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The effects of weather and air pollution on cardiovascular and respiratory mortality in Santiago, Chile, during the winters of 1988–1996

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ABSTRACT: This study quantifies the effects of stressful weather and elevated air pollution levels on cause-specific mortality in Santiago, Chile, during the austral winters from 1988 to 1996. A temporal synoptic index (TSI) is used to form weather classes and air pollution classes. Prior applications of the TSI have formed classes solely on the basis of weather and may have systematically underestimated the impact of air pollution levels on daily mortality. In Santiago, the attribution of increased mortality risk was found to be largely dependent on the type of class formed (weather or pollution). High-mortality weather classes were associated with cold, dry and high-pressure conditions, while high-mortality pollution classes were associated with elevated NO_2 and $PM_{10-2.5}$ concentrations. Cardiovascular disease mortality was more sensitive to weather conditions, and respiratory mortality was more sensitive to pollution levels. Respiratory mortality was most sensitive to stressful conditions at longer lag times (3–6 days), while cardiovascular mortality was most sensitive at shorter lag times (0–2 days). By understanding the relative magnitudes of health risks associated with stressful weather and air pollution conditions we can improve existing air pollution/weather watch systems and better anticipate future risks associated with global climate change. Copyright © 2007 Royal Meteorological Society

KEY WORDS weather; Chile; air pollution; mortality; synoptic climatology; temporal synoptic index

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1. Introduction

The sub-discipline of air pollution epidemiology has developed complex statistical methods to discern the impacts of prolonged exposure to air pollution on human health (Thurston and Kinney, 1994), yet there has been continued concern as to the efficacy of different approaches to control for the potential confounding effects of weather conditions (Health Effects Institute Review Panel, 2003). Concurrently, growing concern over the health consequences of climate change has led to numerous studies of effects of stressful weather conditions on health (Saez *et al.*, 1995; McGregor, 2001; O'Neil *et al.*, 2003; Rainham and Smoyer-Tomic, 2003), which have frequently ignored or minimized the role of air pollution as a possible confounder (Braga *et al.*, 2002; Curriero *et al.*, 2002). While many researchers have speculated that the combined impacts of weather and pollution are 'interactive' (e.g. WHO, 1996; McGregor, 1999; Patz and Balbus, 2001), there have been few attempts to quantify whether the combined effects are additive and independent, antagonistic, or synergistic (WHO, 1996). The Temporal Synoptic Index has been widely applied as a biometeorological approach to evaluating the relative importance of weather and air pollution's impacts on health (Kalkstein, 1991; Pope and Kalkstein, 1996; Jamason *et al.*, 1997; Kalkstein *et al.*, 1997; Kalkstein and Greene, 1997; Greene *et al.*, 1999; Guest *et al.*, 1999; McGregor *et al.*, 1999; Smoyer *et al.*, 2000). This method allows the researcher to consider the composite effect of multiple meteorological elements on a given health outcome rather then considering each element in isolation. Repeated applications of this method have found weather to be a better predictor of summertime mortality than pollution (e.g. Kalkstein, 1991, Kalkstein *et al.*, 1997; Smoyer *et al.*, 2000). The present study asks whether the same findings hold true during the winter in Santiago, Chile, a temperate city with one of the most severe air pollution problems in Latin America. We employ a dual-classification scheme, grouping days based on weather and in a separate analysis, based on air pollution. We aim to:

1. Identify synoptic weather conditions associated with elevated mortality and/or pollution levels during the austral winter months;
2. Evaluate the relative importance of weather conditions and pollution concentrations in explaining periods of elevated mortality;

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3. Determine whether the relative importance of weather and pollution differs if the study period is classified on the basis of pollution conditions rather than weather conditions.

1.1. Prior applications of TSI

The TSI is a method for defining homogenous weather classes (WCs), or air masses, based on principal components analysis of hourly observations of standard meteorological variables (Kalkstein *et al.*, 1997). Once classes have been defined, weather patterns that have a significant association with a given health outcome can be identified. The question of which environmental variable or variables might be responsible for causing the elevated mortality on an 'offensive' WC day is approached by calculating descriptive statistics for each WC, e.g. is the 'offensive' air mass also the hottest or most humid? Were the mean pollution levels for this class above or below other classes?

Kalkstein (1991) found that high mortality in St Louis, Missouri was associated with a hot anti-cyclonic tropical air mass, and that pollution concentrations were not related to the differences in mean mortality among the different WCs. Fluctuations in mortality within the oppressive air mass appeared to be unrelated to any of the six pollutants considered. Further, there was no WC with both high mortality and high levels of pollution in any of the ten major US cities considered in a cursory analysis. In later work, Kalkstein *et al.* (1997) found that in Birmingham, Cleveland and Philadelphia total suspended particulates (TSP) and ozone did not contribute to the elevated mortality that occurred during and after an offensive weather event. In Birmingham and Philadelphia, Smoyer *et al.* (2000) found that the hottest air mass had the highest mean mortality, but not the highest pollution levels, and that no pollution variables were statistically significant predictors of mortality levels on 'offensive' air mass days. Both studies conclude that mortality levels are more sensitive to 'offensive' weather events than to high concentrations of ozone or TSP.

These results fundamentally disagree with epidemiological studies showing that increases in particulate matter were associated with significant increases in mortality in St Louis (Dockery *et al.*, 1992), Philadelphia (Schwartz and Dockery, 1992) and Birmingham (Schwartz, 1993); findings that remained robust to changes in model specifications to correct for relatively lax convergence criteria used in the original analyses (Health Effects Institute, 2003). The apparent disagreement in results of the TSI method and longitudinal time series analyses led to a re-examination of the importance of weather as a potential confounder of pollution's effect on mortality. In Philadelphia (Samet *et al.*, 1998) and Provo, Utah (Pope and Kalkstein, 1996) researchers compared the use of the TSI with alternative methods to control for the effect of weather on the air pollution-mortality relationship. Both studies differed from a 'traditional' Kalkstein approach in that the analysis was not limited to one season, no 'offensive' WCs were defined, and regressions were performed on the full dataset rather than on a subset of 'offensive' weather days. Both studies found little evidence that weather modified the effect of pollution on mortality.

1.2. The joint action of stressful weather and air pollution conditions

Studies of the health effects of air pollution conducted in the 1960s and earlier tended to ignore the weather's potential to confound or modify the pollution–health relationship (Lave and Seskin, 1970). By the 1970s air pollution time-series studies frequently included model terms to control for the confounding effects of temperature (Ware *et al.*, 1981). Recent studies generally find that the effect of pollution on mortality remains significant after controlling for the effect of weather variables, season, and other confounders (Rainham and Smoyer-Tomic, 2005; Schwartz, 2005; Pope and Dockery, 2006). Owing to the continuing debate as to the adequacy of the controls for weather (Health Effects Institute Review Panel, 2003), several sensitivity studies tested different parameterizations of the weather terms, finding in each case that the pollution–disease relationships were robust to alternative model specifications for weather (Kinney *et al.*, 1995; Pope and Kalkstein, 1996; Samet *et al.*, 1998; Welty and Zeger, 2005).

Methodological developments in studies of the effects of temperature on mortality have followed a similar course. Early studies often failed to consider the possible influence of air pollution (Braga *et al.*, 2002; Curriero *et al.*, 2002). More recent temperature-mortality studies have incorporated parameterizations to control for the confounding effects of air pollution (Rainham and Smoyer-Tomic, 2003; O'Neill *et al.*, 2005). While the magnitude and sign of the confounding effects may vary by city (O'Neill *et al.*, 2003), in general, temperature's effect on mortality has been found to persist after adjusting for air pollution.

While most studies have considered the potential confounding effects of weather on air pollution and human health, fewer studies have considered if weather can be considered a modifier of air pollution's effects on health. Katsouyanni *et al.* (1993, 2001); Roberts (2004) and Ren and Tong (2006) found that pollution's effect on mortality was enhanced at warmer temperatures. Samet *et al.* (1998) found evidence of effect modification only when weather was represented by synoptic categories like those used in the TSI.

Almost all of the studies discussed above are asymmetrical by design; that is, they attempt to provide an unbiased estimate of the health effects of **either** weather **or** pollution. A few studies have attempted to make simultaneous effect estimates of air pollution and weather in regression models (Sartor *et al.*, 1995; Goodman *et al.*, 2004). Other studies have modelled the joint health effects of air pollution and temperature as continuous functions of both variables (Shumway *et al.*, 1988; Morris and Naumova, 1998; Roberts, 2004; Ren and Tong,

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2006). Kalkstein *et al.*, (1997) carried out a similarly balanced or symmetrical analysis by complementing a weather-based TSI analysis for Philadelphia with a "pollution synoptic index" and found elevated mean mortality in the 'offensive' pollution classes was of a similar magnitude (6.5 and 7.1 excess deaths per day) as the elevated mortality in the 'offensive' weather class (8.9 excess deaths per day). The present study employs the same strategy. Two classifications are carried out for each day in the analysis, one on the basis of weather conditions and the other on the basis of pollution conditions.

1.3. Description of the study area

Time-series analysis studies in Santiago have found statistically significant associations between air pollution and various health endpoints including daily mortality (Ostro *et al.*, 1996; Cifuentes and Lave, 2000), and medical visits for lower respiratory symptoms (Ostro *et al.*, 1999). The polluted condition of Santiago's atmosphere can be attributed to economic, geomorphological, and meteorological factors. The metropolitan region is home to 45% of the nation's population (5.3 of 12 million) and 70% of its industry (Romero *et al.*, 1999). During most of the year, Santiago is subject to nocturnal inversions and subsidence inversions associated with the South Pacific Subtropical Anti-cyclone. Intense thermal inversions occur during 10% of the days in the fall, decreasing in frequency slightly during June and July, when frontal activity is at a maximum. Thirty three percent of the days with intense thermal inversions occur in series of two or more consecutive days and 75% occur during days with low surface pressure (Ulriksen, 1993). Decreased convective mixing traps contaminants in the closed basin formed by the Andes, the Coastal Range, and the Chacabuco hills (Figure 1), leading to increases in contaminant concentrations (Sandoval, 1993). Critical air pollution episodes are associated with synoptic meteorological conditions that lead to the development of a 'coastal low' (Rutllant and Garreaud, 1994). During a coastal low, skies are clear and humidity is low. The descent of warm continental air and the penetration of sunlight lead to increased surface temperatures. The initial phase of the coastal low is associated with weak easterly winds. The coastal low breaks up as it propagates southward, eventually bringing cold humid maritime air into the Maipo River Valley (Ulriksen, 1993).

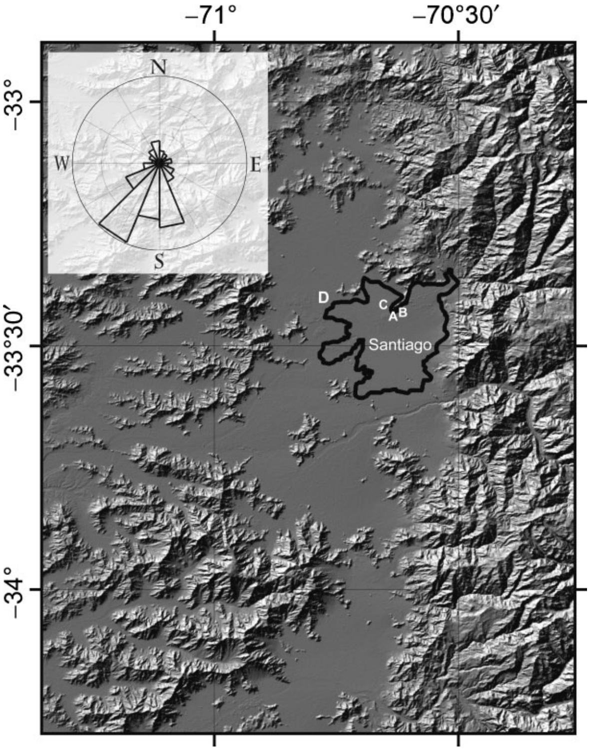

Figure 1. Santiago sits in the Maipo River Valley which is closed to the east by the Andes, to the west by the Coastal Range, and to the north by the Chacabuco Hills. The pronounced topography contributes to the stability of the lower troposphere by limiting horizontal advection. The digital elevation model shown here is based on 3-arcsecond data from the Shuttle Radar Topography Mission (USGS, 2006). A windrose for the study period shows that winds are predominantly south-southwesterly. The locations of the air pollution monitoring stations are indicated by the letters A, B and C. NO_2, SO_2 , $PM_{2.5}$ and PM_{10} were recorded at Station B. Ozone was recorded at Station C and CO was recorded at station A. Meterological data were collected at the Arturo Benitez Airport, indicated by the letter D.

2. Methods

2.1. Meteorological data

Weather data were obtained from the National Climatic Data Center's TD-9956 surface data set (NCDC, 1999). Weather data were recorded at Arturo Merino Benitez International Airport (33.38S, 70.78W), which is located 16 km to the west of the city centre (shown in Figure 1). Temperature, dew point, wind speed and wind direction were recorded hourly, while the percentage of the sky obscured by clouds (sky coverage) and the sea-level pressure were recorded every 3 h. Wind speed and wind direction were converted into northerly and easterly scalars. The percentage of observations missing from the data record for each variable is shown in Table I. To eliminate missing values from the weather record, a 31 day moving average was calculated for all variables. Anomalies from this moving average were calculated for all of the existing hourly observations. Linear interpolation was used to project anomalies during the periods for which no data were available. Finally, these projected hourly anomalies were added to the moving average values.

2.2. Pollution data

Pollution data were obtained from the Metropolitan Service of Environmental Health of Santiago, which maintains an automated air pollution monitoring network. During the study period, 1988–1996, hourly observations of carbon monoxide (CO), ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) were made at five monitoring stations. Four monitoring stations made cumulative daily measurements of total particulates (PM_{10}) and fine particulates ($PM_{2.5}$), allowing the calculation of coarse

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Table I. Percentage of missing hourly and daily observations that had to be estimated for each variable. Missing ozone and CO values were estimated when possible, based on observations from other monitoring stations. Missing values for all variables were estimated using a linear interpolation procedure described in Section 2.1.

	Missing data (%)		Missing data (%)
Ozone	10^b	Wind direction	8^b
CO	9^b	Wind speed	2^b
$PM_{2.5}$[a]	12^b, 11^c	Cloud cover	14^b
PM_{10}[a]	12^b, 11^c	Temperature	2^b
NO_2[a]	18^b, 1^c	Dew point	2^b
SO_2[a]	26^b, 6^c	Sea-level pressure	8^b

[a] Daily means for these variables were used in the analysis.
[b] Percentage of missing hourly observations.
[c] Percentage of missing daily observations. Daily means were computed for all days with at least 18 hourly observations.

fraction particulates ($PM_{10-2.5}$). For each pollutant, the record with the fewest missing values was chosen as the 'station of record' for the analysis. For ozone and carbon monoxide, when no observation was made at the 'station of record', a value was computed based on linear regression using the station with the data record most highly correlated with the 'station of record'. As in Greene *et al.* (1999) if no measurement was made at the second station, a value was computed based on the next most highly correlated station, until the correlation coefficient dropped below $r = 0.70$. This procedure was followed by the same linear interpolation routine applied to the weather data. The percentage of missing observations that had to be estimated for each variable is shown in Table I.

Station B was the station of record for NO_2, SO_2, $PM_{2.5}$ and PM_{10}. Station B is located in a forested park that parallels a high-volume road. Medium density housing and commercial properties surround the area. Station C/F was the station of record for O_3. Station C/F is located between two large roads with numerous small retail stores and light industries in the vicinity. The correlation coefficient for the station B-station C/F hourly ozone record was 0.71. Station A was the station of record for CO. Station A is located in the centre of the downtown area. The traffic volume is high and the monitoring station is surrounded by tall buildings. The correlation coefficent for station B and station A hourly CO records was 0.58. Stations B, C/F and A were all located in the downtown area within 3 km of each other. A cluster analysis using data from the expanded network (eight stations) in 2000, found that stations B and C/F fell in a sector of the city where ozone data behaved similarly (Gramsch *et al.*, 2006). Station A was not included in this study, but it belongs to the same geographic sector that includes stations B and C/F.

The period of study was restricted to one season because an analysis of the full year would result in WCs that were differentiated by time of year rather than by day-to-day variability in synoptic weather patterns. The austral winter months (June, July and August) were selected because observations of particulate matter were made on a daily basis. In the summer, PM observations were made less frequently and less regularly. Similar to other temperate regions, cardiovascular, respiratory and total mortality all peak during the winter months (Killbourne, 1992). Mean winter cardiovascular, respiratory and total mortality levels exceeded the mean levels during the rest of the year by 32%, 91% and 41%, respectively.

2.3. Mortality data

Mortality data were collected by the Chilean National Institute for Statistics from death certificates (Cifuentes and Lave, 2000). Total deaths by disease were broken down into respiratory, cardiovascular disease (CVD), and other categories based on ICD9 codes (International Classification of Disease, 9th Revision). Excess deaths per day were calculated by removing the mean of the nine winters included in the analysis (e.g. 69.3 total deaths by disease per day) from each day's mortality count.

2.4. Trends and seasonality

The separation of the health effects of pollution and weather is complicated by the fact that mortality rates and pollution levels (except for ozone) peak in the wintertime, which increases the risk of seasonal confounding. This risk is reduced, but not eliminated, by restricting the analysis to the winter (Kinney *et al.*, 1995). The Student's t-test was used to determine whether the slope of the trends (during the austral winter time period) for all pollution, weather and mortality variables was significantly different from zero. No trends were found to be significant ($p < 0.05$).

2.5. Data analysis

The TSI, which utilizes a semi-automated classification scheme based on principal components analysis (Kalkstein *et al.*, 1997), was used to assign each day to a meteorologically homogenous WC, and in a separate analysis, to a group with similar air pollution characteristics, a PC. WCs and PCs with significantly elevated mean mortality levels were identified. To determine what air mass characteristics differed between the high-mortality WCs or PCs and the other classes, the mean values of all weather and pollution variables were calculated. A forward stepwise regression of weather and pollution variables on mortality was applied to determine which combination of variables best predicted the number of deaths for each lag and mortality type.

2.5.1. Principal components and cluster analysis

A matrix was formed with four daily observations (5 and 11 am, and 5 and 11 pm) of the six weather variables (north wind, east wind, temperature, dew point, cloud coverage and sea-level pressure). Variables were normalized by subtracting the mean and dividing by the

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standard deviation. Eigenvectors and eigenvalues were calculated based on the correlation matrix of the 24 variables (six variables × four observations per day). A similar principal component analysis was carried out using 13 pollution variables: the four daily observations of O_3 and CO (5 and 11 am, and 5 and 11 pm), as well as the average daily value of $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, NO_2 and SO_2. Three of the 24 weather principal components, which contained 50.1% of the variance, were retained. Of the 13 pollution principal components, 6 which contained 75.3% of the variance, were retained.

A hierarchical cluster tree was formed by calculating the average Euclidian distance between observations (Average Linkage) or the inner squared distances (Ward's algorithm) (Mathworks Inc., 2002). The relative merits of these two techniques have been discussed at length elsewhere (Kalkstein *et al.*, 1987). Clusters were formed based on the linkage distances (Average Distance) or based on the length of links in the cluster tree relative to other links at the same level of the hierarchy (Inconsistency Coefficient). This produced four sets of weather and pollution classes. The Average Linkage, Average Distance set of 14 WCs and the Ward's Algorithm, Inconsistency Coefficient set of 18 PCs were selected on the basis of the number and size of classes, and the cophenetic correlation coefficient which measures how well the data fit the structure suggested by the classes (Mathworks Inc., 2002). The number of days in each weather and pollution class are shown in Table II. The frequency with which the days occurred in sequences having the same weather or pollution class is shown in Table III.

Table II. Frequency of occurrence of all weather and pollution classes during the austral winters from 1988 to 1996. Only those classes with 30 or more occurrences are retained in the analysis.

Weather class	Number of occurences[a]	Pollution class	Number of occurences[a]
1	249	1	7
2	43	2	16
3	53	3	22
4	100	4	38
5	54	5	12
6	103	6	94
7	70	7	8
8	32	8	14
9	44	9	16
10	17	10	28
11	3	11	20
12	53	12	94
13	6	13	76
14	1	14	135
–	–	15	59
–	–	16	173
–	–	17	15
–	–	18	1

[a] Out of 828 total days.

2.5.2. *Defining 'high-mortality' WCs and 'high-mortality' PCs*

In order to determine which weather and pollution classes potentially posed a risk to human health, a measure of the abundance of high-mortality days within each class was devised. High-mortality days were defined as those days with mortality counts above the 89th percentile of the long-term record. The probability of the occurrence of a high-mortality day in the record as a whole is known: 86 high-mortality days out of a total of 828 days, or roughly 10.4%. This figure was used to calculate an expected number of high-mortality days for a class of a given size. The probability that the number of high-mortality days actually observed in a class occurred by chance, p, was calculated based on the binomial distribution. Classes with $p \leq 0.025$ were designated high-mortality classes, and are shown in Table IV. For clarity, these WCs are labelled 'high-mortality' rather than 'offensive' since the latter designation pre-supposes that weather is causing the high mortality. High-mortality classes were determined with respect to same day mortality as well as mortality lagged one to 6 days after the weather (or pollution) event. Classes with an overabundance of low mortality days (below the 11th percentile) were also identified using an analogous procedure. To ensure adequate statistical power, only classes that occurred on 30 or more days were retained in the analysis. There were 10 WCs of the original 14, and 7 PCs of the original 18 that met these criteria.

In order to determine what characteristics might explain the elevated mortality levels in the high-mortality classes, mean values of the weather, pollution and mortality variables were calculated for each weather or pollution class. Mean weather or pollution values that fell below the 25th percentile or exceeded the 75th percentile were

Table III. Persistence of weather and pollution classes. The number of days that fell in sequences of consecutive days with the same pollution or weather class is shown below.

	Number of days that fall in same-class sequences of specified length										
Sequence length (days)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Total
Weather classification (days)	424	208	87	64	25	6	14	0	0	0	828
Pollution classification (days)	447	182	96	40	30	6	0	8	9	10	828
Weather classification (%)	51	25	11	8	3	1	2	0	0	0	100
Pollution classification (%)	54	22	12	5	4	1	0	1	1	1	100

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Table IV. High-mortality weather classes (WC) and pollution classes (PC) are shown below for total, respiratory and cardiovascular mortality. The frequency column gives the number of high-mortality days that fell into each, as a fraction of the total number of days in each class. The p value gives the probability that the number of high mortality within each class occurred by chance. Classes with $p < 0.025$ were defined as 'high-mortality' classes.

Mortality type	Time lag (days)	High-Mortality weather classes			High-mortality pollution classes		
–	–	Class	[a]Frequency	p value	Class	[a]Frequency	p value
1. Total	0	WC 4	18/100	0.01	n/a	–	–
–	1	WC 8	9/32	<0.01	n/a	–	–
–	2	n/a	–	–	n/a	–	–
–	3	WC 8	10/32	<0.01	PC 13	17/76	<0.01
–	4	n/a	–	–	PC 13	14/76	0.02
–	5	n/a	–	–	PC 13	15/76	0.01
–	6	n/a	–	–	PC13, PC16	17/76, 27/173	<0.01, 0.02
2. Respiratory	0	WC 4	19/100	0.01	n/a	–	–
–	1	WC 4	18/100	0.01	n/a	–	–
–	2	n/a	–	–	n/a	–	–
–	3	WC 8	8/32	0.01	PC 13	15/76	0.01
–	4	WC 7	15/70	<0.01	PC 13	14/76	0.02
–	5	WC 4	19/100	0.01	PC 13	15/76	0.01
–	6	WC 4	19/100	0.01	PC 13	14/76	0.02
3. Cardiovascular	0	WC 8	8/32	0.01	n/a	–	–
–	1	WC 8, WC 3	9/32, 11/53	<0.01, 0.02	PC 15	12/59	0.02
–	2	WC 3	13/53	<0.01	n/a	–	–
–	3–6	n/a	–	–	n/a	–	

considered noteworthy and are shown in shaded cells in Table V. By highlighting those variables that fall in the outer quartiles of the distribution, we provide a standard criterion for discussing the characteristics of the high-mortality weather and pollution classes.

2.5.3. *Multiple regression*

Forward stepwise multiple regression was used to determine the relative importance of weather and pollution variables in explaining the variation in excess deaths. Multiple regression was applied to the entire study period. Models are reported as significant only when all of the partial regression coefficients in the model were significantly different from zero with a level of certainty corresponding to a 95% simultaneous confidence interval (Mathworks Inc., 2002). The regressions were run for 0–6 days of lag time between the weather/pollution conditions and the mortality counts. The pool of independent variables that could be added to the regression model included the average daily values for the north wind (m/s), east wind (m/s), cloud coverage (%), temperature (°F), dew point (°F), sea-level pressure (mbar), CO (ppm), O_3 (ppb), SO_2 (ppb), NO_2 (ppb), $PM_{2.5}$(μg/m^3), $PM_{10-2.5}$(μg/m^3), PM_{10}(μg/m^3), 'time' and 'day'. Following Smoyer *et al*. (2000), the 'time' variable counts the number of days since the beginning of the winter, and the 'day' variable counts the number of consecutive days with the same WC. Results are shown in Table VI.

2.5.4. *Analysis of the combined effects of weather and air pollution*

Partitioning the independent effects of air pollution and stressful weather conditions is a statistically challenging problem. Much of the day-to-day variability in pollution levels is driven by weather conditions. A contingency table analysis attempts to avoid the problem of co-variability by grouping together days that have been assigned to high-mortality weather **or** high-mortality pollution classes. Estimates of the independent effects of stressful weather or stressful pollution conditions are derived in order to gain insight into the nature of the combined effects of stressful weather and pollution. All of the days in the study period fell into one of four categories:

Group A: days in both a high-mortality WC **and** a high-mortality PC,
Group B: days in a high-mortality WC and **not** in a high-mortality PC,
Group C: days in a high-mortality PC and **not** in a high-mortality WC, or
Group D: days in **neither** a high-mortality WC, **nor** a high-mortality PC.

The chi-square value was calculated to test for the independence in the occurrence of high-mortality weather and pollution classes. Mean total, cardiovascular and respiratory mortality levels were calculated for Groups A,

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Table V. Comparison of the differences between high- and low-mortality weather and pollution classes. Mean weather and pollution anomalies are given for all weather and pollution classes that were defined as high or low mortality at any time lag from zero to six days. Mean values that fell above the 75th percentile are shown in dark shaded cells. Mean values that fell below the 25th percentile are shown in light shaded cells. Note that the principal differences between the high- and low-mortality weather classes are weather variables, while the principal differences between the high- and low-mortality pollution classes are the pollution concentrations.

	Weather class	Temperature (°C)				Dew point temperature (°C)				Sea level pressure (mbar)				NO_2 (ppb)	SO_2 (ppb)	$PM_{2.5}$ (μg/m^3)	$PM_{10-2.5}$ (μg/m^3)	PM_{10} (μg/m^3)
		11 pm	5 am	11 am	5 pm	11 pm	5 am	11 am	5 pm	11 pm	5 am	11 am	5 pm					
High CVD* Mortality	WC 8	−9	−11	−8	−1	−9	−10	−8	−9	5	5	3	1	10	11	16	4	19
	WC 3	−4	−5	−5	−3	−4	−5	−4	−7	6	6	6	5	−6	1	−8	−2	−9
Low CVD Mortality	WC 5	7	10	4	−1	8	10	7	7	−3	−4	−3	−2	−10	−7	−15	−4	−19
	WC 12	6	2	8	10	5	3	6	6	−1	−2	−3	−4	7	0	−3	2	−1
High Respiratory Mortality	WC 8	−5	−6	−4	0	−5	−6	−5	−5	5	5	3	1	10	11	16	4	19
	WC 4	−2	−4	0	2	−3	−4	−3	−2	1	1	0	−1	18	8	17	9	25
	WC 7	−1	−2	1	2	−1	−2	−1	1	−4	−3	−4	−4	20	9	3	7	11
Low Respiratory Mortality	WC 12	3	1	5	6	3	1	3	3	−1	−2	−3	−4	7	0	−3	2	−1
	WC 2	0	−2	3	6	−1	−2	0	0	0	0	−3	−4	13	6	1	6	7
	WC 5	4	5	2	−1	4	6	4	4	−3	−4	−3	−2	−10	−7	−15	−4	−19
	Pollution class	Temperature (°C)				Dew Point Temperature (°C)				Sea Level Pressure (mbar)				NO_2 (ppb)	SO_2 (ppb)	$PM_{2.5}$ (μg/m^3)	$PM_{10-2.5}$ (μg/m^3)	PM_{10} (μg/m^3)
		11 pm	5 am	11 am	5 pm	11 pm	5 am	11 am	5 pm	11 pm	5 am	11 am	5 pm					
High CVD	PC 15	−1	−1	0	2	0	−1	0	1	1	0	−1	−1	19	2	46	24	69
Low CVD Mortality	PC 12	0	1	−1	−2	1	2	1	0	0	0	1	2	−17	−6	−6	−5	−11
	PC 14	0	0	0	0	0	0	1	1	0	0	0	0	−10	−6	−27	−12	−39
	PC 16	2	2	0	−2	1	2	1	0	−1	−1	0	1	−22	−11	−42	−16	−58
High Resp. Mort.†	PC 13	−1	−2	1	3	−2	−2	−2	−1	1	0	−1	−1	45	18	20	26	45

CVD = cardiovascular disease.
Resp. Mort.† = Respiratory Mortality.

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B, C and D at all time lags for which high-mortality classes were defined for both weather and pollution. Results are shown in Table VII.

3. Results

3.1. High-risk synoptic weather patterns

The first objective of this study was to identify the synoptic weather conditions that promote increased human mortality and/or high concentrations of air pollution. In general, cold, dry, high-pressure conditions brought on by a strong Pacific Anti-cyclone (WC3 and WC8) were associated with high-mortality levels 0–3 days after the weather event occurred. Similar dry, cold, polluted conditions have been linked to elevated hospital admissions for asthma in New York City (Jamason *et al.*, 1997) and respiratory ailments in Birmingham, England (McGregor *et al.*, 1999). McGregor (1999) suggested that under these conditions, cold, dry air can dehydrate the respiratory tract, sensitizing it to injury by air pollutants. Increased mortality and pollution concentrations were associated with a synoptic weather pattern identified as the 'coastal low' by Garreaud *et al.* (2002) (Figure 2), with increasing temperature and cloudiness throughout the day (WC4, PC13, PC15).

3.2. Persistence of weather and pollution classes

The persistence of weather and pollution classes was quantified as the number of times that the same weather or pollution class occurred in sequence (Table III). More days in the weather classification fell in sequences between 2 and 4 days than in the pollution classification. For longer sequences, there were three sequences in the pollution classification that lasted 7 days or more, *versus* only two for the weather classification. More importantly, one of the extended pollution sequences was a series of 10 days belonging to PC13, a 'high-mortality' PC, while neither of the extended weather sequences belonged to a 'high-mortality' WC. There was a sizable mortality peak that began during this 10-day sequence and was most sustained for respiratory mortality. The near-coincidence of these peaks contributed to some of the differences observed between the cardiovascular and respiratory mortality response.

3.3. Differences in the cardiovascular and respiratory mortality response

All mortality types (total, respiratory, cardiovascular) demonstrated some sensitivity to both stressful weather conditions and stressful pollution levels. High-mortality weather and pollution classes were defined for all mortality types (Table IV). However, there were pronounced differences between cardiovascular mortality and respiratory mortality with respect to the type of environmental stressor (weather or pollution), the stressor variable (temperature or dew point, NO_2 or particulates), and the timing of the stressful conditions that provoked the greatest mortality response.

Cardiovascular mortality was more sensitive to weather conditions than to pollution levels. WC3 and WC8 were defined as high cardiovascular mortality classes over a 3-day period, while the sole high cardiovascular mortality pollution class (PC15) was defined as high-mortality only at a single time lag (one-day lag, see Table IV). None of the mean pollution values of WC3 fell in the outer quartile range (Table V). The dominance of the weather effect on cardiovascular mortality was reinforced by the results of the multivariate regression: temperature was significantly associated with cardiovascular mortality at all time lags, while there was only one instance in which a pollution variable was included in the regression model ($PM_{10-2.5}$, with a 2-day lag, see Table VI).

Respiratory mortality appears to be more sensitive to pollution levels than cardiovascular mortality. WC8 was associated with both high cardiovascular mortality and high respiratory mortality and therefore does not shed light on differences between the two mortality types. However, WC4 and WC7, which are high mortality only with respect to respiratory disease, have mean pollution levels in the highest quartile of the daily pollution level distribution (see the bold values in the dark cells in Table V). In contrast, the high cardiovascular mortality WC, WC3, does not have any mean pollution levels in the highest quartile. Further evidence of respiratory mortality's pollution sensitivity is the long-lasting effect of the high respiratory mortality PC, PC13. While the high cardiovascular mortality PC (PC15) was defined for only one day (lag 1), PC13 was associated with high respiratory mortality beginning on the third day after the pollution event and persisting at least as long as 6 days afterward. Finally, NO_2 was positively associated with respiratory mortality in five of the seven multivariate models, compared to only one cardiovascular model that included a pollutant variable ($PM_{10-2.5}$).

Among the weather variables considered, cardiovascular mortality was most sensitive to temperature while respiratory mortality was most sensitive to dew point temperature (humidity). Respiratory mortality was associated with dew point at all of the lags considered (0–6 days) and with temperature at none, while cardiovascular mortality was associated with temperature at all lags and with dew point at none (Table VI). The definition of high-mortality WCs provides further evidence of the different sensitivities. WC8 was the coldest and driest of the 10 classes. WC8 was defined as high-risk with respect to both cardiovascular mortality and respiratory mortality. WC3 was the second coldest WC, and was defined as high-risk with respect to cardiovascular mortality. WC4 was the second driest WC and was defined as high-risk with respect to respiratory mortality (Tables IV and V).

Among the pollution variables considered, cardiovascular mortality was most sensitive to $PM_{10-2.5}$, while respiratory mortality was most sensitive to NO_2. Of all of the PCs, PC13 and PC15 were the most polluted. PC13 was associated with high respiratory mortality at lags three to six (Table IV) and PC15 was associated with high cardiovascular mortality with a one-day lag

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Table VI. Results of stepwise regression of weather and pollution variables on total, respiratory and cardiovascular mortality for the winters of 1988–1996. Only those regressions with an the overall F statistic significant at the $\alpha < 0.05$ level are shown. Variables are listed from largest to smallest absolute partial correlation coefficient.

Mortalitytype	Time Lag (days)	Explanatory variable					Model r^2
Total	0	−Dwpt	−Time	$+NO_2$	$-O_3$	$-SO_2$	0.15
–	1	−Dwpt	−Time	$+NO_2$	$-O_3$	$-SO_2$	0.19
–	2	−Dwpt	−Time	$+NO_2$	−Temp	$-SO_2$	0.25
–	3	−Time	$+NO_2$	−CO	−Temp	$-SO_2$	0.25
–	4	−Time	−Temp	$+NO_2$	−CO	$-PM_{2.5}$	0.26
–	5	−Time	$+NO_2$	−Dwpt	−CO	−Temp	0.29
–	6	−Time	−Dwpt	$+NO_2$	$-SO_2$	$-O_3$	0.26
Respiratory	0	−Dwpt	−Time	+Sky	−CO	–	0.11
–	1	−Dwpt	−Time	$+NO_2$	−CO	+Sky	0.15
–	2	−Dwpt	−Time	+Sky	$+NO_2$	−CO	0.16
–	3	−Dwpt	−Time	−CO	$+NO_2$	+Sky	0.18
–	4	−Dwpt	−Time	$-O_3$	–	–	0.19
–	5	−Time	−Dwpt	−CO	$+NO_2$	$-SO_2$	0.21
–	6	−Time	−Dwpt	−CO	$+NO_2$	–	0.20
Cardiovascular	0	−Temp	–	–	–	–	0.06
–	1	−Temp	−Time	–	–	–	0.08
–	2	−Temp	$+PM_{10-2.5}$	−Time	–	–	0.11
–	3	−Temp	−Time	–	–	–	0.08
–	4	−Temp	−Time	–	–	–	0.09
–	5	−Temp	−Time	+Sky	–	–	0.10
–	6	−Time	−Temp	+Sky	–	–	0.08

Sky is the percentage of the sky obscured by cloud cover.
Dwpt is dew point temperature, a measure of humidity.
SLP is sea level pressure.
Time is number of days since the beginning of the winter.

(Table IV). PC13 has the highest mean NO_2 levels (45 ppb *vs* 19 ppb for PC15), while PC15 has the highest $PM_{2.5}$ concentrations (46 ug/m^3 *vs* 20 ug/m^3 for PC13, see Table V). In the multivariate regressions, the only pollutant that respiratory mortality was positively associated with was NO_2, the only pollutant cardiovascular mortality was associated with was $PM_{10-2.5}$ (Table VI).

The final difference between cardiovascular and respiratory mortality involves the temporal structure of the mortality response to the environmental stressor/s. The cardiovascular mortality response was greatest at short lag times (0–2 days), while the respiratory mortality response was greatest at longer time lags (3–6 days). For example, high cardiovascular mortality WCs were only defined at short time lags (0–2 days), while high respiratory mortality lags were defined at short and long time lags (0–1, and 3–6 days). Similarly, high cardiovascular mortality PCs were only defined with a one-day lag, while high respiratory mortality PCs were defined at lags of 3–6 days (Table IV). WC8 was associated with both high cardiovascular mortality at zero and one-day lags and with high respiratory mortality at a 3-day lag. Figure 3 shows a general decreasing trend in excess cardiovascular deaths in the days subsequent to a stressful weather or pollution event, while excess respiratory deaths gradually increase over the same period. Using a distributed lag model, Goodman *et al*. (2004) found that temperature and black smoke effects were more prolonged for respiratory mortality than cardiovascular mortality in Dublin. Similarly, Zanobetti *et al*. (2003) found elevated cardiovascular mortality declined more rapidly than respiratory mortality after exposure to PM_{10}. These findings underscore the importance of examining a full range of lag times when attempting to quantify the relative importance of weather *versus* pollution.

3.4. Mortality response among different age groups

Total deaths by disease were stratified into three broad age categories: infants, adults and the elderly. The timing and magnitude of the age-specific total mortality response to WC3, PC13 and WC8 are shown in Figure 4. A prolonged mortality response is only observed in the elderly population. Deaths among the elderly represent 70% of the mortality among all age groups. Adult mortality only responded to cold, dry, high-pressure conditions (WC8), with significant excess deaths occurring on the day immediately following the stressful weather event. Infant mortality was an infrequent occurrence (on average 3.3 deaths per day during the winter). The infant mortality response to stressful weather or pollution conditions was statistically indistinguishable from zero.

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Table VII. Results of contingency table analysis of combined effects of stressful weather and air pollution. All days fell into one of four categories: days in both high-mortality weather and pollution classes (group A, upper left cell), days only in high-mortality weather classes (group B, upper right cell) or in high-mortality pollution classes (group C, lower left cell), and days in neither a high-mortality weather nor high-mortality pollution class (group D, lower right cell). Mean excess mortality was calculated for the four subgroups in the six instances in which there were co-occurring high-mortality weather and pollution classes. Mean mortality is shown in the lower right-hand corner of each cell; the number of days that fell in that category (the n of the population for which the mean was calculated) is shown in the upper left hand corner of each cell.

1. Total Mortality, 3 day lag

	PC13	Other PC's
WC8	4 16.0	28 6.5
Other WC's	72 3.6	724 -1.0

$p\chi = 0.51$, $p_{A-(B+C)} = 0.12$

2. CVD Mortality, 1 day lag

	PC15	Other PC's
WC3, WC8	5 4.8	80 2.6
Other WC's	54 1.7	689 -0.4

$p\chi = 0.64$, $p_{A-(B+C)} = 0.83$

3. Resp. Mortality, 3 day lag

	PC13	Other PC's
WC8	4 6.0	28 1.7
Other WC's	72 1.5	724 -0.4

$p\chi = 0.51$, $p_{A-(B+C)} = 0.36$

4. Resp. Mortality, 4 day lag

	PC13	Other PC's
WC7	16 3.2	54 1.5
Other WC's	60 1.7	698 -0.5

$p\chi < 0.001$, $p_{A-(B+C)} = 0.99$

5. Resp. Mortality, 5 day lag

	PC13	Other PC's
WC4	18 3.3	82 1.5
Other WC's	58 0.4	670 -0.5

$p\chi = 0.001$, $p_{A-(B+C)} = 0.54$

6. Resp. Mortality, 6 day lag

	PC13	Other PC's
WC4	18 2.2	82 1.5
Other WC's	58 1.4	670 -0.6

$p\chi = 0.001$, $p_{A-(B+C)} = 0.61$

$p\chi$ = p-value for the chi-square test of independence of occurrence of high-mortality weather and pollution classes.
$p_{A-(B+C)}$ = p-value for the difference between the mean mortality of group A and the sum of groups B and C.
CVD = Cardiovascular disease, *Resp.* = Respiratory Disease.

3.5. Combined effects of weather and air pollution

There were six instances when both high-mortality weather and high-mortality pollution classes were defined for the same mortality type, at the same time lag (Table VII). Based on the chi-squared values, the occurrence of high-mortality weather and pollution classes was found to be independent in the first three instances and not independent in the last three, perhaps because the high-mortality classes in question, WC4, WC7 and PC13, all had high NO_2 concentrations. In every case, the days belonging to both high-mortality and high-pollution classes (group A) had higher mean mortality levels than the days belonging to either a high-mortality WC (group B) or a high-mortality PC (group C). However, the group A days were few in number, and in no instance was the difference between A and B or A and C significant (Student's t-test, $\alpha = 0.05$). In four of the six instances the mortality levels for group A also exceeded the sum of the mean mortality for groups B and C suggesting that the combined effect of weather and pollution on mortality could be synergistic. However, these differences were not large enough to be considered statistically significant (Student's t-test, $\alpha = 0.05$).

4. Discussion

Prior applications of the TSI based only on WCs (Kalkstein, 1991, 1993; Smoyer *et al.*, 2000) have concluded that mortality levels are more sensitive to weather conditions than to air pollution concentrations. This is not a surprising result. The aim of the cluster analysis is to maximize the variance between classes. If a classification is carried out based on weather data, then subsequent analysis of air pollution concentrations will show that one of the classes has the highest mean pollution levels. However, because weather data were used to classify the days rather than pollution, the maximum pollution levels will likely deviate from mean pollution levels to a lesser degree than the most extreme WC conditions deviate from the climatological mean. Since the 'extreme' weather presents a greater perturbation from mean conditions, it is probable that mortality rates will be higher for this class than for the class with 'extreme' pollution levels.

This was the case in the present study. The principal differences between the high- and low-mortality WCs were the temperature, dew point, and pressure levels, while the principal differences between the high- and low-mortality PCs were the NO_2 and particulate matter concentrations (Table V). Therefore, if the question of what environmental factors contribute most to elevated mortality levels is addressed by forming WCs, the answer is temperature, dew point and pressure. If the question is addressed by forming PCs the answer is particulate matter or NO_2; the conclusions are dependent on what information was used to perform the classification, weather or

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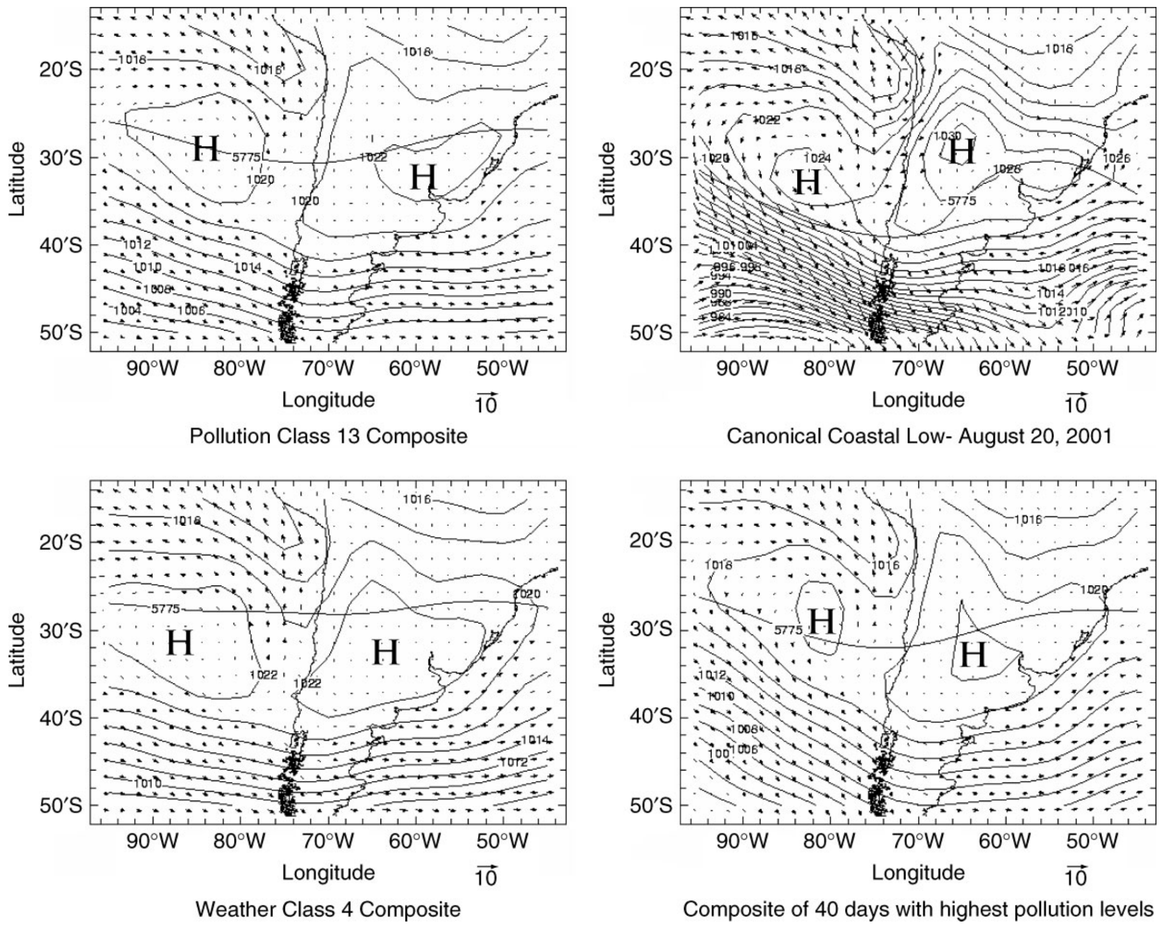

Figure 2. Four different variations of the 'coastal low' pressure system associated with elevated air pollution levels in Santiago, Chile. Mean sea-level pressure is shown with 200 Pa contours. Surface winds are shown as arrow vectors with a reference wind vector (m/s) shown at the bottom right of each panel. The line crossing the isobars is the 5775 m geopotential height at 500 hPa. Composite images show less small-scale variability than the one-day canonical coastal low shown in the upper right (Garreaud and Rutllant, 2002), however, the large-scale patterns are similar. The gridded fields shown above are derived from the NCEP-NCAR reanalysis dataset (Kalnay *et al*., 1996).

pollution data. Thus, the dual classification scheme used in this study puts more of an equal emphasis on weather and pollution than past applications of the TSI to the analysis of weather, air pollution, and mortality, and may help to reconcile the differences between the results of TSI studies and the results of air pollution epidemiology studies.

The formation of synoptic PCs is an important difference between the present study and prior TSI studies (Kalkstein, 1991; Kalkstein *et al*., 1997; Smoyer *et al*., 2000), however, there are other methodological differences that may help to explain why an association between pollution and mortality was found in Santiago, but has been largely absent elsewhere. The most salient of these differences is the fact that earlier studies were restricted to the summer season while this study focuses on the austral winter. Therefore any direct comparison of the results needs to be viewed with caution since the interrelationships between weather, pollution and mortality may be strongly dependent on the season being analysed (Nawrot *et al*., 2007). Other differences include the greater number of air pollutants that were available for Santiago (NO_2, SO_4, CO, O_3, $PM_{2.5}$, PM_{10}) than for earlier studies (only O_3 and TSP were used in Smoyer *et al*., 2000 and Kalkstein *et al*., 1997). The present study considered the effects of air pollution and weather conditions on respiratory, cardiovascular, and total mortality, while earlier studies considered only total mortality. Finally, a longer range of lag times was examined in this study (0–6 days) than in earlier studies (0–3 days in Smoyer *et al*., 2000 and Kalkstein, 1991). All of these factors may have contributed to the present studies' finding that high-mortality PCs had elevated pollution levels and that total and respiratory mortality were significantly associated with NO_2 at multiple time lags.

5. Conclusions

This aim of this study was to identify those weather patterns associated with elevated mortality and pollution, and to evaluate the relative importance of weather conditions and pollution concentrations in explaining periods of elevated mortality in Santiago, Chile. Two of the WCs identified as high mortality had high pollution levels: a cold high-pressure system (WC8), and a coastal low-pressure trough (WC4) which inhibits vertical mixing over Santiago. In multivariate regression models, NO_2

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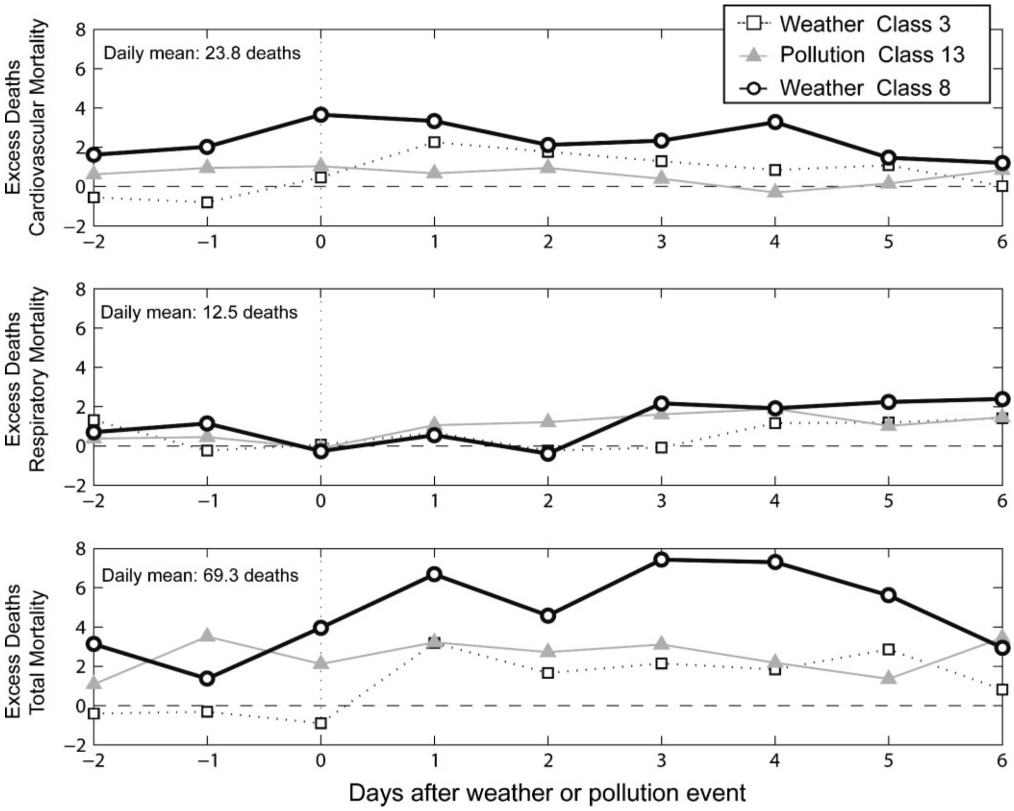

Figure 3. Timing and magnitude of the cardiovascular, respiratory, or total mortality response to WC3, WC8 and PC13. The mean magnitude of the mortality response is shown on the y-axis, as measured by the excess number of deaths. The timing of the mortality response is shown on the x-axis in terms of the number of days before or after the high-risk weather or pollution event. The daily mean is the average number of deaths that occurred for each mortality type during the winters of 1988–1996. Excess deaths are the departure from this average.

was found to have a significant positive association with total and respiratory mortality, though the relationship was weaker than that of temperature or dew point with mortality. Cardiovascular mortality was most sensitive to temperature and particulates at short time lags, while respiratory mortality was most sensitive to dew point and NO_2 at longer time lags. In Santiago, estimates of the combined effects of stressful weather and pollution conditions suggest that a synergistic mechanism may be at work for total mortality and respiratory mortality at some of the time lags considered. The attribution of increased mortality risk was largely dependent on the type of class formed, e.g. high-mortality WCs had cold, dry, high-pressure conditions, while high-mortality PCs had elevated NO_2, SO_2, or $PM_{10-2.5}$ concentrations. In general, forming classes with reference to pollution conditions will result in an estimate of greater health risks associated with air pollution than if classes are formed solely on the basis of weather conditions. By better understanding the timing and magnitude of the mortality response to stressful weather and pollution events we can improve our ability to provide useful forecasts of stressful weather and pollution conditions to susceptible populations, allowing hospitals to better manage their resources, and permitting emergency planners to better anticipate the population's demand for services. This type of historical ecological study can also be used to help predict mortality responses to future climate conditions.

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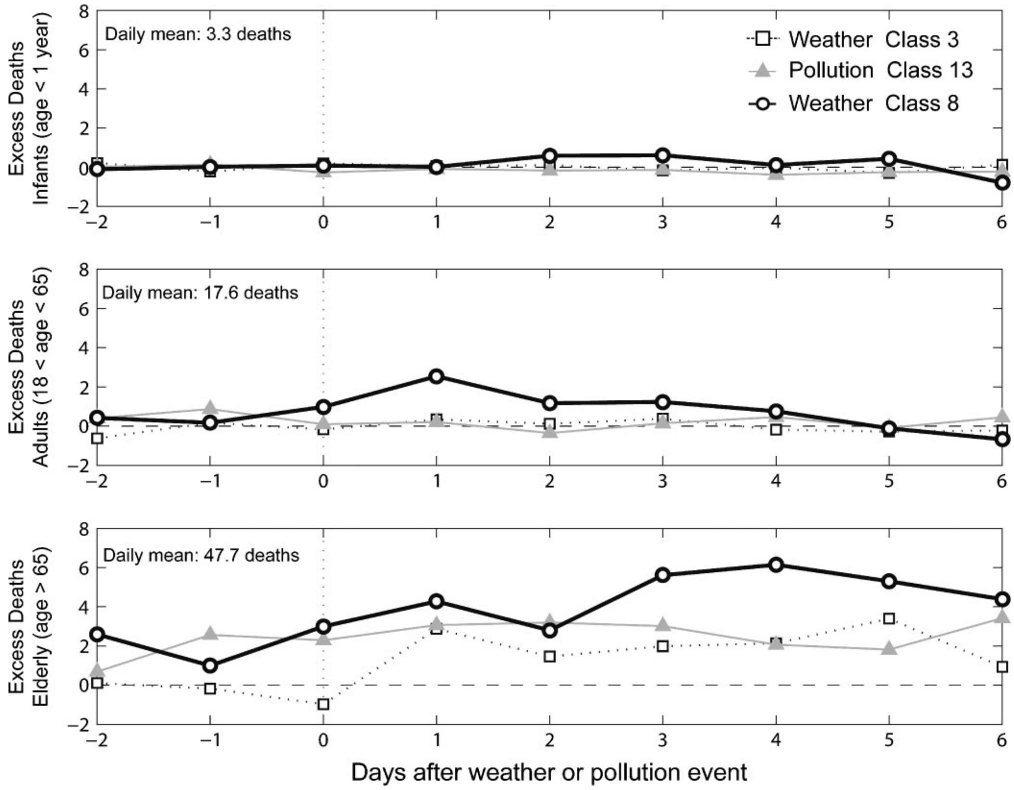

Figure 4. Timing and magnitude of the age-specific total (deaths by disease) mortality response to WC3, WC8 and PC13. Figure description is the same as that given in the Figure 3 legend.

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