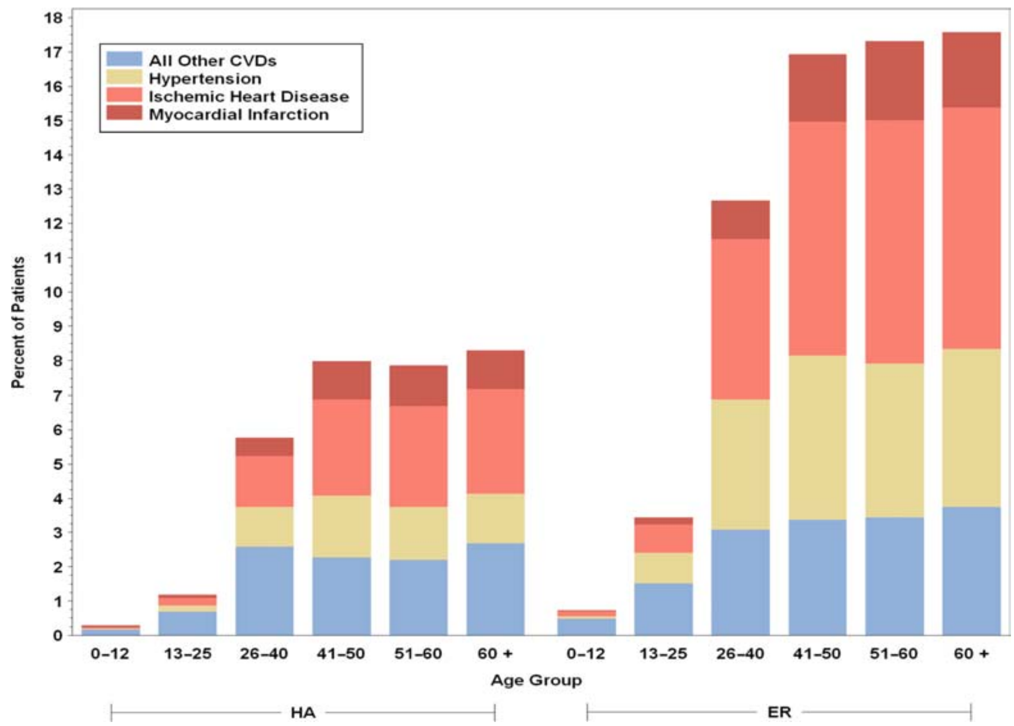

Figure 4. Percentage of ER visits and hospital admissions according to age categories and by leading CVDs observed during the study.

frequently. Ischemic heart disease followed by HTN and MI were the most common causes of admissions in this age group. ER visits due to IHD followed by HTN and MI were more frequent in the 51–60 age groups. The percentage distribution observed in the 41–50 or 60 + years of age and older group was slightly decreased relative to that observed for the 51–60 years old. The lack of increased ER visits and hospital admissions in children between 0–12 years of age is not surprising, since young children are usually kept home, are less exposed to outdoor air pollution and are less likely than older adults to suffer from cardiovascular disease. This observation is consistent with earlier studies in developed countries by Schwartz and Dockery,[65] showing that the increased risk of deaths was greatest in the elderly, and was greatest for cardiovascular disease. A more detailed examination of particulate matter-related risk by deciles of age[66] showed the risk beginning to increase at approximately 40 years of age and reaching its maximum for those 75 years of age and older.

Figure 5 shows the mean daily temperature and humidity during the study period.

Temperature and humidity varied between 15°C and 35°C (mean ~30°C except 20.4°C in the cold season) and between 24% and 88%, respectively, reflecting the subtropical climate in Karachi. The winter season in Karachi is dominated by cold, dry air (mean humidity = 57%) and ground-based inversion occur frequently and increases the concentration of pollutants. Consequently, people are likely to go outdoors and are expected to have higher risks of ambient air pollution exposure. In contrast, summer season is governed by high temperature and humidity (mean temperature = 30°C; mean humidity = 74%), people generally use air conditioning, thus expected to be less exposed to outdoor air pollution.

Descriptive statistics of $PM_{2.5}$ concentrations and meteorological variables are presented in Table 2. The one-year monitoring data revealed that the mass concentration of Karachi $PM_{2.5}$ at the Korangi site showed a seasonal variation with higher values in winter (112 $\mu g/m^3$) and autumn (106 $\mu g/m^3$), lower values in spring (94.8 $\mu g/m^3$), and the lowest in summer (87.5 $\mu g/m^3$), whereas at the Tibet Center site the ranking was winter > summer > spring > autumn. Low boundary layer heights combined with increased emissions from heating sources and biomass burning may lead to high $PM_{2.5}$ concentrations in the winter at both the sites. However, better dispersion of pollutants caused by the increased boundary layer heights and precipitation in summer may likely lower the $PM_{2.5}$ concentrations. The same findings were also observed in the urban area of Beijing,[67] with the highest $PM_{2.5}$ concentrations observed in the winter and the lowest concentrations found in the summer.

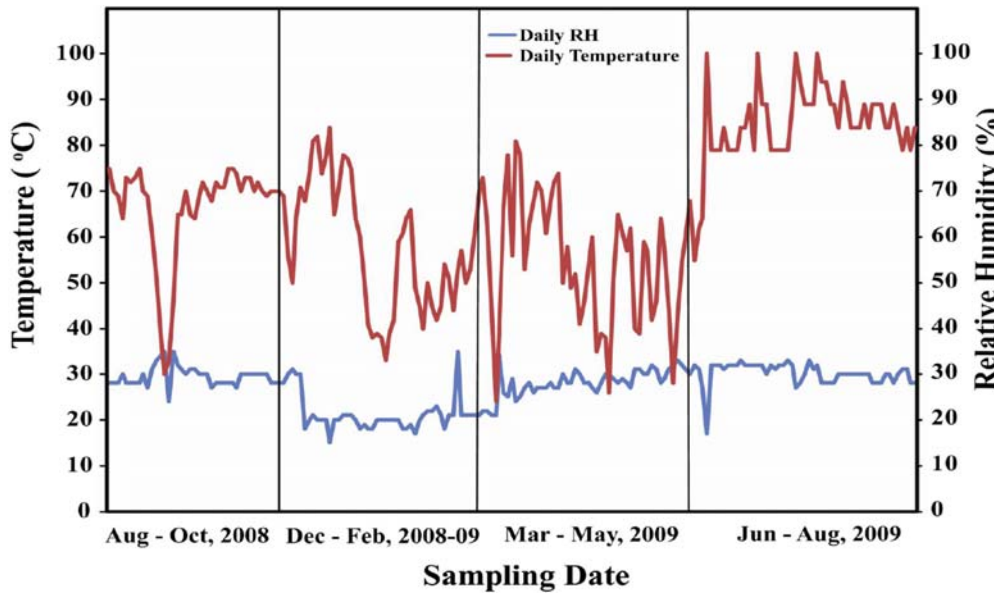

Figure 5. Plots of 24-hour mean temperature and relative humidity in Karachi, August 2008 – August 2009.

Air quality index (AQI) is a good indicator of daily air quality and its implications for short-term health. The higher the AQI value, the greater the level of air pollution and health risk. The AQI was calculated (http://airnow.gov/index.cfm?action=resources.conc_aqi_calc) for $PM_{2.5}$ at Korangi and Tibet Center (Fig. 6), with the highest pollutant-specific value reported as a "level of health concern" (moderate: 16 – 35 μg/m^3, unhealthy for sensitive groups: 36 – 65 μg/m^3, unhealthy: 66 – 150 μg/m^3, very unhealthy: 151 – 250 μg/m^3, and hazardous: 251 – 300 μg/m^3). Based on the air quality index, it is evident that there were 19% days of unhealthy air quality for sensitive groups, 67% days of unhealthy

Table 2. Summary statistics of daily $PM_{2.5}$ concentrations and meteorological variables by season in Karachi, Pakistan, August 2008 – August 2009.

Variable	Mean ± SD[a]	Minimum	25th[b]	50th[b]	75th[b]	Maximum
Fall						
$PM_{2.5}$ (μg/m^3, Korangi)	106.40 ± 58.50	38.5	64.7	83.7	136.7	246.6
$PM_{2.5}$ (μg/m^3, Tibet Center)	57.90 ± 29.50	27.4	40.5	50.8	59.4	167.3
Temperature (°C)	29.50 ± 2.10	24.00	28.00	30.00	30.00	35.00
Humidity (%)	65.90 ± 10.80	30.00	65.00	70.00	72.00	75.00
Pressure (in Hg)	29.72 ± 0.09	29.57	29.65	29.73	29.78	29.97
Winter						
$PM_{2.5}$ (μg/m^3, Korangi)	111.60 ± 39.70	32.80	88.00	104.00	131.00	206.80
$PM_{2.5}$ (μg/m^3, Tibet Center)	104.30 ± 57.40	41.90	72.20	81.90	116.40	268.80
Temperature (°C)	20.40 ± 2.70	15.00	20.00	20.00	21.00	35.00
Humidity (%)	56.80 ± 15.10	24.00	44.00	56.00	70.00	84.00
Pressure (in Hg)	30.01 ± 0.07	29.88	29.95	30.01	30.07	30.14
Spring						
$PM_{2.5}$ (μg/m^3, Korangi)	94.80 ± 46.60	36.30	61.60	87.40	107.00	278.90
$PM_{2.5}$ (μg/m^3, Tibet Center)	71.10 ± 24.30	44.30	54.00	63.00	81.00	156.10
Temperature (°C)	28.80 ± 2.20	24.00	27.00	28.00	31.00	33.00
Humidity (%)	56.00 ± 12.90	26.00	46.00	57.50	64.50	81.00
Pressure (in Hg)	29.81 ± 0.07	29.65	29.77	29.82	29.85	30.01
Summer						
$PM_{2.5}$ (μg/m^3, Korangi)	87.50 ± 24.20	29.70	74.80	87.00	100.00	145.40
$PM_{2.5}$ (μg/m^3, Tibet Center)	73.20 ± 15.70	40.80	65.00	73.00	81.00	131.90
Temperature (°C)	30.20 ± 2.50	17.00	28.00	30.00	32.00	33.00
Humidity (%)	73.70 ± 6.40	62.00	69.00	74.00	78.00	88.00
Pressure (in Hg)	29.52 ± 0.10	29.38	29.46	29.49	29.59	29.79

[a]Standard deviation; [b]Percentiles.

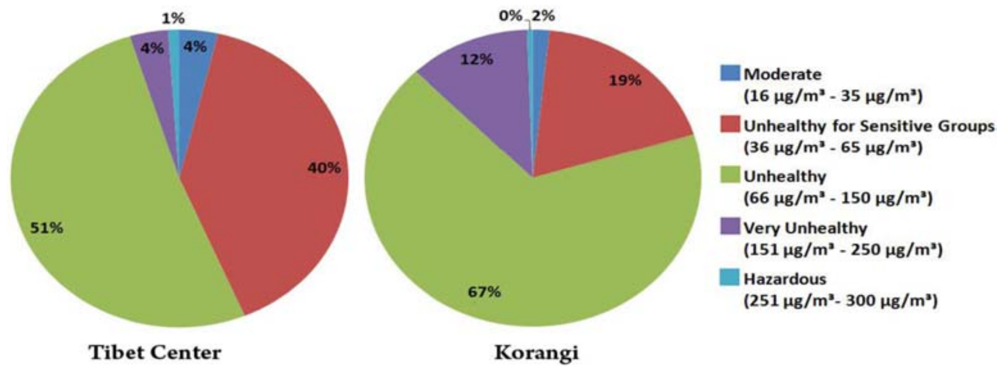

Figure 6. Air Quality Index (AQI) at Korangi and Tiber Center in Karachi, Pakistan, August 2008–August 2009.

air quality, and 12% days of very unhealthy air quality during the entire study period at Korangi site. A study by Luginaah et al.,[15] found associations between ambient air pollution and daily hospital admission of respiratory diseases especially among females in the Windsor, Canada "area of concern". The mean PM_{10} concentration was 50.6 ± 35.5 μg/m^3 and based on the air quality index, there were 165 days of poor air quality, 583 days of moderate air quality, and 1,352 days of good air quality during the entire study period (>2000 days). On the basis of the multi-pollutant index (MPI), Gurjar et al.,[68] report Dhaka, Beijing, Cairo, and Karachi as the most polluted, whereas Osaka-Kobe, Tokyo, Sao Paulo, Los Angeles, New York, and Buenos Aires as the least polluted megacities.

$PM_{2.5}$ concentrations in Karachi are among the highest ever documented in the world. The World Health Organization's (WHO) 24 h air quality guideline for $PM_{2.5}$ is 20 μg/m^3.[69] The mean concentrations of $PM_{2.5}$ in Karachi were in "exceedance" by a factor of at least five, implying that airborne fine particles in Karachi have significant adverse impacts on health.

The time-series analysis showed evidence of positive associations of ambient fine particle air pollution, meteorological factors, and seasonal parameters with ER visits and hospital admissions due to cardiovascular diseases in Karachi. Table 3 presents the relative risk estimates of hospital data per 50 μg/m^3 in pollution. As a result of there being fewer data observed for $PM_{2.5}$ concentrations in the range 251–300 μg/m^3, we have combined this category with $PM_{2.5}$ (201–251 μg/m^3). Note that although fine particulate air pollution was measured at two different sites, Korangi and Tibet Center, increases in same day $PM_{2.5}$ concentrations were associated with an increase in ER visits and HAs at both sites. Statistically strongest relationships were observed for HAs (RR = 1.613, 95% CI = 1.274–2.043 for Korangi; RR = 2.036, 95% CI = 1.424–2.911 for Tibet Center) for $PM_{2.5}$ concentrations (151–200 μg/m^3). Unexpectedly the relations were found to be less strong at the very highest $PM_{2.5}$ concentrations – possibly residents avoid going outside on days of extreme pollution. This analysis provides to the growing evidence linking ambient particulate matter with daily morbidity in developing countries.

Table 3. Relative risk estimates (95% CI) of cardiovascular hospital admissions and ER visits associated with 50 μg/m³ increase in $PM_{2.5}$ (μg/m³), during 2008–2009.

	Relative Risk			
	Korangi		Tibet Center	
$PM_{2.5}$ (μg/m^3)[a]	ER Visits	Hospital Admissions	ER Visits	Hospital Admissions
$51 < PM_{2.5} < 100$	1.155 (0.935, 1.427)	1.243** (1.028, 1.503)	0.980 (0.838, 1.147)	1.057 (0.927, 1.205)
$101 < PM_{2.5} < 150$	1.186 (0.951, 1.479)	1.321*** (1.086, 1.607)	1.168 (0.927, 1.472)	1.025 (0.832, 1.263)
$151 < PM_{2.5} < 200$	1.339** (1.037, 1.730)	1.613**** (1.274, 2.043)	1.342* (0.940, 1.914)	2.036**** (1.424, 2.911)
$201 < PM_{2.5} < 300$[b]	1.421 (1.013, 1.993)	1.559** (1.087, 2.237)	1.190 (0.882, 1.606)	1.284* (0.951, 1.733)

*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$; ****$p < 0.001$.
[a] $PM_{2.5}$ concentrations of less than 50 μg/m^3 were used as reference.
[b] Two categories were combined.

There have been a number of epidemiologic studies in developed countries that have reported significant associations between short-term exposures to ambient particulate air pollution and cardiovascular mortality. Studies reporting particulate matter associations with cardiovascular hospitalizations have been more recent. Our findings complement substantial evidence on positive associations between day-to-day variation in $PM_{2.5}$ concentrations and hospitalizations for cardiovascular diseases in developed countries. Dominici et al.,[35] reported a positive association of $PM_{2.5}$ with risk for hospital admission for cardiovascular and respiratory diseases in 204 US urban counties for 1999–2002. The largest association was for heart failure, which had a 1.28% (95% CI, 0.78%–1.78%) increase in risk per 10 $\mu g/m^3$ increase in same-day $PM_{2.5}$. Ito et al.,[70] analyzed Medicare admission data for Detroit, Michigan for 1992–1994, along with size fractionated particle concentration data from a nearby monitoring station in Windsor, Ontario and showed positive associations of $PM_{2.5}$ for hospitalization for ischemic heart disease, heart failure, pneumonia, and chronic obstructive pulmonary disease (COPD). A study by Haley et al.,[36] that analyzed cardiovascular disease hospitalizations in New York State between 2001 and 2005 found the strongest association with heart failure. The increased risk (95% CI) of hospitalizations per 10 $\mu g/m^3$ increase in $PM_{2.5}$ was found to be 0.46% and 1.51% for ischemic heart disease and heart failure, respectively. Mean concentrations of $PM_{2.5}$ reported in this study for various locations in New York State and New York City ranged from 11.1 to 15.5 $\mu g/m^3$. Relative risk estimates (95% CI) for all cardiovascular diseases from our study indicate that an increase in $PM_{2.5}$ concentrations of 10 $\mu g/m^3$ at Korangi and Tibet Center is associated with an increase in 1.6% HAs and 1.3% and 1.6% ER visits, respectively. The mean annual concentration of $PM_{2.5}$ at Korangi and Tibet Center is 100.1 and 76.6 $\mu g/m^3$, respectively. At these levels, the risk associated with ambient particulate concentration far exceeds that which has been observed in developed countries.

Our study has strengths and limitations. The strengths include the site of study, which is includes the largest public hospital in the country for heart diseases serving the population of the urban metropolitan city of Karachi. The study design and the quality of hospital data are also major strengths. Moreover, our results are consistent with those in developed countries relating CVD hospitalizations to exposure to particulate air pollution. Limitations of this study are the same as in other studies of this kind. First, we assume that air pollutant concentrations measured at fixed sites serve as a proxy for the personal exposure during the study period. Factors such as outdoor and indoor emission sources, time spent outdoors, time spent indoors, life style, and smoking may influence the validity of this assumption. However, personal exposure assessment is not realistic. Second, the potential miscoding and diagnosis of CVD events may introduce a bias in daily time-series analyses. We used only primary diagnosis, an approach that should diminish misclassification of outcomes. Third, we monitored only HAs and ER visits and did not have information about outpatient or physician office visits, ER visits and hospitalizations at other hospitals. In addition, our study does not include patients with CVD who did not seek treatment, or died at home or en-route to the hospital. We also cannot distinguish multiple hospitalizations for one individual from those for several individuals. For these reasons our study is likely to under-represent the true risk of ambient air pollution to the residents of Karachi. In spite of these limitations our results provide strong evidence that significant morbidity is associated with $PM_{2.5}$ air pollution.

CONCLUSIONS

This study is one of the first to investigate the relationship between particulate air pollution and cardiovascular diseases in a mega city in a developing country where particulate levels are extraordinarily high. The $PM_{2.5}$ levels averaging about 5–7 fold higher than the WHO guideline on a "good" day, and with frequent peaks at levels as high as 279 $\mu g/m^3$. Particulates were measured at two sites, one more industrial than the other, but in general the patterns over time were similar. Our studies show, as has been demonstrated elsewhere in developed countries, that higher levels of $PM_{2.5}$ are associated with a striking elevation in rates of ER visits and hospitalizations for cardiovascular diseases (ischemic heart disease, hypertension, myocardial infarction). Because of the striking levels of air pollution that we have documented, it is imperative that further investigation of health outcomes in mega cities of developing countries be performed.

AUTHOR CONTRIBUTIONS

Drs. David Carpenter, Zafar Fatmi and Haider Khwaja: Responsible for the overall project, reviewing the air pollution monitoring data, hospital data, and the statistical data anlaysis;
Daniel Malashock and Zafar Aminov: Statistical data anlaysis of air pollution and hospital;

Dr. Azhar Siddique: Responsible for managing the air pollution monitoring sites, data review, and analysis.
Dr. Jahan Zeb Qurashi: Involved in organizing and operationalizing the data collection, and technical assistance for the measurement of air pollution monitoring methods.
Dr. Ambreen Kazi: Involved in designing and operationalizing the data collection methods, particularly training of field staff regarding data collection for health from the hospitals, monitoring quality of data, cleaning and preparation of the data for analysis.

Acknowledgements

This work was supported by Pakistan-US Science and Technology Cooperative Program (administered by National Academy of Sciences) under the grant # PGA-7251-07-010. Authors would like to thank Wadsworth Center, NYSDOH, University at Albany, Higher Education Commission, Pakistan, Aga Khan University Hospital, and NICVD, Karachi and physicians who provided and collected the health data used in this study. We owe a particular debt of gratitude to Ms. Kelly Robbins, Drs. Vincent Dutkiewicz, Amber Sinclair, Aneeta Khoso, Sumayya Saied, Ms. Naseem Parvez Ali, and Mr. Kamran Khan who assisted us in all aspects of this work.

REFERENCES

[1] Atkinson RW, Anderson HR, Strachan DP, Bland JM, Bremner SA, Ponce de Leon A. Short-term associations between outdoor air pollution and visits to accident and emergency departments in London for respiratory complaints. *Eur Respir J*. 1999;13:257–265.
[2] Bell ML, Samet JM, Dominici F. Time-series studies of particulate matter. *Annu Rev Public Health*. 2004;25:247–280.
[3] Bell ML, Ebisu K, Peng RD, Walker J, Samet JM, Zeger SL, Dominici F. Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999–2005. *Am J Epidemiol*. 2008;168:1301–1310.
[4] Brunekreef B. Health effects of air pollution observed in cohort studies in Europe. *J Expo Sci Environ Epidemiol*. 2007;17(Suppl 2):S61–S65.
[5] Burnett RT, Smith-Doiron M, Stieb D, Cakmak S, Brook JR. Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. *Arch Environ Health*. 1999;54:130–139.
[6] Burnett RT, Brook J, Dann T, Delocla C, Philips O, Cakmak S, Vincent R, Goldberg MS, Krewski D. Association between particulate- and gas-phase components of urban air pollution and daily mortality in eight Canadian cities. *Inhal Toxicol*. 2000;12:15–39.
[7] Burnett RT, Goldberg MS. Size fractionated particulate mass and daily mortality in eight Canadian cities. *Revised Analyses of Time-Series of Air Pollution and Health*. Boston, MA: Special Report; Health Effects Institute; 2003:85–90.
[8] Dockery DW, Pope AC III, Xu X, Spengler JD, Ware JH, Fay ME. An association between air pollution and mortality in six U.S. cities. *N Engl J Med*. 1999;329:1753–1759.
[9] Dockery DW. Health effects of particulate air pollution. *Ann Epidemiol*. 2009;19:257–263.
[10] Goldberg MS, Burnett RT, Bailar JC III, Brook J, Bonvalot Y, Tamblyn R, Singh R, Valois MF, Vincent R. The association between daily mortality and ambient air particle pollution in Montreal, Quebec. 2. Cause-specific mortality. *Environ Res*. 2001;86:26–36.
[11] Health Effects Institute. 2000. National Morbidity, mortality, and air pollution study. HEI Report 94, Part 2.
[12] Ibald-Mulli A, Timonen KL, Peters A, Heinrich J, Wölke G, Lanki T, Buzorius G, Kreyling WG, de Hartog J, Hoek G, ten Brink HM, Pekkanen J. Effects of particulate air pollution on blood pressure and heart rate in subjects with cardiovascular disease: a multicenter approach. *Environ Health Perspect*. 2004;112:369–377.
[13] Ito K, Mathes R, Ross Z, Nadas A, Thurston G, Matte T. Fine particulate matter constituents associated with cardiovascular hoapitalizations and mortality in New York city. *Environ Health Perspect*. 2011;119:467–473.
[14] Lin M, Chen Y, Villeneuve PJ, Burnett RT, Lemyre L, Hertzman C. Gaseous air pollutants and asthma hospitalization of children with low household income in Vancouver, British Columbia, Canada. *Am J Epidemiol*. 2004;159:294–303.
[15] Luginaah IN, Fung KY, Gorey KM, Webster G, Wills C. Association of ambient air pollution with respiratory hospitalization in a government-designated "area of concern": the case of Windsor, Ontario. *Environ Health Perspect*. 2005;113:290–295.
[16] Mann JK, Tager IB, Lurmann F, Segal M, Quesenberry CP Jr, Lugg MM, Shan J, Van Den Eeden SK. Air pollution and hospital admissions for ischeamic heart disease in persons with congestive heart failure or arrhythmia. *Environ Health Perspect*. 2002;110:1247–1252.
[17] NRC (National Research Council). *Committee on Research Priorities for Airborne Particulate Matter. Research Priorities for Airborne Particulate Matter, IV: Continuing Research Progress*. Washington, DC: National Academies Press; 2004.
[18] Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *J Med Assoc*. 2002;287:1132–1141.
[19] Pope CA III, Dockery DW. Health effects of fine particulate air pollution: lines that connect. *J Air Waste Manage Assoc*. 2006;56:709–742.
[20] Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. The National morbidity, mortality, and air pollution study. Part II: morbidity and mortality from air pollution in the United States. *Res Rep Health Eff Inst*. 2000;94:5–70.
[21] Schwartz J, Marcus A. Mortality and air pollution in London: a time series analysis. *Am J Epidemiol*. 1990;131:185–194.
[22] Schwartz J. What are people dying of on high air pollution days? *Environ Res*. 1994;64:26–35.
[23] Schwartz J. Airborne particles and daily deaths in 10 US cities. *Revised Analyses of Time-Series of Air Pollution and Health. Special Report*. Boston, MA: Health Effects Institute; 2003:211–218.

[24] Sunyer J, Ballester F, Tertre AL, Atkinson R, Ayres JG, Forastiere F, Forsberg B, Vonk JM, Bisanti L, Tenias JM, Medina S, Schwartz J, Katsouyanni K. The association of sulfur dioxide air pollution levels with hospital admissions for cardiovascular diseases in Europe (The APHEA 2 study). *Eur Heart J*. 2003;24:752–760.
[25] WHO (World Health Organization). *Air Quality Guidelines for Europe*. WHO Regional Publications, European Series, No. 91. 2nd ed. Copenhagen: WHO Regional Office for Europe; 2000.
[26] Zanobetti A, Schwartz J. Cardiovascular damage by airborne particles: are diabetics more susceptible? *Epidemiology*. 2002;13:588–592.
[27] Atkinson RW, Anderson HR, Sunyer J, Ayres J, Baccini M, Vonk JM, Boumghar A, Forastiere F, Forsberg B, Touloumi G, Schwartz J, Katsouyanni K. Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. Air pollution and health: a European approach. *Am J Respir Crit Care Med*. 2001;164:1860–1866.
[28] Chen L, Verrall K, Tong S. Air particulate pollution due to bushfires and respiratory hospital admissions in Brisbane, Australia. *Int J Environ Health Res*. 2006;16:181–191.
[29] Klemm RJ, Mason R. Replication of reanalysis of Harvard six-city mortality study. *Revised Analyses of Time-Series of Air Pollution and Health, Special Report*. Boston, MA: Health Effects Institute; 2003:165–172.
[30] Liu X, Lessner L, Carpenter DO. Association between residential proximity to fuel-fired power plants and hospitalization rate for respiratory diseases. *Environ Health Perspect*. 2012;120:807–810.
[31] Ostro B, Broadwin R, Green S, Feng WY, Lipsett MJ. Fine particulate air pollution and mortality in nine California counties: results from CALFINE. *Environ Health Perspect*. 2006;114:29–33.
[32] Ostro B, Roth L, Malig B, Marty M. The effects of fine particle components on respiratory hospital admissions in children. *Environ Health Perspect*. 2009;117:475–480.
[33] Analitis A, Katsouyanni K, Dimakopoulou K, Samoli E, Nikoloulopoulos AK, Petasakis Y, Touloumi G, Schwartz J, Anderson HR, Cambra K, Forastiere F, Zmirou D, Vonk JM, Clancy L, Kriz B, Bobvos J, Pekkanen J. Short-term effects of ambient particles on cardiovascular and respiratory mortality. *Epidemiology*. 2006;17:230–233.
[34] COMEAP. *Cardiovascular Disease and Air Pollution. A Report by the Committee on the Medical Effects of Air Pollutant's Cardiovascular Sub-Group*. London, United Kingdom: United Kingdom Department of health; 2006.
[35] Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *J Am Med Assoc*. 2006;295:1127–1134.
[36] Haley VB, Talbot TO, Felton HD. Surveillance of the short-term impact of fine particle air pollution on cardiovascular disease hospitalizations in New York State. *Environ Health*. 2009;8:42.
[37] Le Tertre A, Medina S, Samoli E, Forsberg B, Michelozzi P, Boumghar A, Vonk JM, Bellini A, Atkinson R, Ayres JG, Sunyer J, Schwartz J, Katsouyanni K. Short-term effects of particulate air pollution on cardiovascular diseases in eight European cities. *J Epidemiol Community Health*. 2002;56:773–779.
[38] Park SK, O'Neill MS, Vokonas PS, Sparrow D, Schwartz J. Effects of air pollution on heart rate variability: the VA normative aging study. *Environ Health Perspect*. 2005;113:304–309.
[39] Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. *J Am Med Assoc*. 2008;299:2172–2179.
[40] Peng RD, Bell ML, Geyh AS, McDermott A, Zeger SL, Samet JM, Dominici F. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. *Environ Health Perspect*. 2009;117:957–963.
[41] Samet JM, Dominici F, Curriero F, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 US cities, 1987–1994. *N Engl J Med*. 2000;343:1742–1749.
[42] Schwartz J. Air pollution and hospital admissions for heart disease in eight U.S. counties. *Epidemiology*. 1999;10:17–22.
[43] Simpson R, Williams G, Petroeschevsky A, Best T, Morgan G, Denison L, Hinwood A, Neville G, Neller A. The short-term effecst of air pollution on daily mortality in four Australian cities. *Aust N Z J Public Health*. 2005;29:205–212.
[44] Zanobetti A, Schwartz J. The effect of particulate air pollution on emergency admissions for myocardial infarction: a multicity case-crossover analysis. *Environ Health Perspect*. 2005;113:978–982.
[45] Zanobetti A, Schwartz J. The effect of fine and coarse particulate air pollution on mortality: a national analysis. *Environ Health Perspect*. 2009;117:898–903.
[46] Chen R, Chu C, Tan J, Cao J, Song W, Xu X, Jiang C, Ma W, Yang C, Chen B, Gui Y, Kan H. Ambient air pollution and hospital admission in Shanghai, China. *J Hazard Mater*. 2010;181:234–240.
[47] Dominici F, Samet JM, Zeger SL. Combining evidence on air pollution and daily mortality from the twenty largest US cities: a hierarchical modeling strategy. *J R Stat Soc Ser A*. 2000;163:263–302.
[48] Ostro B, Broadwin R, Lipsett MJ. Coarse and fine particles and daily mortality in the Coachella Valley, California: a follow-up study. *J Expo Anal Environ Epidemiol*. 2000;10:412–419.
[49] Zeka A, Zanobetti A, Schwartz J. Short term effects of particulate matter on cause specific mortality: effects of lags and modification by city characteristics. *Occup Environ Med*. 2005;62:718–725.
[50] Cifuentes LA, Vega J, Kopfer K, Lave LB. Effect of the fine fraction of particulate matter versus the coarse mass and other pollutants on daily mortality in Santiago, Chile. *J Air Waste Manage Assoc*. 2000;50:1287–1298.
[51] Dockery DW, Schwartz J, Spengler JD. Air pollution and daily mortality: association with particulates and acid aerosols. *Environ Res*. 1992;59:362–373.
[52] Dominici F, Peng RD, Zeger SL, White RH, Samet JM. Particulate air pollution and mortality in the United States: did the risks change from 1987 to 2000? *Am J Epidemiol*. 2007;166:880–888.
[53] Schwartz J, Dockery DW, Neas LM. Is daily mortality associated specifically with fine particles? *J Air Waste Manage Assoc*. 1996;46:927–939.
[54] Lee JT, Kim H, Hong YC, Kwong HJ, Schwartz J, Christiani DC. Air pollution and daily mortality in seven major cities of Korea, 1991–1997. *Environ Res Sect A*. 2000;84:247–254.
[55] Li X, Gilmour PS, Donaldson K, MacNee W. In vivo and in vitro proinflammatory effects of particulate air pollution (PM10). *Environ Health Perspect*. 1997;105:1279–1283.

[56] WHO (World Health Organization). *World Health Report 2002. Reducing Risk, Promoting Healthy Life*. Geneva, Switzerland: WHO; 2002.
[57] Parekh PP, Khwaja HA, Khan AR, Naqvi RR, Malik A, Shah SA, Khan K, Hussain G. Ambient air quality of two metropolitan cities of Pakistan and its health implications. *Atmos Environ*. 2001;35:5971–5978.
[58] Barletta B, Meinardi S, Simpson IJ, Khwaja HA, Blake DR, Rowland FS. Mixing ratios of volatile organic compounds (VOCs) in the atmosphere of Karachi, Pakistan. *Atmos Environ*. 2002;36:3429–3443.
[59] Gurjar BR, Jain A, Sharma A, Agarwal A, Gupta P, Nagpure AS, Lelieveld J. Human health risks in megacities due to air pollution. *Atmos Environ*. 2010;44:4606–4613.
[60] Linn WS, Szlachcic Y, Gong H Jr, Kinney P, Berhane K. Air pollution and daily hospital admissions in metropolitan Los Angeles. *Environ Health Perspect*. 2000;108:427–434.
[61] Sinclair AH, Edgerton ES, Wyzga R, Tolsma D. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. *J Air Waste Manage Assoc*. 2010;60:163–175.
[62] Krzyzanowski M, Cohen A, Anderson R, and the WHO Working Group. Quantification of health effects of exposure to air pollution. *Occup Environ Med*. 2002;59:791–793.
[63] Stone E, Schauer J, Quraishi TA, Mahmood A. Chemical characterization and source apportionment of fine and coarse particulate matter in Lahore, Pakistan. *Atmos Environ*. 2010;44:1062–1070.
[64] Hilbe JM. *Negative Binomial Regression*. Cambridge, UK: Cambridge University Press; 2007. ISBN-13:9780521857727.
[65] Schwartz J, Dockery DW. Increased mortality in Philadelphia associated with daily air pollution concentrations. *Am Rev Respir Dis*. 1992;145:600–604.
[66] Schwartz J. Air pollution and hospital admissions for the elderly in Detroit, Michigan. *Am J Respir Crit Care Med*. 1994;150:648–655.
[67] Zhao X, Zhang X, Xu X, Xu J, Meng W, Pu W. Seasonal and diurnal variations of ambient PM2.5 concentration in urban and rural environments in Beijing. *Atmos Environ*. 2009;43:2893–2900.
[68] Gurjar BR, Butler TM, Lawrence MG, Lelieveld J. Evaluation of emissions and air quality in megacities. *Atmos Environ*. 2008;42:1593–1606.
[69] WHO (World Health Organization). *Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Global update 2005: Summary of risk assessment*. Geneva, Switzerland: WHO; 2006.
[70] Ito K, De Leon SF, Lippmann M. Associations between ozone and daily mortality: analysis and meta-analysis. *Epidemiology*. 2005;16:446–457.