

Air pollution and cardiovascular and respiratory disease: Rationale and methodology of CAPACITY study

Katayoun Rabiei⁽¹⁾, Sayed Mohsen Hosseini⁽²⁾, Erfan Sadeghi⁽³⁾, Tohid Jafari-Koshki⁽⁴⁾,
Mojtaba Rahimi⁽⁵⁾, Mansour Shishehforoush⁽⁶⁾, Ahmadreza Lahijanzadeh⁽⁷⁾,
Babak Sadeghian⁽⁸⁾, Elham Moazam⁽⁹⁾, Mohammad Bagher Mohebi⁽¹⁰⁾,
Victoria Ezatian⁽¹¹⁾, Nizal Sarrafzadegan⁽¹⁾

Original Article

Abstract

BACKGROUND: Considering the high level of air pollution and its impact on health, we aimed to study the correlation of air pollution with hospitalization and mortality of cardiovascular (CVD) and respiratory diseases (ResD) (CAPACITY) to determine the effects of air pollutants on CVD and ResD hospitalizations and deaths in Isfahan, Iran.

METHODS: Hourly levels of air pollutants including particulate matter (PM), carbon monoxide (CO), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and ozone (O₃), information of CVD and ResD admissions and death certificate were obtained respectively from Department of Environment (DOE), Iran, hospitals and cemetery. Time series and case-crossover model were used to find the impact of air pollutants. This paper only summarizes the descriptive findings of the CAPACITY study.

RESULTS: The total number of hospitalized patients were 23781 in 2010 and 22485 in 2011. The most frequent cause of hospitalization and death was ischemic heart diseases in both years. While the mean annual levels of O₃, CO, and PM₁₀ were lower in 2011 than in 2010, NO₂ and SO₂ levels higher in 2011. In both years, PM₁₀ was similarly increased during last month of fall, late spring and early summer. In 2011, the PM_{2.5} and PM₁₀ monthly trend of change were similar.

CONCLUSION: The CAPACITY study is one of the few large-scale studies that evaluated the effects of air pollutants on a variety of CVD and ResD in a large city of Iran. This study can provide many findings that could clarify the effects of these pollutants on the incidence and burden of both disease groups.

Keywords: Air Pollution, Cardiovascular Diseases, Respiratory Tract Diseases

Date of submission: 19 Apr. 2017, *Date of acceptance:* 15 July 2017

Introduction

Air pollution is undoubtedly associated with a variety of diseases, and thus serves as an indirect cause of mortality.^{1,2} According to the World Health Organization (WHO) report for 2012, three million deaths throughout the world were attributable to

ambient air pollution. Cardiovascular diseases (CVDs) and respiratory disease (ResD) were responsible for respectively 72% and 14% of these deaths.³

Numerous studies, mainly in the developed countries, have evaluated the relationships between air pollution and death or hospitalization due to ResD

1- Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

2- Department of Biostatistics and Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran

3- Noncommunicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran

4- Road Traffic Injury Research Center AND Department of Statistics and Epidemiology, School of Health, Tabriz University of Medical Sciences, Tabriz, Iran

5- Department of Anesthesiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

6- Isfahan Disaster Management Office, Isfahan Governor's Office, Isfahan, Iran

7- Khouzestan Department of Environment, Ahvaz, Iran

8- Central Laboratory and Air Pollution Monitoring, Isfahan Province Environmental Monitoring Center, Isfahan Department of Environment, Isfahan, Iran

9- Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

10- Information Technology Offices, Isfahan University of Medical Sciences, Isfahan, Iran

11- Isfahan Meteorological Offices, Isfahan, Iran

Correspondence to: Nizal Sarrafzadegan, Email: nsarrafzadegan@gmail.com

and CVDs.⁴⁻⁷ However, there is a shortage of similar research in developing countries where rapid population growth and its consequences such as an increase in air pollution generally raise the disease burden. The mentioned relationships can even be confounded by climatic factors,⁸ poor air quality management policies, and inefficient monitoring of environmental factors. The absence of a comprehensive patient information systems have turned the evaluation of the health effects of air pollution in developing countries into a challenge and necessitated further large-scale studies in these areas.⁹

Iran, a developing country, has witnessed a rise in air pollution during the recent years. In 2012, 26267 Iranians died due to air pollution and WHO identified Iran as one of the most polluted countries in the world.¹⁰ Although growing research attention has been paid to the subject, only few studies have been performed at large-scale level and have examined the simultaneous effects of pollutants on CVD- and ResD-related hospitalizations and deaths.^{11,12}

As an industrial city and the third large metropolis in Isfahan, Iran, has to deal with the problem of air pollution. According to Isfahan cohort study, CVDs are more frequent in Isfahan, even among the youth and women, than in many other populations.¹³ Moreover, the high levels of CVD risk factors, particularly unhealthy lifestyle, would gradually increase the incidence of these diseases in the city. The prevalence of diabetes and hypertension in Isfahan has been estimated at 5.6% and 17.3%, respectively¹⁴ and 21.8% of the man population of the city are smokers.¹⁵ The daily sodium intake in the city is 4309.6 ± 1344.4 mg¹⁶ and over half of the population do not have adequate levels of physical activity.^{17,18} The city is surrounded by numerous industrial factories including Mobarakeh Steel Company, Isfahan Steel Company, Isfahan Oil Refinery, and power plants. Following the population growth in recent years, the numbers of motor vehicles and daily commutes, and thus, the levels of air pollutants have increased in the city.¹⁹

Therefore, we performed the correlation of air pollution with hospitalization and mortality of CVD and ResD (CAPACITY). This study evaluated the effects of different pollutants including particulate matter (PM) 10 and 2.5, carbon monoxide (CO), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and ozone (O₃), on two major outcomes of CVD and ResD-related hospitalization and death, under controlled climatic conditions. In this article, we report the rational, methodology and basic descriptive results of the CAPACITY study.

Materials and Methods

The CAPACITY study was performed in Isfahan from March 2010 to March 2012. Two methods, time series and case-crossover designs, were adopted for the purpose of the study. It is noteworthy that this paper reported the methodology of the CAPACITY study, including data collection, management, and statistical models of data analysis, in detail. However, only descriptive findings of the CAPACITY study were discussed and all other findings will be presented in future publications.

The city of Isfahan (32.6546 °N, 51.6680 °E) covers an area of 493.82 km² in the center of Iran, along with the foothills of Zagros mountains and Zayanderud plain. With a population of 2240249 in 2016 (2067821 people in 2011), Isfahan is the third largest metropolis in Iran.^{20,21} It is located 1574 m above sea level with a mean temperature of 15.6 °C, and a mean annual precipitation of 125 ml. It has an arid climate categorized as cold desert climates in the Köppen-Geiger system.²² However, as Zayanderud has recently changed from a permanent to a seasonal and sometimes even dried out river, Isfahan currently has drier climate.¹⁰

Owing to its industrial conditions and large factories, Isfahan has a relatively high population density.²³ Two thermal power plants are located near Isfahan. Shahid Montazeri Power Plant in the north of the city is one of the largest power plants in the country and generates 1616 MW per day. Isfahan Power Plant, located 75 km southwest of Isfahan, generates 954 MW per day.²⁴ Two large steel companies are also located in the west and southwest of Isfahan. There is also a large cement plant in the west of the city and an oil refinery in the north²⁵ (Figure 1).

The studied population consisted of all residents of Isfahan who were admitted either to hospitals of Isfahan or died due to a confirmed diagnosis of CVDs or ResDs based on the International Classification of Diseases-10 (ICD-10).²⁶

Hospitals with coronary care units (CCU), emergency wards for cardiac or respiratory patients or cardiology, internal medicine, and respiratory diseases wards (where the target patients were likely to be admitted) in Isfahan were identified in coordination with the Deputy of Treatment. A total of 15 eligible hospitals including 8 universities, 4 private, 1 military, and 2 social insurance hospitals, were identified at the time of the study.

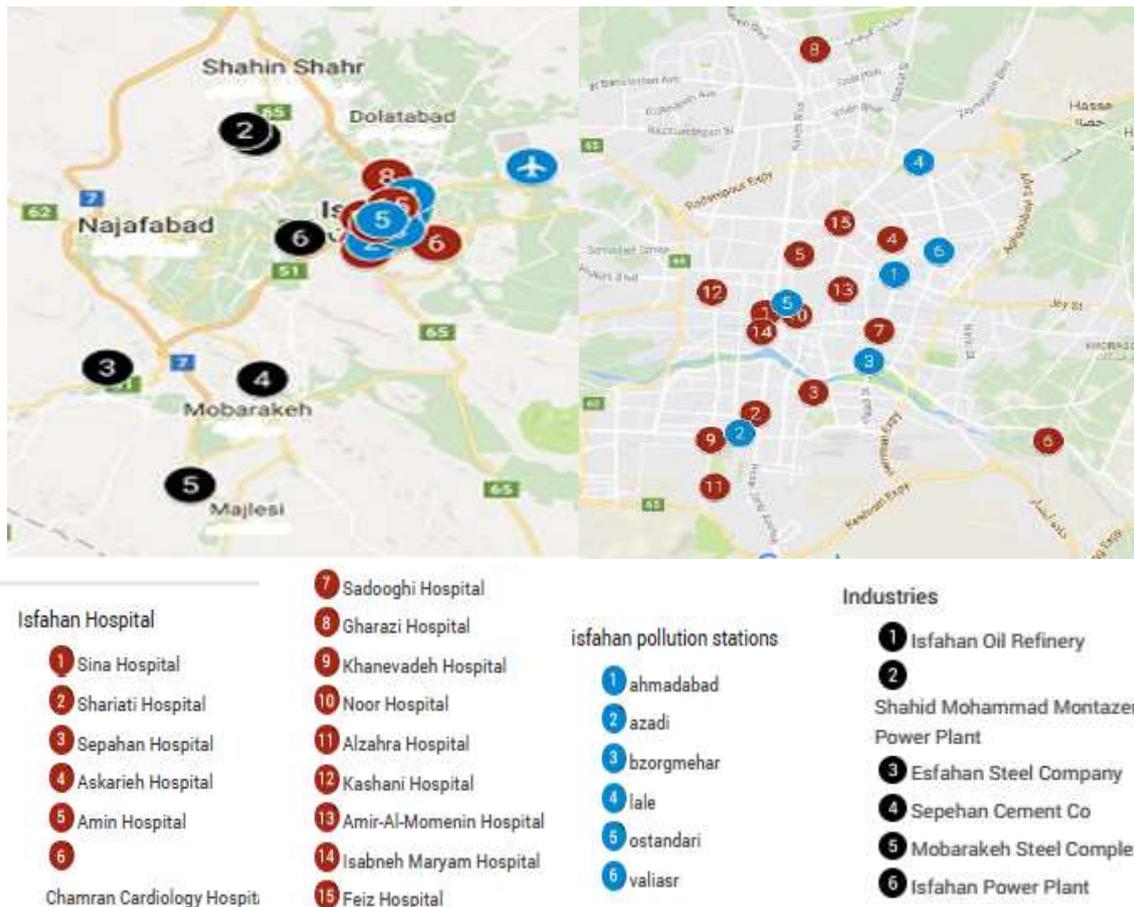


Figure 1. The location of air pollution monitoring stations in Isfahan, Iran, meteoritic data

Patients' information was collected through the hospital information system (HIS). Trained experts in medical records used patients' files to extract information like treatment, dates of admission and discharge, diagnosis, prescribed medications, lab results, and performed invasive procedures, as well as administrative and accounting information, such as incurred costs, insurance coverage, and health subsidies during the hospitalization period. Then, they entered the data into the HIS. However, clinical examination was not recorded in the system. Data entry was supervised by the treatment deputy of relevant university. The HIS of all hospitals in the country are constantly evaluated and monitored by the Office of Statistics and Information Technology of the Ministry of Health.²⁷

15 hospitals in Isfahan met the criteria and considered in this study. However, only eight hospitals used the HIS in 2010. The medical record experts of these hospitals entered the final diagnosis for each patient (recorded in patient files by relevant physicians) in the HIS. The diagnoses were recorded based on ICD-10 codes. All emergency admitted patients diagnosed with codes I00-I99 (for

circulatory diseases) and J00-J99 (for ResD) were enrolled. The demographic characteristics of the patients (name, father's name, file number, national identification number, sex, age, occupation, home and work address, and insurance coverage) and disease-related information (admission time and unit, type of referral, and final diagnosis) were then extracted by the hospital medical records experts.

In the remaining seven hospitals without HIS, patient files were archived based on the final diagnosis (ICD-10 codes). Therefore, medical record experts were asked to extract the paper files of all patients with CVD or ResD with a diagnosis of I00-I99 or J00-J99. The above-mentioned information was then collected and entered into a designed reporting software package.

In 2011, all hospitals used the HIS, and thus the described procedure used in hospitals with HIS was followed to extract data.

Since all patients with I00-I99 and J00-J99 diagnoses were included, the search results were filtered based on the address (packages) to identify Isfahan residents. Patients' files in each hospital were re-evaluated by two experts to ensure that only Isfahan

residents were included. After extracting the data from all hospitals, the address of 1500 randomly selected patients were checked to confirm not only their place of residence, but also the data management adopted by hospital medical records experts.

In order to obtain mortality data of 2010 and 2011 categorized by cause of death, data were collected from Isfahan's cemetery. The cause of death recording and categorization system in Iran was developed in 2004. In this system, the main cause of death is extracted from death certificates issued by relevant physicians and recorded (as ICD-10 codes) in collaboration with health deputies of universities of medical sciences, the Forensic Medicine Organization, municipalities, and organizations for civil registration.²⁴ In this study, the characteristics (name, father's name, sex, dates of birth, date and cause of death, and address) of individuals who died of CVDs (I00-I99) and ResDs (J00-J99) were obtained.

Hourly records of air pollutants were collected from air pollution monitoring stations and managed in Microsoft Excel files by the lab experts of Isfahan's Department of Environment. In 20th March 2010, to 19th March 2012, PM₁₀, CO, NO₂, O₃, and SO₂ levels were automatically measured and recorded every hour. PM_{2.5} data were also recorded on 20th March 2011, to 19th March 2012. All stations were constantly monitored and calibrated by the lab experts of Isfahan's Department of Environment. SO₂, O₃, NO₂, and CO levels were determined by ultraviolet (UV) fluorescence, UV absorption, chemiluminescence, and infrared absorption spectroscopy methods, respectively. PM₁₀ and PM_{2.5} measurements were performed using beta attenuation monitoring.²⁸

The experts of Isfahan's Department of Environment (DOE) examined the collected data and eliminated the outliers by checking the correlation of trend of data in all stations. In order to determine the mean daily levels of pollutants, the average 24-hour levels at each station were first separately calculated. The obtained values in all stations were then averaged to calculate the mean levels in Isfahan. Files related to 24-hour levels at different stations and the whole city were finally used to develop time series and case-crossover files.

Daily temperature, dew point, wind speed, sea level pressure, and visibility data were also collected from Isfahan's Meteorological Organization to eliminate their confounding effects on air pollution and the consequent hospitalization. In order to ensure the accuracy of the collected data, they were

compared with available satellite data (an archive of all climatic data recorded at meteorological stations since 1950).²⁹

In order to create the required files, identification (ID) code was assigned to each row of data in all files (including the patients, deceased, pollutants, and meteorological data). The IDs were developed based on dates, in a way that a specific yyyy/mm/dd/hh code was allocated to each point of pollutant data (8760 points of data in each year). Considering the nature of the data, the IDs were unique in the air pollutants and meteorological data files. However, since several individuals could die or be hospitalized on any particular day, the IDs could be repeated in the patients and deceased files. One-to-many merging methods were thus administered to build the files. Based on the created file the missing data for air pollutants were shown.

Time series and case-crossover methods were simultaneously applied for data analysis for all objectives of the CAPACITY study. All data analyses were conducted using R version 3.2.3. A confidence interval (CI) of 95% was considered in both Poisson and conditional regression methods. In this paper, we presented only the descriptive findings of the CAPACITY study.

Results

The mean annual O₃, CO, and PM₁₀ levels were lower in the second year. In contrast, NO₂ and SO₂ levels increased by 1.5 and 1.8 times, respectively (Table 1). In both years, the highest mean levels of NO₂ and SO₂ were detected in January. The greatest mean levels of PM₁₀ in the first and second years of study were seen in January and April, respectively (Figure 2). In the second year, the mean NO₂ and SO₂ levels were higher than 50 part per billion (ppb) on 182 days. These levels were higher than 100 ppb in about 30 days (in fall and winter in case of SO₂ and sometimes in spring in case of NO₂). In the first year, however, the mean levels of these two pollutants were higher than 50 ppb only on 50 days. Furthermore, the SO₂ and NO₂ levels were higher than 60 ppb on only one and five days, respectively. In both years, PM₁₀ increased on similar days of the last month of fall, late spring, and early summer. In the second year, the increments in PM_{2.5} had a similar trend to that of PM₁₀.

The total number of hospitalized patients in Isfahan was 23781 in the first year and 22485 in the second year of study. The mean age of the selected individuals in the first and second years was 52.55 ± 25.26 and 54.98 ± 23.59 years, respectively.

Table 1. Descriptive data of the pollutants in 20th March 2010 to 19th March 2012 in Isfahan, Iran

Variable	Observed data (%)	Mean \pm SD	Min	Max
First year				
O ₃ (ppb)	91.53	36.40 \pm 6.33	20.87	51.98
CO (ppm)	94.30	6.07 \pm 1.57	2.49	9.99
SO ₂ (ppb)	92.52	27.26 \pm 9.30	9.00	69.91
NO ₂ (ppb)	91.40	33.48 \pm 7.04	17.38	67.59
PM ₁₀ ($\mu\text{g}/\text{m}^3$)	67.42	161.98 \pm 40.91	39.63	358.10
Second year				
O ₃ (ppb)	46.23	28.17 \pm 21.15	1.33	132.24
CO (ppm)	80.50	3.97 \pm 2.13	0.01	31.84
SO ₂ (ppb)	94.36	49.06 \pm 37.51	0.02	284.00
NO ₂ (ppb)	67.43	48.36 \pm 32.95	0.01	377.65
NO (ppb)	70.19	79.58 \pm 39.59	1.70	545.60
PM ₁₀ ($\mu\text{g}/\text{m}^3$)	46.23	117.94 \pm 70.24	7.67	1227.50
PM _{2.5} ($\mu\text{g}/\text{m}^3$)	75.32	54.64 \pm 37.10	1.66	500.23

SD: Standard deviation; O₃: Ozone; CO: Carbon monoxide; SO₂: Sulfur dioxide; NO₂: Nitrogen dioxide; PM: Particulate matter; ppb: Part per billion; ppm: Part per million

Moreover, 53% of the patients in both years were men. The frequency of CVDs in the mentioned years were 18397 (77.36%) and 16990 (75.56%) individuals, respectively. Table 2 presents the frequency of different causes of hospitalization and the mean age of the patients. Ischemic heart disease was responsible for the greatest numbers of hospitalizations in both years. Among the ResDs, chronic lower ResDs was the most frequent cause of hospitalization in both 2010 (n = 1583, 29.40%) and 2011 (n = 1,415, 25.75%). In both years, all diseases, except for hypertension, were more prevalent in men than in women.

The largest numbers of hospitalization for ischemic heart diseases, hypertension, and heart failure were seen in winter 2011 and fall 2011. The greatest hospitalization frequency for all ResDs was in the winters of both years (Figure 3).

Discussion

The world's first severe air pollution and smog events occurred in Pennsylvania and London in the mid-20th century, after World War II.^{30,31} Increased mortality following these events highlighted the health effects of air pollutants and motivated health policymakers to perform epidemiological studies to determine such impacts. As a result, the first studies on air pollution were conducted.^{29,32,33} Over time, similar studies were performed in different developed countries and air pollution reduction strategies were implemented accordingly. Considering the trend of population growth in Iran and the consequent increase in the number of motor vehicles, changes in lifestyle, and industrial developments in Iran, further researches are required to clarify the health effects of population growth and industrial development, particularly air pollution.

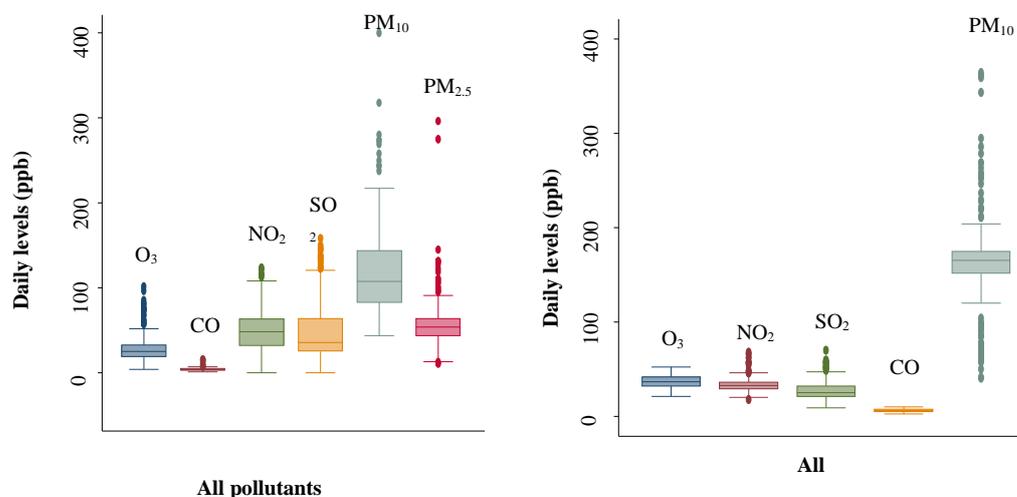


Figure 2. The distribution of daily levels of pollutants 20th March 2010 to 19th March 2012
O₃: Ozone; CO: Carbon monoxide; NO₂: Nitrogen dioxide; SO₂: Sulfur dioxide; PM: Particulate matter

Table 2. Frequency of patients admitted to hospitals of Isfahan, Iran, due to cardiovascular and respiratory diseases

Diseases (ICD codes)	First year (March 20, 2010, to March 19, 2011)			Second year (March 20, 2011, to March 19, 2012)		
	Frequency [n (%)]	Age (mean \pm SD)	Men [n (%)]	Frequency [n (%)]	Age (mean \pm SD)	Men [n (%)]
All cardiovascular diseases (I00-I99)	18397 (77.36)	57.53 \pm 21.39	9642 (52.41)	16990 (75.56)	59.63 \pm 19.15	8813 (51.87)
Hypertensive diseases (I10-I15)	1805 (7.59)	64.61 \pm 14.65	667 (36.95)	2046 (9.10)	64.34 \pm 14.86	785 (38.10)
Ischemic heart diseases (I20-I25)	8810 (37.05)	56.83 \pm 20.02	4763 (54.07)	8075 (35.91)	58.39 \pm 17.30	4276 (53.10)
Conduction disorders, cardiac arrest (I44-I46)	458 (1.93)	62.14 \pm 24.40	266 (58.08)	507 (2.25)	62.25 \pm 23.85	279 (55.03)
Cardiac arrhythmias (I47-I49)	839 (3.53)	52.89 \pm 23.73	401 (47.79)	761 (3.38)	56.58 \pm 23.43	352 (46.44)
Congestive heart failure (I50.0)	958 (4.03)	61.90 \pm 23.91	537 (56.05)	840 (3.74)	65.51 \pm 20.41	483 (57.57)
Cerebrovascular diseases (I60-I69)	2088 (8.78)	66.31 \pm 18.95	1077 (51.58)	1766 (7.85)	69.25 \pm 15.00	934 (53.01)
Other cardiovascular diseases	3439(14.46)	49.61 \pm 23.74	1931 (56.15)	2995 (13.32)	52.75 \pm 22.45	1714 (57.32)
All respiratory disease (J00-J99)	5384 (22.64)	35.50 \pm 29.64	3088(57.36)	5495 (24.44)	40.60 \pm 29.49	3178 (57.83)
Acute upper respiratory infections (J00-J06)	358 (1.51)	12.60 \pm 16.65	207 (57.98)	286 (1.27)	12.08 \pm 17.52	169 (59.30)
Influenza due to seasonal influenza virus (J10)	5 (0.02)	27.40 \pm 4.28	3 (60.00)	4 (0.02)	46.00 \pm 22.72	3 (75.00)
Pneumonia (J12, J13, J14, J15, J16, J17, J18)	1085 (4.56)	39.27 \pm 32.20	607 (55.94)	1126 (5.01)	40.20 \pm 32.71	621 (55.45)
Acute bronchitis and bronchiolitis (J20- J21)	143 (0.60)	22.86 \pm 26.05	81 (56.64)	184 (0.82)	14.14 \pm 23.05	111 (60.33)
Chronic lower respiratory disease (J40-J47)	1583 (6.66)	49.66 \pm 27.15	856 (54.11)	1415 (6.29)	52.77 \pm 25.32	800 (56.62)
Other respiratory diseases	2210 (9.29)	28.09 \pm 26.76	1334 (60.39)	2046 (9.10)	64.34 \pm 14.86	775 (38.10)
Total	23781 (100)	52.55 \pm 25.26	12730 (53.54)	22485 (100)	54.98 \pm 23.59	11991 (53.49)

ICD: International classification of diseases; SD: Standard deviation

Owing to considerable development in Isfahan, a major employment and industrial hub in Iran, during the past 50 years, the city is now facing several problems including air pollution. Studies to quantify the health impacts of air pollution in this city are hence critical. In the CAPACITY study, we aimed to determine the effects of air pollutants on various diseases. Therefore, we collected the CVD and ResD-related mortality and hospitalization data (a total of 54266 cases) over a two-year period from relevant organizations. We also evaluated 266926 hourly records from six air pollution monitoring stations.

According to the initial results of CAPACITY study, the mean annual levels and most mean daily levels of pollutants in 2010 and 2011 were higher

than the standard levels determined by the WHO.³⁴ While the WHO allows $PM_{10} > 50 \mu g/m^3$ on only 35 days of the year, the mean daily levels of this pollutant were higher than $50 \mu g/m^3$ on over 80% of the days in both years. Moreover, SO_2 and NO_2 levels were considerably increased in 2011. Based on the WHO guidelines, the standard 24-hour and annual SO_2 levels should be respectively below 48 and 19 ppb. The mean annual levels of this pollutant were higher than the allowed level in both years. It was actually 2.5 times higher than the allowed level in 2011. The mean daily levels of this gas were also higher than the allowed level in over half the year in 2011. In 2010, the number of days with high SO_2 levels was much lower than that in 2011.

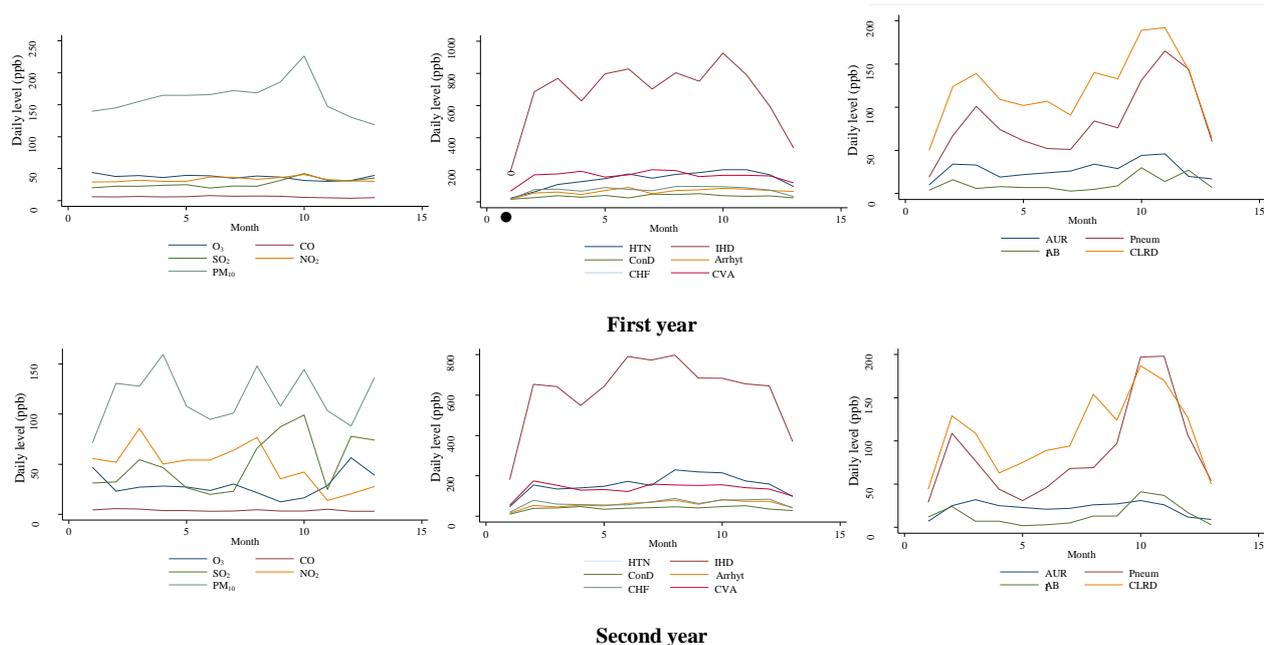


Figure 3. Trends of monthly changes in the mean levels of pollutants and frequency of hospitalizations in 20th March 2010 to 19th March 2012

O₃: Ozone; CO: Carbon monoxide; NO₂: Nitrogen dioxide; SO₂: Sulfur dioxide; PM: Particulate matter; HTN: Hypertensive diseases; IHD: Ischemic heart diseases; ConD: Conduction disorders and cardiac arrest; Arrhyt: Cardiac arrhythmias; CHF: Congestive heart failure; CVA: Cerebrovascular diseases; AURI: Acute upper respiratory infections; Pnum: Pneumonia; AB: Acute bronchitis and bronchiolitis; CLRD: Chronic lower respiratory disease

As stated by the WHO, the mean annual NO₂ levels should be less than 21 ppb. The mean level of this pollutant was 34 ppb in 2010 and 49 ppb in 2011. Therefore, the air pollution status in 2010 and 2011 was worse than the WHO recommendations. According to the available statistics, fuel oil and diesel consumption were higher and gas consumption was lower in 2011 compared to 2010. Since the largest amounts of SO₂ are produced in power plants run on fuel oil and high-sulfur diesel, higher levels of this pollutant in 2011 can be related to the increased use of these two fossil fuels.

Similar to previous research in other countries, the CAPACITY study used the HIS to collect the frequency of the selected diseases. Since health and mortality-related data are recorded in various national systems including the civil registration and hospital records, benefiting from the existing data seems to be the optimum and cost-effective choice for many studies. Registration systems have also been used in a large number of studies on air pollution. For instance, a study in Taiwan used the National Health Insurance (NHI) Program, which covers over 98% of the population, and the case-crossover design to evaluate the relationship between PM₁₀ levels and ischemic heart disease hospitalizations.³⁵ A case-crossover study in South Africa on the relationship between respiratory,

cardiovascular, and cerebrovascular mortality and different pollutants obtained mortality data from the Health Information and Technology Department.³⁶ In an eight-year study, Wichmann et al. examined the relationship between PM₁₀ levels and hospitalization for myocardial infarction. They extracted the diagnoses, as well as patients' age and sex, from the National Ambulatory Care Reporting System (NACRS) database maintained by the Canadian Institute for Health Information (CIHI).³⁶

The HIS has introduced to Iran's health system about 10 years ago. The Ministry of Health has evaluated and monitored the system three times ever since. Owing to the data recorded in the HIS, the system can serve as an invaluable source of information in various studies. Nevertheless, the possible use of different approaches to data entry in 2010 and 2011 might have been responsible for the decreased rate of hospitalization in 2011.

Research on the health effects of pollutants is relatively new in Iran. Recent increases in pollutants in different cities in the country, especially in the western and southwestern areas, have necessitated studies on the relationship between pollutants and disease incidence, mortality and generally its burden on health. Most previous studies, however, have adopted the WHO's air quality (AirQ) model to examine the burden of disease caused by air

pollutants in various cities of Iran. A previous study estimated the proportion of cardiovascular and respiratory mortality attributable to air pollutants in 2011 in Tehran.³⁷ A series of studies in Ahwaz used the AirQ model to calculate the proportion of cardiovascular and respiratory mortality attributable to PM₁₀, CO, SO₂, and NO₂.^{38,39} Another study in Sanandaj, Iran, used the same software to determine the proportion of cardiovascular and respiratory mortality attributable to PM₁₀ in 2013.⁴⁰

One of the few efforts to directly measure health impacts was performed by Ebrahimi *et al.* who evaluated the relations between dust storm and cardiovascular and respiratory admissions. The study subjects were patients with cardiovascular and ResDs who received medical services from the Center for Disaster Management and Medical Emergencies (CDMME) in Sanandaj during dust event days. According to Pearson correlation analysis, the incidence of dust storm significantly increased the frequency of emergency admissions.⁴¹ While the mentioned study only evaluated the effects of PM₁₀ during dust event days on emergency admissions, the present research applied the time series and case-crossover designs to examine the effects of all pollutants during the whole year.

Qorbani *et al.* were among the first to use the case-crossover design in Iran. They sought to clarify the relationship between admissions for the acute coronary syndrome and CO and PM₁₀ levels 24 hours before admission among 250 patients in a hospital in Tehran. Their findings indicated a significant association between the risk of admission and CO levels 24 hours before admission [odds ratio (OR) = 1.18]. However, no such a relation was observed in case of PM₁₀.¹² Despite its novelty in 2012, this study had a small sample size. Khamutian *et al.* adopted the time series design and found significant relationships between CO, NO₂, and O₃ levels and admissions for asthma to seven large hospitals in Kermanshah.⁴² Although the study evaluated all emergency admissions to seven large hospitals during two years, they only studied the relation between PM₁₀ levels and asthma.

A number of studies have also assessed the associations between various diseases and air pollution in Isfahan. Mansourian *et al.* conducted a time series analysis to determine the relationship between ResD admissions in children and different air pollutants during 2005 and 2006. They randomly selected 120 children who were hospitalized for ResDs. Poisson regression analysis revealed significant associations between the admission rate

and SO₂-CO, SO₂-PM₁₀, and PM₁₀-CO levels ($\beta = 0.937, 0.930, \text{ and } 0.952$, respectively).⁴³ Meanwhile, in the CAPACITY study, the relationship between five air pollutants with all CVD and ResD hospitalization and mortality in all age groups were measured. A case study during 2005-2009 reported the higher frequency of cardiovascular mortality in more polluted cities of Isfahan Province.⁴⁴

Apparently, previous studies in Iran have highlighted limited associations between a number of diseases and air pollution indices or some pollutants. However, to the best of our knowledge, this study was the first in Iran and the Middle East region to examine the relationship between cardiovascular and respiratory mortality and hospitalization in general and levels of six pollutants (as quantitative independent variables). The large sample size, the diversity of the pollutants and outcomes, and the simultaneous administration of time series and case-crossover methods have added to its strengths.

This study, however, has some limitations. First, the data was previously collected by the HIS. Although we believe that the emergency and elective admissions could be easily distinguished in the HIS, the systems used in the selected hospitals were not designed by a single company. Thus, it led to differences in the recorded data. Therefore, after descriptive analysis of the collected data, we realized that we should delete the elective patients of our database and consider the only emergency admitted patients. Based on our experience and the increasing interest in the use of data registration systems in scientific research, data entry and usage in the HIS have to be updated.

Conclusion

In conclusion, the CAPACITY study showed that performing large-scale studies, at the level of cities or even the country, requires coordination between and data from several organizations. However, data collection using field questioning at any single organization is both costly and time-consuming. Data collection at this level facilitates the development of various models and the application of different analytical methods. Therefore, the results of the CAPACITY study can be beneficial to the design of future studies, development of research policies aiming at the use of national registration systems, and modification of the existing policies for the extraction of health indices. Moreover, our findings can provide health researchers, authorities, and policymakers with fresh insight into the health impacts of air pollution and

thus facilitate the development of effective preventive strategies. These results can also be compared with the results of similar research in other countries.

Acknowledgments

This study was financially supported by the Crisis Management Office of Isfahan Provincial Governor Office, Iran. The proposal was approved by Isfahan's Department of Environment (ID: 90/7588) and Isfahan Cardiovascular Research Center (ID: 91112). The authors wish to express their gratitude to the Crisis Management Office of Isfahan Provincial Governor Office and Isfahan's DOE for their support.

Conflict of Interests

Authors have no conflict of interests.

References

- Cesaroni G, Badaloni C, Gariazzo C, Stafoggia M, Sozzi R, Davoli M, et al. Long-term exposure to urban air pollution and mortality in a cohort of more than a million adults in Rome. *Environ Health Perspect* 2013; 121(3): 324-31.
- Fischer PH, Marra M, Ameling CB, Hoek G, Beelen R, de Hoek K, et al. Air pollution and mortality in seven million adults: The Dutch environmental longitudinal study (DUELS). *Environ Health Perspect* 2015; 123(7): 697-704.
- World Health Organization. Burden of disease from Ambient Air Pollution for 2012. Geneva, Switzerland: WHO; 2012.
- Anderson JO, Thundiyil JG, Stolbach A. Clearing the air: A review of the effects of particulate matter air pollution on human health. *J Med Toxicol* 2012; 8(2): 166-75.
- Ji M, Cohan DS, Bell ML. Meta-analysis of the Association between Short-Term Exposure to Ambient Ozone and Respiratory Hospital Admissions. *Environ Res Lett* 2011; 6(2).
- Perez L, Grize L, Infanger D, Kunzli N, Sommer H, Alt GM, et al. Associations of daily levels of PM10 and NO(2) with emergency hospital admissions and mortality in Switzerland: Trends and missed prevention potential over the last decade. *Environ Res* 2015; 140: 554-61.
- Pope CA 3rd, Turner MC, Burnett RT, Jerrett M, Gapstur SM, Diver WR, et al. Relationships between fine particulate air pollution, cardiometabolic disorders, and cardiovascular mortality. *Circ Res* 2015; 116(1): 108-15.
- Roberts S. Interactions between particulate air pollution and temperature in air pollution mortality time series studies. *Environ Res* 2004; 96(3): 328-37.
- McGranahan G, Murray F. Air pollution and health in rapidly developing countries. London, UK: Routledge; 2012.
- World Health Organization. Database: Outdoor air pollution in cities: Public health, environmental and social determinants of health (PHE) [Online]. [cited 2011]; Available from: URL: http://www.who.int/phe/health_topics/outdoorair/databases/cities-2011/en
- Hosseinpoor AR, Forouzanfar MH, Yunesian M, Asghari F, Naieni KH, Farhood D. Air pollution and hospitalization due to angina pectoris in Tehran, Iran: A time-series study. *Environ Res* 2005; 99(1): 126-31.
- Qorbani M, Yunesian M, Fotouhi A, Zeraati H, Sadeghian S. Effect of air pollution on onset of acute coronary syndrome in susceptible subgroups. *East Mediterr Health J* 2012; 18(6): 550-5.
- Talaei M, Sarrafzadegan N, Sadeghi M, Oveisgharan S, Marshall T, Thomas GN, et al. Incidence of cardiovascular diseases in an Iranian population: The Isfahan Cohort Study. *Arch Iran Med* 2013; 16(3): 138-44.
- Shirani S, Kelishadi R, Sarrafzadegan N, Khosravi A, Sadri G, Amani A, et al. Awareness, treatment and control of hypertension, dyslipidaemia and diabetes mellitus in an Iranian population: The IHHP study. *East Mediterr Health J* 2009; 15(6): 1455-63.
- Sarrafzadegan N, Baghaei A, Sadri G, Kelishadi R, Malekafzali H, Boshtam M, et al. Isfahan healthy heart program: Evaluation of comprehensive, community-based interventions for non-communicable disease prevention. *Prevention and Control* 2006; 2(2): 73-84.
- Mohammadifard N, Khaledifar A, Khosravi A, Nouri F, Pourmoghadas A, Feizi A, et al. Dietary sodium and potassium intake and their association with blood pressure in a non-hypertensive Iranian adult population: Isfahan salt study. *Nutr Diet* 2017; 74(3): 275-82.
- Rabiei K, Kelishadi R, Sarrafzadegan N, Sadri G, Amani A. Short-term results of community-based interventions for improving physical activity: Isfahan Healthy Heart Programme. *Arch Med Sci* 2010; 6(1): 32-9.
- Sarrafzadegan N, Kelishadi R, Esmailzadeh A, Mohammadifard N, Rabiei K, Roohafza H, et al. Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran. *Bull World Health Organ* 2009; 87(1): 39-50.
- Gandomkar A. A Statistical Study of Isfahan Air Polluted Days. Proceedings of the 4th International Conference on Chemical, Ecology and Environmental Sciences (ICEES'2015); 2015 Dec. 15-16; Pattaya, Thailand.
- Islamic Republic of Iran Vice Presidency for Strategic Planning and Supervision Statistical Centre of Iran. Selected findings of national population and housing census, 2011 [Online]. [cited 2011]; Available from: URL: <https://www.amar.org.ir/Portals/1/Iran/90.pdf>
- Uganda Bureau of Statistics. National Population

- and Housing Census 2014; Main Report [Online]. [cited 2016]; Available from: URL: <https://unstats.un.org/unsd/demographic/sources/census/wphc/Uganda/UGA-2016-05-23.pdf>
22. Peel MC, Finlayson BL, McMahon TA. Updated world map of the Koppen-Geiger climate classification. *Hydrol Earth Syst Sci* 2007; 11: 1633-44.
 23. Abbasnia M, Tavousi T, Khosravi M, Toros H. Interactive effects of urbanization and climate change during the last decades (A case study: Isfahan city). *Eur J Sci Technol* 2016; 4(7).
 24. Khosravi A, Aghamohamadi S, Kazemi E, Pour Malek F, Shariati M. Mortality profile in Iran (29 provinces) over the years 2006 to 2010. Tehran, Iran: Ministry of Health and Medical Education; 2013. p. 413-4.
 25. Encyclopædia Iranica. Isfahan xiv. modern economy and industries (2) Isfahan City: xiv. Modern Economy and Industries [Online]. [cited 2016]; Available from: URL: <http://www.iranicaonline.org/articles/isfahan-xiv2-industries-of-isfahan-city>
 26. World Health Organization. International Statistical Classification of Diseases and Related Health Problems. Geneva, Switzerland: WHO; 2010.
 27. Abedian S, Bitaraf E. The Framework for Evaluation of Hospital Information System in Iran. Tehran, Iran: The office of statistics and Technology-Ministry of Health; 2010.
 28. Sepehrnia S. Instructions for air pollution monitoring stations: Iran Department of Environment [Online]. [cited 2015]; Available from: URL: <https://www.doe.ir/Portal/file/?681739>
 29. Gordon EL. History of the Modern Environmental Movement in America [Online]. [cited 2012]; Available from: URL: https://photos.state.gov/libraries/mumbai/498320/fernandesma/June_2012_001.pdf
 30. Schrenk HH. Air pollution in Donora, PA: Epidemiology of the unusual smog episode of October 1948. Washington, DC: Federal Security Agency, Public Health Service, Bureau of State Services, Division of Industrial Hygiene; 1949.
 31. Wilkins ET. Air pollution and the London fog of December, 1952. *J R Sanit Inst* 1954; 74(1): 1-15.
 32. Brimblecombe P. The Clean Air Act after 50 years. *Weather* 2006; 61(11): 311-4.
 33. Stern AC. History of air pollution legislation in the United States. *J Air Pollut Control Assoc* 1982; 32(1): 44-61.
 34. World Health Organization. Air quality guidelines. Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide [Online]. [cited 2006]; Available from: URL: <http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/pre2009/air-quality-guidelines.-global-update-2005.-particulate-matter,-ozone,-nitrogen-dioxide-and-sulfur-dioxide>
 35. Chiu HF, Peng CY, Wu TN, Yang CY. Short-term effects of fine particulate air pollution on ischemic heart disease hospitalizations in Taipei: A case-crossover study. *Aerosol Air Qual Res* 2013; 13(5): 1563-9.
 36. Wichmann J, Voyi K. Ambient air pollution exposure and respiratory, cardiovascular and cerebrovascular mortality in Cape Town, South Africa: 2001-2006. *Int J Environ Res Public Health* 2012; 9(11): 3978-4016.
 37. Naddafi K, Hassanvand MS, Yunesian M, Momeniha F, Nabizadeh R, Faridi S, et al. Health impact assessment of air pollution in megacity of Tehran, Iran. *Iranian J Environ Health Sci Eng* 2012; 9(1): 28.
 38. Geravandi S, Goudarzi G, Salmanzadeh S, Beyt Mashal S, Mohammadi M, Naiemabadi A. Determination of cardiovascular deaths and hospital admissions due to respiratory disease for particulate matter less than 10 microns exposure in Ahvaz city during 2010-2012. *J Rafsanjan Univ Med Sci* 2016; 14 (10): 853-64. [In Persian].
 39. Goudarzi G, Geravandi S, Saeidimehr M.J, Mohammadi M, Vosoughi Niri S, Salmanzadeh S, et al. Estimation of health effects for PM10 exposure using of Air Q model in Ahvaz City during 2009. *Iran J Health Environ* 2015; 8(1): 117-26. [In Persian].
 40. Hosseini G, Maleki A, Amini H, Mohammadi S, Hassanvand MS, Giasi O, et al. Health impact assessment of particulate matter in Sanandaj, Kurdistan, Iran. *J Adv Environ Health Res* 2014; 2(1): 54-62.
 41. Ebrahimi SJ, Ebrahimpour L, Eslami A, Bidarpoor F. Effects of dust storm events on emergency admissions for cardiovascular and respiratory diseases in Sanandaj, Iran. *J Environ Health Sci Eng* 2014; 12: 110.
 42. Khamutian R, Najafi F, Soltanian M, Shokoozadeh MJ, Poorhaghighat S, Dargahi A, et al. The association between air pollution and weather conditions with increase in the number of admissions of asthmatic patients in emergency wards: A case study in Kermanshah. *Med J Islam Repub Iran* 2015; 29: 229.
 43. Mansourian M, Javanmard SH, Poursafa P, Kelishadi R. Air pollution and hospitalization for respiratory diseases among children in Isfahan, Iran. *Ghana Med J* 2010; 44(4): 138-43.
 44. Rashidi M, Ghias M, Ramesht MH. Geographical epidemiology of death due to cardiovascular diseases in Isfahan Province, Iran. *J Isfahan Med Sch* 2011; 29(125): 13-9. [In Persian].
- How to cite this article:** Rabiei K, Hosseini SM, Sadeghi E, Jafari-Koushki T, Rahimi M, Shishehforoush M, et al. **Air pollution and cardiovascular and respiratory disease: Rational and methodology of CAPACITY study.** *ARYA Atheroscler* 2017; 13(6): 264-73.