Temperature, Air Pollution, and Hospitalization for Cardiovascular Diseases among Elderly People in Denver

Petra J. M. Koken,[1] Warren T. Piver,[1] Frank Ye,[1] Anne Elixhauser,[2] Lola M. Olsen,[3] and Christopher J. Portier[1]

[1]National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA; [2]Agency for Healthcare Research and Quality, Rockville, Maryland, USA; [3]National Aeronautics and Space Administration, Greenbelt, Maryland, USA

Daily measures of maximum temperature, particulate matter ≤ 10 μm in aerodynamic diameter (PM_{10}), and gaseous pollution (ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide) were collected in Denver, Colorado, in July and August between 1993 and 1997. We then compared these exposures with concurrent data on the number of daily hospital admissions for cardiovascular diseases in men and women > 65 years of age. Generalized linear models, assuming a Poisson error structure for the selected cardiovascular disease hospital admissions, were constructed to evaluate the associations with air pollution and temperature. After adjusting the admission data for yearly trends, day-of-week effects, ambient maximum temperature, and dew point temperature, we studied the associations of the pollutants in single-pollutant models with lag times of 0–4 days. The results suggest that O_3 is associated with an increase in the risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease. SO_2 appears to be related to increased hospital stays for cardiac dysrhythmias, and CO is significantly associated with congestive heart failure. No association was found between particulate matter or NO_2 and any of the health outcomes. Males tend to have higher numbers of hospital admissions than do females for all of the selected cardiovascular diseases, except for congestive heart failure. Higher temperatures appear to be an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure, and are associated with a decrease in the frequency of visits for coronary atherosclerosis and pulmonary heart disease. *Key words:* **acute myocardial infarction, air pollution, cardiac dysrhythmias, cardiovascular diseases, CO, congestive heart failure, coronary atherosclerosis, generalized estimating equations, NO_2, O_3, PM_{10}, Poisson regression, pulmonary heart disease, SO_2, temperature.** *Environ Health Perspect* **111:1312–1317 (2003). doi:10.1289/ehp.5957 available via *http://dx.doi.org/* [Online 19 May 2003]**

There is substantial epidemiologic literature indicating a link between air pollution and cardiovascular morbidity and mortality. This includes not only studies of episodic pollution such as occurred during 1930 in the Meuse Valley (Firket 1931), 1948 in Pennsylvania (Shrenk et al. 1949), and 1952 in London (Ministry of Health 1954) but also of the generally low concentrations found in urban areas. Studies have been carried out in North America (Burnett et al. 1997a, 1997b; Morris et al. 1995; Morris and Naumova 1998; Schwartz 1999; Schwartz and Morris 1995; Zanobetti et al. 2000), in Western Europe (Atkinson et al. 1999; Ballester et al. 2001; Diaz et al. 2001; Hoek et al. 2001; Prescott et al. 1998), in Tokyo, Japan (Piver et al. 1999), and in Hong Kong, China (Wong et al. 1999). Most of these studies showed a predominant effect of particulates and carbon monoxide on cardiovascular admissions (Ballester et al. 2001; Burnett et al. 1997b; Morris et al. 1995; Morris and Naumova 1998; Schwartz 1999; Schwartz and Morris 1995; Wong et al. 1999). However, the Tokyo study (Piver et al. 1999) suggests an independent effect of nitrogen dioxide. Furthermore, the studies in Canada (Burnett et al. 1997a) and Spain (Diaz et al. 2001) demonstrated consistent effects for sulfur dioxide and/or ozone on cardiovascular hospital admissions. Several reports have addressed the issue of weather and mortality; extreme temperatures have been associated with increased daily mortality in numerous regions of the world (Braga et al. 2001; Kunst et al. 1993). Mortality has also been observed to increase during periods of 3 or more days of unusual temperatures during summer or winter, showing that temperature variability is an important determinant of human health effects (Braga et al. 2001, 2002; Saez et al. 1995).

It has been suggested that weather and temperature may modify the effects of air pollution on health both at high temperatures (Katsouyanni et al. 1993) and low temperatures (Morris and Naumova 1998). The Intergovernmental Panel on Climate Change (IPCC; 1996) has projected that atmospheric concentrations of carbon dioxide could double in the next 50–100 years. A doubling of atmospheric concentrations of CO_2 could result in an increase in average global surface air temperatures of 1–3°C because of the greenhouse effect. In addition, because approximately 65% of atmospheric CO_2 comes from combustion of fossil fuels, increasing concentrations of CO_2 could also be accompanied by increasing concentrations of other air pollutants, particularly in large urban areas. An increase in surface air temperatures could accompany a greater frequency and duration of heat waves. According to the IPCC (1996), the frequency of extremely hot days in temperate climates approximately doubles for every 2–3°C increase in temperature during the average summer. Because heat waves often occur in large metropolitan areas during warm summer months, these large cities could experience an increase in the incidence of heat-related morbidity and mortality (McMichael et al. 1996). To address this specific issue, we focused our research on the months of the year when the frequency of exposure to high daily maximum temperatures (T_{max}) and high air pollutant concentrations would be the greatest. The present study focuses on the months of July and August (1993–1997) in Denver, Colorado.

Studies have documented associations between daily variations in air pollution and cardiovascular deaths and hospital admissions (Dockery et al. 2000). Mechanisms for the effects of air pollution on cardiovascular mortality and morbidity may include changes in blood coagulability (Seaton et al. 1995) and changes in the nervous system control of the heart, possibly leading to arrhythmias (Peters et al. 2000). Mechanisms linking temperature to cardiovascular mortality and morbidity have also been postulated. The blood viscosity and cholesterol levels have been found to increase with high temperatures (Keatinge et al. 1986), whereas blood pressure and fibrinogen levels increase during winter, although outdoor temperature does not seem to determine the seasonal variation in fibrinogen (van der Bom et al. 1997). In many epidemiology studies with respiratory and cardiovascular diseases, regression models include adjustments for seasonal climate variability to isolate the contributions of air pollution on the daily number of deaths or hospital admissions for these diseases. In contrast to using seasonal adjustments for the entire year, we focused on the months of July and August, partially to avoid potential bias in the type of seasonal adjustment to be used and partially to focus on short time-frame changes in temperature.

Address correspondence to P.J.M. Koken, National Institute of Environmental Health Sciences, MD A3-06, PO Box 12233, Research Triangle Park, NC 27709 USA. Telephone: (919) 541-2271. Fax: (919) 541-1479. E-mail: koken@niehs.nih.gov

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Materials and Methods

Setting. Denver once was among the most polluted cities in the United States, with a brown cloud as a constant reminder of its air pollution woes. The city regularly exceeded the federal air pollution standards for 200 days/year, every year in the late 1970s. Air pollution in Denver mainly derives from motor vehicle exhaust emissions, with industrial pollution playing a minor role. Denver's air pollution levels are also exacerbated by temperature inversions resulting from Denver's geographic location. During a temperature inversion, a warm, less-dense inversion layer of air overlies colder, denser air, forming a "lid" that traps pollutants below it. In Denver the trapping effect is even more pronounced because long periods of calm weather and light winds trap pollutants against nearby mountains. The local government has undertaken sizable efforts to reduce air pollution; the city has now complied with Clean Air Act regulations for particulates, CO, and O_3 (U.S. EPA 2001) and has cut its pollution dramatically. Nonetheless, the remaining levels of pollutants may continue to have health effects, even at their improved levels. In this study, we defined Denver as all of Denver County.

Hospital admission data. The numbers of daily hospital admissions to all 11 hospitals in Denver County were obtained for the months of July and August during 1993–1997. July and August are of particular interest because these are the months with highest temperatures, combined with relatively high levels of outdoor activity during which exposure would be maximized. The data were provided by the Agency for Healthcare Research and Quality (AHRQ; Rockville, MD). The AHRQ maintains state-specific hospital discharge databases as part of the Healthcare Cost and Utilization Project (HCUP 2001). Data elements included admission date, age, sex, and discharge diagnoses. The study population was restricted to men and women > 65 years of age admitted to the hospitals with a primary discharge diagnosis of the following causes [coded using *International Classification of Diseases, 9th Revision-CM* (*ICD-9-CM*); Centers for Medicare & Medicaid Services 2003]: acute myocardial infarction (*ICD-9-CM* 410.00–410.92), coronary atherosclerosis (*ICD-9-CM* 414.00–414.05), pulmonary heart disease (*ICD-9-CM* 416.0–416.9), cardiac dysrhythmias (*ICD-9-CM* 427.0–427.9), and congestive heart failure (*ICD-9-CM* 428.0). These particular diseases were chosen because they include a mixture of acute and chronic cardiovascular diseases. Admissions resulting from viral infections (e.g., influenza) and chronic pulmonary dysfunctions (e.g., embolisms, hypertension, thrombosis, aneurysms) were excluded. Observations were available for all diseases on all the days of the study period (310 total days). The unit of analysis was the daily number of admissions for males and females > 65 years of age per 10,000 residents. The numbers of residents in Denver per sex and age for the years 1993–1997 were derived from the Population Estimates Program of the U.S. Census Bureau (2000). From 1993 to 1997, the total population of males and females > 65 years of age has declined from about 64,000 to about 60,000. The percentage of males and females in the > 65 age group was 38% and 62%, respectively.

Environmental data. Air pollution data were extracted from the U.S. Environmental Protection Agency (EPA) Aerometric Information Retrieval System (AIRS) (U.S. EPA 2002). Daily concentrations of the U.S. EPA's criteria air pollutants were obtained from all of the monitoring stations in Denver County. These pollutants included NO_2, SO_2, O_3, CO, and particulate matter ≤ 10 μm in aerodynamic diameter (PM_{10}). The PM_{10} level was collected over a 24-hr period, whereas gaseous air pollutants were measured hourly. For each day, the 24-hr arithmetic average reading was determined for each station, and then an arithmetic average was calculated over all stations. During July and August of 1993–1997, three monitoring stations measured PM_{10} in Denver. PM_{10} measurements were available for 298 (96%) of the possible days during the study periods (July–August 1993–1997). O_3 was monitored at two stations during the study periods, and data were available for 310 (100%) of the days. NO_2 and SO_2 were measured at one site in all 5 years, with 303 (98%) and 310 (100%) of the days available, respectively. CO was monitored at three stations from 1993 to 1995 and four stations in 1996 and 1997; data were available on all days during the study periods.

Daily 24-hr meteorologic measurements such as T_{max} and dew point temperature (DPT) were provided by the National Climate Data Center (NCDC 2002). During July and August of 1993–1997, three measurement stations were located in Denver County. These meteorologic measurements were available on all days during the study period and were averaged over all stations.

Modeling approach. We used general linear models (GLMs; McCullagh and Nelder 1989) to analyze the frequency of hospital admissions for a given day as a function of environmental exposures. Poisson error structure was assumed because hospital admissions are generally rare events. In a classic Poisson regression, the model assumes

$$\log [E(Y_i)] = \beta \mathbf{X}_i, \qquad [1]$$

where $\mathbf{X}_i$ is the matrix of covariates on day i, Y_i is the morbidity count on day i, and E denotes the expected value. Unlike the normal distribution, which is completely determined by its two parameters, the mean μ and the variance σ^2, the relationship between the mean and variance for a Poisson variate is a fixed relationship. Given a Poisson distribution with parameter λ, this relationship is $\mu = \sigma^2 = \lambda$.

In the present study, explicit adjustments for seasonal patterns were not necessary because we used only data for July and August from each year. In addition, the daily number of hospital admissions for each disease and the daily levels of each environmental variable in July and August within any given year were assumed to be independent of daily disease counts and environmental levels from the previous years. Although the hospital admission and environmental data are treated as independent from year to year, within a 2-month period in a given year the number of hospital admissions and the levels of the environmental variables for a given day could be correlated with the data for each of these variables from previous days. To account for potential delays in disease incidence after important exposures, lag times of 1–4 days for each of the environmental variables were included as additional model covariates. Model covariates were also centered using their means. Besides an intercept term and indicator variables for sex (0 = female, 1 = male), day of the week, and year of study, all GLM models included an offset or normalizing factor to account for population changes during 1993–1997. The application of an offset is a computational procedure to treat the population size (PS) as a reference value and does not require an additional parameter in the Poisson regression:

$$\log [E(Y_i)] = \log(\mathrm{PS})\, \beta \mathbf{X}_i. \qquad [2]$$

Parameters in the Poisson regression models were estimated using the generalized estimating equations (GEEs) of Liang and Zeger (1986) to account for the possibility of overdispersion and serial correlation (Lipsitz et al. 1994; Schwartz 1993). Overdispersion refers to the increase in the variance of the distribution of the disease counts that can occur when the underlying population is not homogeneous with respect to risk of morbidity. Serial correlation refers to a situation where the daily number of hospital admissions on 2 days close to each other in time is correlated. The GEE for estimating β is an extension of the independence estimating equation for correlated data. The covariance matrix of Y_i is modeled as

$$V = \phi A^{1/2} R(\alpha) A^{1/2}, \qquad [3]$$

where A is an $n \times n$ diagonal matrix with the variance of Y_i as the diagonal element, $R(\alpha)$ is the $n \times n$ working correlation matrix that is fully specified by the vector of parameters α,

and ϕ is the overdispersion parameter (Liang and Zeger 1986; SAS/STAT Software 1997). The working correlation structure for daily number of hospital admissions within a year was assumed to be autoregressive with the following structure:

$$\text{corr}(Y_i, Y_{i'}) = \alpha^{|i-i'|}. \quad [4]$$

α is estimated empirically from the data, and ϕ is estimated from the residual χ^2 using the method of McCullagh and Nelder (1989). Missing values were treated as being missing completely at random and were dropped from the analyses, but appropriate care was taken to ensure that autoregressive parameters were estimated with the proper lags.

Before adding the air pollution variables to the models, the effects of the T_{max} and DPT were investigated. For each cardiovascular disease, the daily admissions per 10,000 population were regressed against the T_{max} and DPT with various lag times from 0 to 4 days. The lags for T_{max} and DPT that minimized the deviance were kept fixed for the subsequent analyses incorporating the effect of the air pollutants. Residuals of each model were examined to check whether there were discernible patterns and autocorrelation by means of residual plots and partial autocorrelation function plots, respectively (Schwartz et al. 1996). Once we determined the optimal model for temperature-related effects on hospital admissions (core model), we examined the association between exposure to one air pollutant and daily numbers of hospital admissions per 10,000 population. Each air pollutant was entered linearly (with a log link function) into the regression, and lags between 0 and 4 days were examined. Because of the large number of pollutants and lags tested, emphasis was placed on the consistency of associations across lags and measures, and only the more highly significant findings are discussed. To examine the effect of a period of time with consistently above-median temperatures, the same analyses were carried out containing a variable describing the number of days in a row when maximum daily temperatures were greater than or equal to its 50th percentile. Additional analyses were conducted for each sex separately but resulted in insufficient sample sizes and are not reported here. Other strategies for model choice (e.g., forward, backward elimination) and autocorrelation formulations (exchangeable, unstructured) did not significantly alter the results and are not presented here.

We used PROC GENMOD (SAS System for Windows, Release 8.00; SAS Institute, Cary, NC) in the analysis.

Results

Table 1 shows the mean and variance of the daily numbers of hospital admissions for the cardiovascular diseases per 10,000 population in Denver during the study period. The highest mean daily rate of hospital admissions was observed in males for coronary atherosclerosis (0.74/10,000) and in females for congestive heart failure (0.52/10,000).

Figure 1 shows the annual daily average number of hospital admissions for cardiovascular diseases per 10,000 population for males and females. In general, there appears to be a greater incidence for males than for females, and for most of the diseases a slight increase in daily average number of hospital admissions per 10,000 population was observed during 1993–1997. As a result, the models for each disease include classification variables for annual trends and for sex.

Table 2 contains the summary statistics of the environmental data in Denver during the study period. Levels of pollutants were generally low if examined in light of U.S. EPA National Ambient Air Quality Standards (U.S. EPA 2001). All of the average pollutant levels would have easily met the standards.

Table 3 shows the correlations among the air pollution and weather variables. O_3 presented positive correlation with T_{max}, negative correlations with other environmental variables, and almost no correlation with PM_{10} (0.03). It showed the strongest correlation with T_{max} (0.41), and CO (–0.40). NO_2 presented high positive correlations with CO (0.73), PM_{10} (0.56), and SO_2 (0.46). The correlations observed for O_3 can be explained by the fact that O_3 is a summertime pollutant caused by the reaction of volatile organic compounds, CO, and NO_2 in the presence of sunlight. The correlations seen in Table 3 between PM_{10}, NO_2, and SO_2 probably exist because secondary particles are formed from gaseous precursors, including the SO_x and NO_x. No consistent trends over the 5 years of this study were seen in the average daily concentrations of the environmental variables.

The single-pollutant GLMs were evaluated based on sequentially identifying factors that significantly reduce the residual error. Table 4 summarizes the results of the single-pollutant analysis for the different cardiovascular diseases in the > 65-year-old population of Denver for up to 4 lag days. The most statistically significant association from the single-pollutant measures investigated, whether positive or negative, is presented. The coefficients from Table 4 can be interpreted in terms of increased daily hospital admissions. For example, the model for coronary atherosclerosis results in a statistically significant 2-day lag effect of O_3 on daily coronary atherosclerosis hospital admissions. An increase in the daily average level of O_3 from 20 ppb (25th percentile) to 29.7 ppb (75th percentile; Table 2) is statistically associated with an increase in daily hospital admissions for coronary atherosclerosis of $(e^{0.012(29.7-20.0)} - 1) \times 100\% = 12.3\%$ with a 95% confidence interval (CI) of 3.96–21.4%. The percentage change in risk and the 95% CI associated with a 25–75th percentile increase in T_{max}, DPT, and/or pollutant measure are reported together with the p-value in Table 4. The estimates for the overdispersion factor for the individual models (not shown) were nearly equal to 1.0, so adjustment of the standard errors was not necessary.

The results indicate that T_{max} at either lag 0 or 1 has a significant association with all cardiovascular diseases except for cardiac dysrhythmias. T_{max} is positively associated (increasing T_{max} leads to increasing hospital admissions) with both acute myocardial infarction ($p < 0.01$) and congestive heart failure ($p = 0.02$). In contrast, the T_{max} is negatively associated with the observed number of hospital admissions for coronary atherosclerosis ($p < 0.01$) and pulmonary heart disease

Table 1. Means and variances of the daily numbers of hospital admissions for males and females > 65 years of age per 10,000 population in Denver, July–August 1993–1997.

	Males		Females	
Disease	Mean	Variance	Mean	Variance
Acute myocardial infarction	0.51	0.20	0.31	0.08
Coronary atherosclerosis	0.74	0.36	0.40	0.10
Pulmonary heart disease	0.08	0.03	0.06	0.02
Cardiac dysrhythmias	0.36	0.14	0.29	0.08
Congestive heart failure	0.48	0.19	0.52	0.15

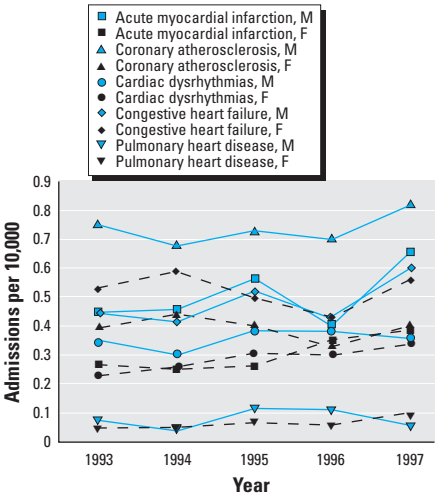

Figure 1. Annual daily average number of hospital admissions for cardiovascular diseases per 10,000 population for males (M) and females (F) > 65 years of age in Denver, July–August 1993–1997.

($p < 0.01$). A 25–75th percentile increase in T_{max} (from 83 to 93.5°F) is associated with an 18, 13, 28, and 13% change in risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, pulmonary heart disease, and congestive heart failure, respectively. T_{max} has no significant association with cardiac dysrhythmia hospital admissions ($p > 0.05$). A 1-day lag DPT association was observed for coronary atherosclerosis (negative, $p < 0.01$) and for congestive heart failure (positive, $p < 0.01$). A 25–75th percentile increase in DPT (from 44.2 to 53.3°F) is associated with a 9 and 16% change in risk of hospitalization for coronary atherosclerosis and congestive heart failure, respectively.

Levels of O_3 are positively associated with the number of coronary atherosclerosis (lag 2, $p < 0.01$) and pulmonary heart disease (lag 1, $p < 0.01$) hospital admissions and negatively associated with the number of acute myocardial infarction hospital admissions (lag 0, $p < 0.01$). A 25–75th percentile increase in average daily O_3 concentrations (from 20 to 29.7 ppb) is associated with an 18, 12, and 21% change in risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease, respectively. Marginal positive associations are seen for current-day SO_2 concentrations with hospital admissions for cardiac dysrhythmias ($p = 0.055$) and for the level of CO with congestive heart failure (lag 3, $p = 0.046$). A 25–75th percentile increase in average daily SO_2 concentrations (from 3.8 to 7.2 ppb) is associated with a 9% change in risk of hospitalization for cardiac dysrhythmias. An increase from 0.8 to 1.1 ppm in average daily CO is associated with an 11% change in risk of hospitalization for congestive heart failure. No significant associations were found between particulate matter or NO_2 for any lag day and any of the health outcomes.

Sex is an important risk factor in all of the selected cardiovascular diseases, except for congestive heart failure. Males had higher numbers of hospital admissions than did females ($p = 0.01$). When exposed to both higher temperatures and O_3, males are associated with a 68, 82, and 17% increased risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease, respectively. Also, males have a 23% increased risk of hospitalization for cardiac dysrhythmias compared with women.

Inclusion of a variable describing the number of days in a row when maximum daily temperatures were greater than or equal to its 50th percentile (88.5°F; Table 2) had no effect on the model parameter estimates.

Discussion and Conclusions

The purpose of this study was to determine if exposures to higher temperatures and air pollutant concentrations were significantly associated with hospital admissions for cardiovascular diseases. Hospital admissions represent morbidity data, rather than mortality data, and represent a more immediate response to higher temperatures and/or air pollutant concentrations. Studies of morbidity effects can strengthen the consistency of findings regarding the biologic plausibility of mortality effects of temperature and air pollution. This study was conducted during July–August, a period of time when outdoor levels of air pollution likely are a better reflection of actual exposure, given that individuals spend more time outdoors in summer than in winter, and the time when temperatures are usually the highest of the year.

From the results, it is clear that there is heterogeneity in the association of individual components of air pollution and temperature with the disease end points. No association was found between particulate matter or NO_2 and any of the health outcomes. A large number of daily time-series studies have reported associations between particulate matter and hospitalizations. Most of these studies have focused on respiratory hospital admissions rather than cardiovascular diseases and do not address an issue similar to the one studied in this study. Some recent studies have reported associations between particulate matter and hospitalizations for cardiovascular diseases (Schwartz 1999; Schwartz and Morris 1995), and others have not (Burnett et al. 1997a). Burnett et al. (1997a) could not identify particulate mass as an independent risk factor beyond that attributable to climate and gaseous air pollution. All of these studies have analyzed full-year data, whereas the present study focused on July–August only. A seasonal particulate matter effect might exist, as was seen in a study of Cook County, Illinois (Styer et al. 1995) in which a significant effect of particulate matter on cardiovascular mortality numbers was found in spring and fall, but no significant effect was found in winter and summer.

The significant associations between July–August concentrations of CO and specific cardiovascular diseases are confirmed in a large number of year-round studies (Ballester et al. 2001; Burnett et al. 1997b; Morris et al. 1995; Morris and Naumova 1998; Schwartz 1999; Schwartz and Morris 1995). Morris et al. (1995) found that CO showed a consistent, significant association with hospital admissions for congestive heart failure. Burnett et al. (1997b) demonstrated a similar effect in investigation of 10 Canadian cities. The limited data from laboratory studies on the combined effects of air pollution with either heat stress or cold stress seem to support the possibility of enhanced toxicity of CO associated with extreme temperatures (Yang et al. 1988). Studies in Chicago, Illinois (Morris and Naumova 1998), and Tucson, Arizona (Schwartz 1997), failed to demonstrate an increase in the effect of CO at high temperatures. It is possible that the cut point for the high temperature range was not sufficiently high in the Chicago study, whereas the summer CO levels were not high enough in the Tucson study.

We found a significant negative association of O_3 with hospital admissions for acute myocardial infarction and a positive association for coronary atherosclerosis and pulmonary heart disease. Only three studies that we reviewed showed evidence of a consistent association between O_3 and cardiovascular admissions. Prescott et al. (1998) found that cardiovascular admissions for patients ≥ 65 years of age had a significant (negative) association with O_3. Burnett et al. (1997a) showed that O_3 was most strongly associated with

Table 2. Summary statistics for daily levels of environmental variables in Denver, July–August 1993–1997.

Variable	Source	No.	Mean	Minimum	Percentile 25th	Percentile 50th	Percentile 75th	Maximum	SD
NO_2 (ppb)	AIRS	303	32.7	13.0	28.0	33.2	37.9	51.3	7.24
SO_2 (ppb)	AIRS	310	5.7	0.4	3.8	5.3	7.2	18.9	2.94
O_3 (ppb)	AIRS	310	25.0	5.4	20.0	25.2	29.7	40.2	6.61
CO (ppm)	AIRS	310	0.9	0.3	0.8	0.9	1.1	1.6	0.27
PM_{10} (μg/m^3)	AIRS	298	24.2	7.0	20.0	24.0	28.0	51.6	6.25
T_{max} (°F)	NCDC	310	87.4	62.0	83.0	88.5	92.5	99.0	7.37
DPT (°F)	NCDC	310	48.6	26.8	44.2	49.3	53.3	62.4	6.23

Data from U.S. EPA (2002) and NCDC (2002).

Table 3. Pearson correlation coefficients of environmental variables for Denver, July–August 1993–1997.

	T_{max}	DPT	NO_2	SO_2	O_3	CO	PM_{10}
T_{max}	1.00	–0.42	0.34	0.26	0.41	0.11	0.38
DPT	—	1.00	–0.12	–0.15	–0.26	0.01*	–0.24
NO_2	—	—	1.00	0.46	–0.30	0.73	0.56
SO_2	—	—	—	1.00	–0.10	0.21	0.36
O_3	—	—	—	—	1.00	–0.40	0.03*
CO	—	—	—	—	—	1.00	0.25
PM_{10}	—	—	—	—	—	—	1.00

*$p > 0.05$.

hospitalization for cardiac diseases in Toronto in the summer. In Hong Kong, Wong et al. (1999) found a significant relation of O_3 with hospital admissions for cardiovascular diseases. However, most of the reviewed studies do not suggest an impact of O_3 on the number of hospitalizations attributable to cardiovascular disease (Ballester et al. 2001; Morris et al. 1995; Morris and Naumova 1998; Schwartz 1997; Schwartz and Morris 1995).

It is noteworthy to mention the association between SO_2 and cardiac dysrhythmias. The physiopathologic mechanisms of SO_2 causing cardiovascular damage are insufficiently understood, and more research is needed in this area. Only two studies that we reviewed showed SO_2 as being positively associated with daily hospital admissions for cardiac diseases (Burnett et al. 1997a; Diaz et al. 2001). It is possible that, in this case, SO_2 is serving as a general indicator of air pollution exposure rather than a direct causal initiator of cardiovascular damage.

Sex appeared to be an important risk factor in all of the selected cardiovascular diseases except for congestive heart failure. Males tend to have higher numbers of hospital admissions than do females.

Higher temperatures *a*) appear to be an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure; *b*) are associated with a decrease in the frequency of visits for coronary atherosclerosis and pulmonary heart disease; and *c*) have no significant effect on visits for cardiac dysrhythmias. It is possible that patients with chronic cardiovascular conditions (coronary atherosclerosis and pulmonary heart disease) avoid outdoor exposures during periods of peak heat, resulting in the negative association. In contrast, exposures to higher air pollutant concentrations (except for particulate matter and NO_2) appear to have a positive effect on the number of hospital admissions for cardiovascular diseases. According to Bernard et al. (2001), climate change may affect exposures to air pollutants by *a*) affecting weather and thereby local and regional pollution concentrations; *b*) affecting anthropogenic emissions, including adaptive responses involving increased fuel combustion for power generation; *c*) affecting natural sources of air pollutant emissions; and *d*) changing the distribution and types of aeroallergens. According to Bernard et al. (2001), it is expected that, in the future, the pollutants of concern are likely to remain, as now, particulate matter—both from its primary sources and from the secondarily formed particles—and photochemical pollution with O_3. Emissions of SO_x and NO_x due to power generation might increase, but control technologies are available and should be able to control such emissions.

The present study is limited because it uses environmental monitoring data to represent ambient concentrations. The fact that different pollutants have not been measured at the same monitoring stations (e.g., NO_2 was measured only at one site, and other pollutants at three or four sites) can affect the estimated correlations between the pollutants. Besides this, environmental monitoring data do not necessarily represent individual exposures. This could result in associations between exposures and hospital admissions that are spurious. Also, measurement errors resulting from differences between the population-average exposure and ambient levels cannot be avoided. However, this kind of measurement error is likely to cause a bias toward the null and underestimates the pollutant effects (Zeger et al. 2000). Many individual risk factors, such as smoking, diet, cholesterol level, and obesity, either do not vary significantly over time or vary slowly. In addition, there is no reason to believe that daily variations in the individual risk factors are correlated with daily changes in air pollution; therefore, they are unlikely to be confounding factors in this study (Schwartz 1997). It is possible that with accurate, individual exposures, the major associations seen in this study may not be all of the associations that are important.

Care should be taken with drawing conclusions about the impact of temperature on morbidity because the estimated adverse health effects from exposures to higher temperatures and air pollutants are small. Uncertainties inherent in the analyses go far beyond the sampling variability that is captured by the standard error of the confidence interval. These uncertainties arise from model misspecification, omitted covariates, and errors in the measurement of covariates considered in the models. Care should also be taken in comparing different studies because discrepancies may reflect regional differences in pollution mixture, climate, flora and fauna, period of data collection, measurement methods of air pollutants, or medical practice patterns. Time series do not give precise information on the relationship between air pollution and health for a particular individual. However, they provide valuable information on the overall health impact of air pollution as measured at fixed-site monitoring stations.

In summary, the results of this study in Denver suggest that O_3 increases the risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease. SO_2 appears to be related to increased hospital stays for cardiac dysrhythmias, and CO is significantly associated with congestive heart failure hospitalization. No association was found between particulate matter or NO_2 and hospitalization for any condition. Males had more hospital admissions for cardiovascular diseases than did females. Higher temperatures appear to be an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure. However, higher temperatures are associated with a decrease in the frequency of visits for coronary atherosclerosis and pulmonary heart disease and have no significant effect on admissions for cardiac dysrhythmias. In contrast, exposures to higher air pollutant concentrations (except for particulate matter and NO_2), even at levels that meet federal air quality standards, appear to have an effect of increasing the number of hospital admissions for cardiovascular diseases as a whole.

Table 4. Summary of results for single-pollutant analysis of hospital admissions for cardiovascular diseases for males and females > 65 years of age in Denver, July–August 1993–1997.

Disease	Model covariate	Single-day lag	β (SE)	Percent change in hospital admissions (95% CI)	*p*-Value
Acute myocardial infarction	T_{max}	0	0.017 (0.007)	17.5 (2.9–34.3)	0.009
	O_3	0	–0.020 (0.006)	–17.6 (⁻26.7–⁻7.5)	0.001
	Male sex	—	0.517 (0.061)	67.7 (48.4–89.5)	< 0.0001
Coronary atherosclerosis	T_{max}	1	–0.014 (0.004)	–12.5 (⁻18.9–⁻5.5)	0.001
	DPT	1	–0.010 (0.003)	–8.7 (⁻13.6–⁻3.6)	0.003
	O_3	2	0.012 (0.004)	12.3 (4.0–21.4)	0.004
	Male sex	—	0.601 (0.038)	82.4 (69.0–96.8)	< 0.0001
Pulmonary heart disease	T_{max}	0	–0.035 (0.008)	–28.3 (⁻38.4–⁻16.5)	< 0.0001
	O_3	1	0.020 (0.008)	21.4 (4.0–41.8)	0.009
	Male sex	—	0.160 (0.062)	17.4 (3.7–32.8)	0.010
Cardiac dysrhythmias	SO_2	0	0.025 (0.013)	8.9 (⁻0.34–18.93)	0.055
	Male sex	—	0.203 (0.028)	22.5 (15.8–29.6)	< 0.0001
Congestive heart failure	T_{max}	1	0.013 (0.005)	13.2 (2.9–24.4)	0.016
	DPT	1	0.016 (0.004)	15.7 (7.6–24.4)	< 0.0001
	CO	3	0.332 (0.166)	10.5 (0.1–22.0)	0.046

CI, confidence interval. The percentage change in the number of admissions for a 25–75th percentile change in each pollutant (or for males compared with females) is presented at its most statistically significant single lag.

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