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Air Pollution and Deaths among Elderly Residents of São Paulo, Brazil: An Analysis of Mortality Displacement

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Running title: Mortality displacement and air pollution in Brazil.

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Abstract

Background: Evaluation of short-term mortality displacement is essential to accurately estimate the impact of short-term air pollution exposure on public health.

Objectives: To quantify mortality displacement by estimating single-day lag effects and cumulative effects of air pollutants on mortality using distributed lag models.

Methods: We performed a daily time series of non-accidental and cause-specific mortality among elderly residents of São Paulo, Brazil, between 2000 and 2011. Effects of particulate matter smaller than 10 μm (PM10), nitrogen dioxide (NO_2) and carbon monoxide (CO) were estimated in Poisson generalized additive models. Single-day lag effects of air pollutant exposure were estimated for lags 0, 1 and 2 day lags. Distributed lag models with lags of 0-10, 0-20 and 0-30 days were used to assess mortality displacement and potential cumulative exposure effects.

Results: PM10, NO_2 and CO were significantly associated with non-accidental and cause-specific deaths in both single-day lag and cumulative lag models. Cumulative effect estimates for 0-10 days were larger than estimates for single-day lags. Cumulative effect estimates for 0-30 days were essentially zero for non-accidental and circulatory deaths, while remaining elevated for respiratory and cancer deaths.

Conclusions: We found evidence of mortality displacement within 30 days for non-accidental and circulatory deaths in elderly residents of São Paulo. We did not find evidence of mortality displacement within 30 days for respiratory or cancer deaths.

Introduction

Air pollution short-term exposure has been associated with a variety of adverse health effects, such as overall, circulatory and respiratory mortality (Anderson et al. 2007; WHO 2006, 2013).

It has been suggested that short-term exposure to air pollution only affects a frail subpopulation having elevated risk of dying due to its poor health condition. Consequently, an air pollution episode could deplete this frail group and advance deaths among some by a limited number of days or weeks, followed by a period with a mortality rate lower than expected. This phenomenon is known as "mortality displacement" or "harvesting effect" (Schwartz 2000a; Zeger et al. 1999). It is important to identify the mortality displacement for public health reasons. If air pollution-related deaths are displaced only by a few days, the public health impact measured in loss of life expectancy would be less than when deaths are brought forward by a much greater period of time (Schwartz 2000a).

As the air pollution effects on mortality could occur in the same day of exposure or in later days, the so-called lag structures need to be investigated to quantify these effects. However, if multiple lags are used in one model, common regression models will be susceptible to collinearity problems, due to the high correlation among exposures on consecutive days. The solution for this problem was the development of distributed lag model (DLM) using smooth functions, such as polynomials, to describe the relationship between lagged exposure of multiple days (Gasparrini et al. 2010; Zanobetti et al. 2000). Recently, the investigation of lag structures with DLM has been improved by several authors for different study types (Armstrong 2006; Gasparrini et al. 2010; Gasparrini 2014; Roberts and Martin 2007; Samoli et al. 2013; Schwartz 2000b). In some time series studies, the DLM has been applied to quantify a cumulative effect

over multiple lagged days (Braga et al. 2001; Filleul et al. 2004; O'Neill et al. 2008; Romieu et al. 2012; Samoli et al. 2009, 2013; Schwartz 2000b) and/or to evaluate the mortality displacement attributable to air pollution (Goodman et al. 2004; Zanobetti et al. 2000, 2002, 2003; Zanobetti and Schwartz 2008).

In most cases, studies that used DLM with lag structures up to 60 days have not found mortality displacement within this time period, which suggests that effects of air pollution on mortality are not simply due to deaths being advanced by a few days or weeks. In these studies, effects based on single-day lags underestimate cumulative effects (Goodman et al. 2004; Zanobetti et al. 2002, 2003; Zanobetti and Schwartz 2008). A European multicity study (Zanobetti et al. 2002, 2003) estimated effects of a 10 $\mu g/m^3$ increase in particulate matter < 10 μm (PM10) and reported that non-accidental, cardiovascular, and respiratory deaths were increased 1.61% [95% confidence interval (95% CI): 1.02, 2.20], 1.97% (95% CI: 1.38, 2.55) and 4.20% (95% CI: 1.08, 7.42), respectively, for cumulative effects up to 40 days. In contrast, corresponding estimates for average exposures on the same day and previous day were only 0.70% (95% CI: 0.43, 0.97), 0.69% (95% CI: 0.31, 1.08) and 0.74% (95% CI: -0.17, 1.66), respectively.

Mortality displacement in US and European populations may differ from displacement in Latin America due to differences in population, health care, and other characteristics. However, to our knowledge, no studies of mortality displacement have been reported based on data from Latin America. In addition, we are not aware of studies that have analyzed mortality displacement in relation to daily time series of nitrogen dioxide (NO_2) and carbon monoxide (CO) exposures.

São Paulo is the largest and most developed city in Brazil, and one of the most polluted cities as well (IEMA 2014). Recently, the Multicity Study of Air Pollution and Mortality in Latin America – ESCALA (Estudio de Salud y Contaminación del Aire en Latinoamérica) (Romieu et al. 2012), reported significant associations between mortality in São Paulo and single-day lagged exposures and short cumulative-lag exposures (up to 3 days) to PM10, encouraging further investigation of these data.

The aim of the present study was to investigate evidence for mortality displacement in the association between air pollution and daily mortality among the elderly residents of São Paulo, Brazil.

Material and Methods

We conducted a daily time series study of the relationship between non-accidental deaths and PM10, NO_2 and CO exposure. The analysis included deaths that occurred among elderly residents (≥ 60 years) of São Paulo, Brazil, between 2000 and 2011.

Numbers of daily deaths (in men and women combined) were obtained from the records kept in the Mortality Information System of the Brazilian Public Health System (DATASUS 2014) and reviewed by the Improvement Program for Mortality Information of the Health Secretariat of São Paulo City (SMSSP 2014). Outcomes were classified according to the International Classification of Diseases 10th edition as all non-accidental causes (all groups except S00 to T98 and V01 to Y98), circulatory diseases (group I), cerebrovascular diseases (codes I60 to I69), respiratory diseases (group J), chronic lower respiratory diseases (codes J40 to J47) and cancer (groups C and D, until code D48).

Air pollutant data were obtained from records provided by the Environmental Company of the State of São Paulo (CETESB 2014). PM10 was measured using beta radiation (10 possible monitors), NO_2 was measured using chemiluminescence (7 possible monitors) and CO with nondispersive infrared (9 possible monitors). Measurements were considered valid if at least 16 hourly measurements were collected in each day for each site. Only sites with at least 16 hourly measurements on each day, and with < 25% of missing data for the whole period, were used in the analysis. In addition, measurements at each site had to be highly correlated with those at other sites (Spearman correlation ≥ 0.80) (Supplemental Material, Table S1) for a site to be included, leaving 3 sites for PM10 and CO (24-hour average and maximum eight-hour moving average, respectively) and 2 sites for NO_2 (24-hour average) (Supplemental Material, Table S2). Missing data for each site were imputed based on linear regressions using data for the same pollutant measured at other sites at the same time. Remaining missing air pollutant data were estimated by an application of cubic smoothed spline with 4 degrees of freedom (df) per year, using the *mtsdi* package (Multivariate Time Series Data Imputation) (Junger and Ponce de Leon 2012) from R software (R Core Team 2014) (Supplemental Material, Table S2).

After imputation, daily city levels were calculated for each pollutant, by averaging all available data across the selected monitoring sites. Daily averages for temperature and relative humidity were obtained from the measurements performed by the Brazilian Institute of Meteorology (1 site) (INMET 2014) and by the Airspace Control Institute of the Brazilian Defense Ministry (2 sites) (ICEA 2014).

The Poisson generalized additive model was fitted to estimate single-day lag effects of air pollutant exposures on lag 0, lag 1 and lag 2 days. Also, the Poisson generalized additive DLM

was fitted for lags up to 30 days for non-accidental and specific-causes of death and up to 40 days for non-accidental deaths (the latter to compare with previous studies of total mortality).

For the DLM analysis, we used a matrix of second degree polynomials to estimate separate effects for cumulative lags of 0-10, 0-20, 0-30, and 0-40 days. A polynomial structure was used to fit a smooth shape for these effects because it has been shown to reduce noise and bias compared with an unconstrained DLM (Schwartz 2000b; Zanobetti et al. 2002).

All Poisson regression analyses were conducted in the R software using *mgcv* (Mixed GAM Computation Vehicle with GCV/AIC/REML smoothness) (Wood 2011) and *dlnm* (Distributed Lag Non-linear Models) (Gasparrini 2011) packages.

Models were adjusted using a thin plate regression spline for temporal trend and seasonality (4 to 7 df per year), mean daily temperature at single-day lags of 3 or 5 days (2 or 3 df) and mean daily relative humidity at single-day lag 3 (2 or 3 df), following the ESCALA project methodology (Romieu et al. 2012). The choice of the most appropriate lags for temperature and relative humidity, as well as the number of df for these variables and for temporal trend and seasonality were based on the Akaike Information Criterion from each model. Categorical variables for weekdays and holidays were also included. Model adjustments were different for each outcome (Supplemental Material, Table S3).

Residual diagnostics were conducted by analyzing (i) scatter plots of deviance residuals for variation around the long-term pattern, (ii) partial autocorrelation function for residual autocorrelation and overfitting, (iii) periodogram for residual seasonality and (iv) Q-Q plots for normality of standardized deviance residuals.

Mortality displacement was assessed by the shape of the association between air pollutants and deaths. When mortality displacement is within the time window analyzed, one expects a

drop in effects for longer lags making them negative until the frail subpopulation pool is replenished. In cumulative effects, mortality displacement results in a decrease towards zero (the effects would cancel out or partially cancel out) and it is expected that the confidence interval for the sum of the relative risks includes 1 (Schwartz 2000a; Zanobetti et al. 2000). The air pollution effect estimates are presented as an increase or decrease in the percentage of deaths, and their 95% CI, for a 10 $\mu g/m^3$ increase in PM10 and NO_2 and for a 1 ppm increase in CO.

A sensitivity analysis was performed using unconstrained DLM up to 30 days, that is, without a polynomial structure to specify the relation between effects and lagged days, for PM10, NO_2, and CO. We performed separate PM10 analyses to evaluate the potential influence of the degrees of freedom specified for the trend variable (specifically, 4 vs. 6 df/year for non-accidental mortality, 5 vs. 6df/year for circulatory mortality, 6 vs. 5 df/year for respiratory and chronic respiratory mortality, and 5 vs. 4 df/year for cerebrovascular and cancer mortality). In addition, we estimated effects of PM10 on deaths among residents of all ages, because it would be expected to have a limited impact on an analysis of mortality. Finally, we repeated the PM10 analyses adjusting for mean temperature over a 0–10 day lag, using exposure-response and lag-response curves according to Gasparrini et al. (2015), instead of the single-day lags of 3 or 5 days used in the primary models.

All analyses were performed using R software, version 3.1.2 (R Core Team 2014). Statistical significance was set at p value < 0.05.

Results

The mean concentrations of PM10, NO_2 and CO for the whole period of analysis were 40.8 $\mu g/m^3$, 51.1 $\mu g/m^3$ and 1.6 ppm, respectively (Table 1). The mean temperature ranged from

8.9°C to 28.9°C and the mean relative humidity from 27.3% to 94.3%. There were among all elderly, on average, 109 deaths per day, of which 45 were for circulatory diseases, 17 for respiratory diseases and 23 for cancer.

PM10, NO_2 and CO exposures were associated with non-accidental deaths and with all specific causes of death evaluated (Table 2). Considering non-accidental deaths, the estimated daily increase was 0.37% (95% CI: 0.20, 0.55), 0.40% (95% CI: 0.21, 0.60) and 1.07% (95% CI: 0.68, 1.47) related to PM10, NO_2 and CO exposure, respectively, on lag 0.

We estimated significant cumulative effects for lag 0-10 for most of causes of death and pollutants that were substantially larger than the estimates for the single lags (Table 3). Cumulative effect estimates for lag 0-20 remained significant for non-accidental deaths associated with PM10 and NO_2 and for respiratory and cancer deaths associated with all pollutants. The cumulative effect estimates for lag 0-30 remained high and significant for respiratory and cancer deaths associated with PM10 and NO_2. Cumulative effect estimates for non-accidental or cerebrovascular mortality at lag 0–30 were not statistically significant for any pollutant and, in general, were close to the null, but associations with circulatory deaths were negative and statistically significant for NO_2 and CO, and nearly significant for PM10.

Cumulative effect estimates for non-accidental deaths increased and then decreased, becoming zero at 27 days for PM10 and 19 days for CO (Figure 1) and at 32 days for NO_2 (not shown). When the analysis was extended to lag 0–40, estimated effects at 40 days were similar to those at 30 days (0.00%; 95% CI: -0.92, 0.92 for PM10, -0.13%; 95% CI: -1.16, 0.91 for NO_2, and -3.03%; 95%CI: -5.37, -0.64 for CO). The pattern was similar for circulatory deaths, with effect estimates crossing the null at 18, 19, and 13 days for PM10, NO_2, and CO, respectively (Figure 1). In contrast, cumulative effect estimates for respiratory deaths remained positive

throughout the 0–30 day lag. Effect estimates for single-day lagged exposures also supported mortality displacement for non-accidental and circulatory deaths, with significant negative associations estimated for exposures lagged by approximately 10-27 days (Supplemental Material, Figure S1).

The effect estimates and pattern in the effect estimates in unconstrained DLM were similar to polynomial DLM (Table 4). The pattern of cumulative effect estimates for PM10 lagged 0-30 days was similar to the main analysis when we modeled the time trend using different degrees of freedom (Supplemental Material, Table S4) and when we included deaths among residents of all ages instead of limiting the analysis to residents ≥60 years of age (Supplemental Material, Table S5). Cumulative effect estimates for PM10 lagged 0–30 days also were consistent with the primary analysis when we adjusted for daily temperature using a 0–10 day cumulative lag (Supplemental Material, Table S6).

Discussion

Few time series studies have addressed mortality displacement and cumulative effects of air pollution in periods of one month. Our findings suggest that in elderly residents of São Paulo, non-accidental mortality was displaced by less than 30 days by the three pollutants studied. However, the displacement patterns varied considerably for specific causes of death.

Mortality displacement

To our knowledge, this is the first study that assessed mortality displacement by air pollution using Brazilian data. São Paulo is a city with both a large population and a long continuous record of daily air pollution monitoring, making this city very suitable for the

analysis we performed. Our findings provide evidence of mortality displacement for non-accidental and circulatory deaths within 30 days, in contrast with other studies of this phenomenon.

One of the first DLM studies analyzed total suspended particulate (TSP) and mortality data from Milan between 1980 and 1989 (Zanobetti et al. 2000). The authors found a significant increase in total mortality up to 45 days (Table 5). Zanobetti et al. (2002, 2003) also analyzed mortality displacement related to PM10 levels in Europe between 1990 and 1997. They did not find evidence of the phenomenon within 40 days for all deaths (Zanobetti et al. 2002) or for circulatory deaths (Zanobetti et al. 2003) based on a meta-analysis of 10 cities (Table 5). Goodman et al. (2004) also did not find evidence of mortality displacement within 40 days for all, circulatory and respiratory deaths related to black smoke (BS) in Dublin between 1980 and 1996 (Table 5).

Previous studies of TSP and deaths in Philadelphia from 1974 to 1988 (Zeger et al.1999) and of particulate matter < 2.5 μm (PM2.5) and circulatory deaths in the Boston area from 1979 to 1986 (Schwartz 2000a) also did not report findings consistent with mortality displacement.

Disease-specific mortality and morbidity patterns, and prevention and treatment policies, differ between Brazil and other countries. These factors may contribute to differences in frailty compared with other populations, and might explain the evidence of mortality displacement in our Brazilian study population. One example was the study carried out between 1996 and 2001 by Martins et al. (2006) using DLM until lag 20. They found evidence of short-term displacement of circulatory hospital admissions among the elderly in São Paulo at cumulative lags of a few days only for PM10 and sulfur dioxide (SO_2).

According to the World Health Organization (WHO), Brazil has higher mortality rates and Disability Adjusted Life Years due to circulatory diseases, also a poorer risk factor profile, such as a greater hypertension prevalence, than countries in Europe or North America (WHO 2011). Also as stated by WHO, Brazil has a low expenditure per capita on health and a high-income inequality, so that prevention and treatment of circulatory disease, and of other diseases, is likely not as good as in high income countries (WHO 2011).

Brazil has a national and free health care system with several specific policies for some diseases and risk factors. However, the low coverage and complicated access for the system probably contribute to a poor health status of many inhabitants. In São Paulo, the coverage of the primary health care system was only 30.4% of the population in December of 2011, the last month evaluated in this study (DAB 2015). According to a national survey carried out in 2013 (IBGE 2015), 39.0% of residences were registered in primary health care units in São Paulo and only 35.0% of them were visited by primary health care teams.

In contrast with non-accidental and circulatory mortality, we did not find evidence of mortality displacement within 30 days for respiratory or cancer mortality. This suggests that cumulative air pollution exposure may shift mortality away from circulatory diseases to other causes of death. We have no ready explanation for this. The patterns differed for different causes of death, and non-causal explanations are also possible. Zanobetti et al. (2003) also did not find evidence of mortality displacement for respiratory deaths related to PM10 exposure in a European multicity study (Table 5). Schwartz (2000a) found no indication for mortality displacement for cardiovascular mortality, whereas some indication was found for pneumonia and chronic obstructive pulmonary disease mortality.

Air pollution can influence the frail subpopulation by, at least, three ways: increasing the mortality rate, increasing the recruitment into the group and delaying the recovery rate of the group. If only the mortality rate increases, mortality displacement probably can be observed. However, if air pollution affects all three mechanisms and increases the frail subpopulation size, larger positive associations between air pollution and mortality may be observed over increasing time intervals (Zanobetti and Schwartz 2008).

Alternatively, deaths from respiratory diseases and cancer may not represent responses to air pollution as acute as those for circulatory diseases (Zanobetti et al. 2003). This may explain the absence of observable mortality displacement over the 30-day time window analyzed in this study.

It is difficult to disentangle the effects of temperature and air pollution. Although adjusting for temperature over longer lags (0–10 days) did not materially alter the evidence in support of mortality displacement (Supplemental Material, Table S6), cumulative effects for some outcomes did change slightly, and we could not adjust for temperature over longer lag periods because of unstable estimates and problems with model convergence.

Associations with single short lags

Single-day lag and cumulative effects up to 5 days indicated significant increases in deaths in association with air pollutant levels, which is in line with results presented in other studies from São Paulo and many studies across the World (Supplemental Material, Tables S7 and S8). Associations between a 10 $\mu g/m^3$ increase and overall and specific-causes of deaths in São Paulo City reported by the ESCALA study (Romieu et al. 2012) were comparable to ours estimates (Supplemental Material, Table S7).

Cancer deaths were included in the present study because it is reasonable to think that individuals who have advanced cancer are also susceptible to air pollution episodes. As short-term exposure to air pollution is not associated with carcinogenesis, the immediate cause of death is likely cardiovascular or respiratory but the underlying cause noted on the death certificate will still be cancer. Positive associations were also reported between cancer deaths and TSP (Villeneuve et al. 2003), NO_2, SO_2 and O_3 (Goldberg et al. 2013) in time series studies.

Cumulative effects until 10 days

Our estimates of cumulative effects over 0-10 days were stronger than estimated effects for single-day lagged exposures, and the cumulative effect estimates remained significant up to lag 10 for all exposures and outcomes except for associations between CO and circulatory and cancer mortality. ESCALA (Romieu et al. 2012) estimated significant cumulative effects for PM10 exposure until lag 3 for São Paulo city, which also were stronger than effect estimates for single-day lags. (Supplemental Material, Table S8). Consistent with previous analyses that used DLM (Zanobetti et al. 2002, 2003) and other cumulative models (Schwartz 2000a), our findings suggest relative risks may be underestimated when based on single-day lag effects.

Conclusion

We found evidence of short-term mortality displacement for non-accidental and circulatory deaths in an elderly Brazilian population. No evidence for mortality displacement within 30 days was found for respiratory and cancer deaths. Additional research is needed to confirm our findings and identify potential mechanisms to explain them.

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Table 1. Daily summary statistics of air pollutants, weather variables and number of deaths among elderly.

	Daily measures					
	Minimum	1st Q	Median	Mean	3rd Q	Maximum
Environment variables						
PM10 ($\mu g/m^3$)	4.6	26.5	37.1	40.8	50.4	158.7
NO_2 ($\mu g/m^3$)	9.2	38.4	48.2	51.1	60.9	150.5
CO (ppm)	0.4	1.0	1.4	1.6	2.0	8.6
Mean Temperature (ºC)	8.9	18.5	21.1	20.8	23.4	28.9
Mean Relative Humidity (%)	27.3	66.9	74.0	72.7	79.9	94.3
Deaths (n)						
Non-accidental	59.0	96.0	108.0	109.1	121.0	178.0
Circulatory	19.0	39.0	45.0	45.2	51.0	84.0
Cerebrovascular	1.0	9.0	11.0	11.5	14.0	28.0
Respiratory	3.0	13.0	17.0	17.0	20.0	42.0
Chronic respiratory	0.0	4.0	6.0	5.9	7.0	18.0
Cancer	7.0	19.0	23.0	22.9	26.0	46.0

1st Q: first quartile; 3rd Q: third quartile.

Table 2. Percent change (95% confidence interval)[a] in number of deaths associated with air pollutant levels for different single-day lags[b].

Deaths	Percent change (95% CI)		
	Lag 0	Lag 1	Lag 2
PM10			
Non-accidental	0.37 (0.20, 0.55)	0.54 (0.36, 0.72)	0.60 (0.40, 0.80)
Circulatory	0.01 (-0.27, 0.29)	0.16 (-0.14, 0.47)	0.40 (0.07, 0.73)
Cerebrovascular	1.60 (0.99, 2.22)	1.44 (0.74, 2.15)	0.04 (-0.58, 0.66)
Respiratory	1.33 (0.83, 1.83)	0.98 (0.41, 1.56)	0.61 (0.11, 1.12)
Chronic respiratory	1.43 (0.58, 2.27)	1.15 (0.18, 2.12)	0.56 (-0.29, 1.41)
Cancer	0.71 (0.27, 1.15)	0.55 (0.04, 1.06)	0.09 (-0.35, 0.54)
NO_2			
Non-accidental	0.40 (0.21, 0.60)	0.50 (0.31, 0.70)	0.58 (0.38, 0.79)
Circulatory	0.31 (0.01, 0.61)	0.42 (0.11, 0.74)	0.55 (0.22, 0.89)
Cerebrovascular	1.51 (0.88, 2.14)	1.32 (0.63, 2.02)	0.17 (-0.48, 0.83)
Respiratory	1.22 (0.71, 1.74)	0.67 (0.10, 1.24)	0.41 (-0.12, 0.95)
Chronic respiratory	1.21 (0.34, 2.08)	0.74 (-0.22, 1.71)	0.49 (-0.42, 1.4)
Cancer	0.93 (0.48, 1.38)	0.48 (-0.01, 0.98)	0.02 (-0.45, 0.49)
CO			
Non-accidental	1.07 (0.68, 1.47)	1.04 (0.64, 1.44)	0.74 (0.32, 1.17)
Circulatory	0.84 (0.23, 1.45)	0.28 (-0.35, 0.92)	-0.14 (-0.78, 0.50)
Cerebrovascular	2.39 (1.08, 3.71)	0.99 (-0.38, 2.39)	0.31 (-0.97, 1.59)
Respiratory	2.54 (1.47, 3.63)	1.66 (0.52, 2.80)	0.72 (-0.33, 1.78)
Chronic respiratory	2.19 (0.41, 4.01)	1.87 (-0.02, 3.79)	1.35 (-0.41, 3.13)
Cancer	1.40 (0.46, 2.35)	0.16 (-0.83, 1.16)	-0.29 (-1.21, 0.63)

[a]Associated with a 10 $\mu g/m^3$ increase in PM10 and NO_2 and with a 1 ppm increase in CO.
[b]Results from a Poisson generalized additive model using single-day lag structures for PM10, NO2 and CO, adjusted by trend, seasonality, temperature, relative humidity, weekdays and holidays.

Table 3. Cumulative percent change (95% confidence interval)[a] in number of deaths associated with air pollutant levels for different cumulative lag structures[b].

Deaths	Percent change (95% CI)		
	Lag 0 to 10	Lag 0 to 20	Lag 0 to 30
PM10			
Non-accidental	1.22 (0.84, 1.60)	0.88 (0.33, 1.44)	-0.10 (-0.82, 0.62)
Circulatory	0.72 (0.11, 1.33)	0.04 (-0.85, 0.93)	-1.11 (-2.21, 0.01)
Cerebrovascular	2.33 (1.14, 3.54)	1.05 (-0.58, 2.71)	0.72 (-1.39, 2.87)
Respiratory	3.40 (2.45, 4.36)	3.45 (2.05, 4,87)	2.81 (0.99, 4.66)
Chronic respiratory	2.95 (1.34, 4.57)	1.58 (-0.75, 3.96)	2.41 (-0.66, 5.57)
Cancer	1.55 (0.75, 2.43)	1.59 (0.50, 2.68)	1.98 (0.58, 3.40)
NO_2			
Non-accidental	1.47 (1.05, 1.89)	1.15 (0.52, 1.78)	0.22 (-0.60, 1.05)
Circulatory	1.34 (0.66, 2.02)	0.55 (-0.46, 1.57)	-1.45 (-2.77, -0.12)
Cerebrovascular	1.99 (0.69, 3.30)	0.62 (-1.20, 2.47)	-0.14 (-2.47, 2.24)
Respiratory	3.18 (2.13, 4.25)	3.15 (1.58, 4.76)	2.98 (0.94, 5.06)
Chronic respiratory	2.83 (1.03, 4.66)	0.83 (-1.81, 3.54)	1.34 (-2.09, 4.90)
Cancer	1.84 (0.93, 2.76)	2.38 (1.05, 3.72)	2.35 (0.67, 4.06)
CO			
Non-accidental	2.01 (1.05, 2.97)	0.41 (-0.99, 1.83)	-1.47 (-3.29, 0.39)
Circulatory	1.18 (-0.30, 2.68)	-0.11 (-3.29, 1.11)	-4.22 (-7.05, -1.30)
Cerebrovascular	3.54 (0.70, 6.45)	0.88 (-3.09, 5.01)	0.34 (-4.78, 5.74)
Respiratory	6.41 (3.96, 8.92)	5.96 (3.36, 9.69)	3.21 (-1.32, 7.94)
Chronic respiratory	5.39 (1.37, 9.57)	1.81 (-3.91, 7.86)	2.82 (-4.59, 10.80)
Cancer	1.36 (-0.64, 3.41)	3.50 (0.50, 6.58)	2.85 (-0.96, 6.81)

[a]Associated with a 10 $\mu g/m^3$ increase in PM10 and NO_2 and with a 1 ppm increase in CO.
[b]Results from a Poisson generalized additive distributed lag model, constrained with a second degree polynomial, using cumulative lag structures of lags 0-10, 0-20 and 0-30 days for PM10, NO_2 and CO, adjusted by trend, seasonality, temperature, relative humidity, weekdays and holidays.

Table 4. Cumulative percent change (95% confidence interval)[a] in number of deaths, of lag 0-30 days, associated with air pollutant levels from an unconstrained model[b].

Deaths	Percent change (95% CI)		
	PM10	NO_2	CO
Non-accidental	-0.03 (-0.77, 0.71)	0.32 (-0.51, 1.16)	-1.40 (-3.24, 0.48)
Circulatory	-0.98 (-2.10, 0.16)	-1.30 (-2.64, 0.05)	-3.91 (-6.78, -0.94)
Cerebrovascular	0.45 (-1.68, 2.63)	-0.40 (-2.75, 2.00)	1.05 (-4.16, 6.54)
Respiratory	2.82 (0.97, 4.71)	3.02 (0.95, 5.24)	3.31 (-1.26, 8.09)
Chronic respiratory	2.04 (-1.07, 5.24)	0.98 (-2.49, 4.56)	2.72 (-4.74, 1.08)
Cancer	1.98 (0.57, 3.41)	2.53 (0.83, 4.26)	3.15 (-0.70, 7.15)

[a]Associated with a 10 $\mu g/m^3$ increase in PM10 and NO_2 and with a 1 ppm increase in CO. [b]Results from an unconstrained Poisson generalized additive distributed lag model using cumulative lag structures of lags 0-10, 0-20 and 0-30 days for PM10, NO_2 and CO, adjusted by trend, seasonality, temperature, relative humidity, weekdays and holidays.

Table 5. Cumulative percent change (95% confidence interval) in number of non-accidental, circulatory and respiratory deaths by 10 μg/m^3 increase in particulate air pollution among studies.

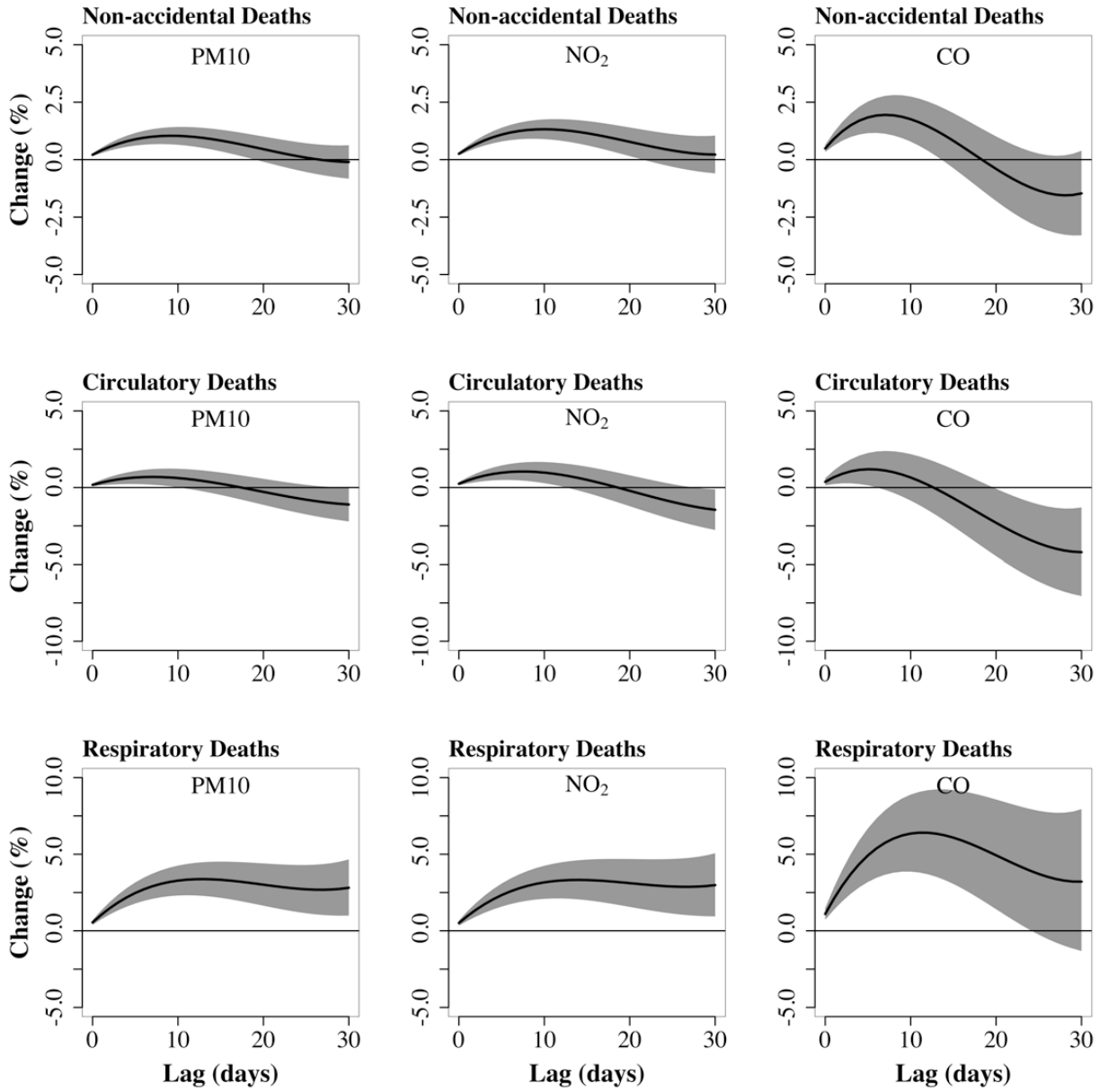
Study	Age group	Air pollutant	Period	Percent change[a] (95% CI)	
				Cumulative	Single lag
Non-accidental deaths					
São Paulo[b] (this study)	Elderly	PM10	Lag 0 to 40	0.00 (-0.92, 0.92)	0.37 (0.20, 0.55)[c]
Milan (Zanobetti et al. 2000)[b]	All ages	TSP	Lag 0 to 45	6.70 (3.80, 9.60)	2.20 (1.40, 3.10)
Boston (Schwartz 2000a)[d]	All ages	PM2.5	60-day window	3.75 (3.20, 4.30)	2.10 (1.50, 4.30)
10 European Cities (Zanobetti et al. 2002)[b]	All ages	PM10	Lag 0 to 40	1.57 (0.26, 2.88)	0.70 (0.43, 0.97)
Dublin (Goodman et al. 2004)[b]	All ages	BS	Lag 0 to 40	1.10 (0.80, 1.30)	0.40 (0.30, 0.60)
Circulatory deaths					
São Paulo[b] (this study)	Elderly	PM10	Lag 0 to 30	-1.11 (-2.21, 0.01)	0.01 (-0.27, 0.29)[e]
10 European Cities (Zanobetti et al. 2003)[e]	All ages	PM10	Lag 0 to 40	1.72 (1.20, 2.25)	0.69 (0.31, 1.08)
Dublin (Goodman et al. 2004)[b]	All ages	BS	Lag 0 to 40	1.10 (0.70, 1.50)	0.40 (0.20, 0.70)
Respiratory deaths					
São Paulo[b] (this study)	Elderly	PM10	Lag 0 to 30	2.81 (0.99, 4.66)	1.33 (0.83, 1.83)[e]
10 European Cities (Zanobetti et al. 2003)[e]	All ages	PM10	Lag 0 to 40	2.62 (0.19, 5.11)	0.74 (-0.17, 1.66)
Dublin (Goodman et al. 2004)[b]	All ages	BS	Lag 0 to 40	3.60 (3.00, 4.30)	0.20 (0.00, 0.50)

[a]Interquartile range increase in Zanobetti et al. (2000) and 10 μg/m^3 increase in other studies. [b]Distributed lag model constrained with polynomial structure. [c]Lag 0. [d]STL (standard template library) algorithms with LOESS (locally weighted smoothing). [e]Unconstrained distributed lag model..

Figure 1. Cumulative percent change[a] in number of deaths associated with air pollutant levels of lag 0-30 days[b].

[a]Associated with a 10 μg/m^3 increase in PM10 and NO_2 and with a 1 ppm increase in CO. [b]Results from a Poisson generalized additive distributed lag model, constrained with a second degree polynomial, using cumulative lag structures of lags 0-30 days for PM10, NO_2 and CO, adjusted by trend, seasonality, temperature, relative humidity, weekdays and holidays. The shadow area represents 95% CI.

Figure 1.


Non-accidental Deaths
PM10
Non-accidental Deaths
NO2
Non-accidental Deaths
CO
Circulatory Deaths
PM10
Circulatory Deaths
NO2
Circulatory Deaths
CO
Respiratory Deaths
PM10
Respiratory Deaths
NO2
Respiratory Deaths
CO
Change (%)
Lag (days)