Time scale effects in acute association between air-pollution and mortality

Myrto Valari, Lucio Martinelli, Edouard Chatignoux, James Crooks and Val Garcia

Myrto Valari:

NRC Post-doc at the U.S Environmental Protection Agency, Atmospheric Modeling Division

U.S. Environmental Protection Agency

109 T.W. Alexander Drive

Research Triangle Park, NC 27711

Valari.Myrto@epa.gov

Lucio Martinelli:

Laboratoire de Physique de la Matière Condensée

Ecole Polytechnique, 91128 Palaiseau Cedex, France

Edouard Chatignoux:

Observatoire Régional de Santé Ile-de-France

21/23, rue Miollis 75732 Paris Cedex 15, France

e.chatignoux@ors-idf.org

James Crooks:

U.S Environmental Protection Agency, Atmospheric Modeling Division

U.S. Environmental Protection Agency

109 T.W. Alexander Drive

Research Triangle Park, NC 27711

26 Crooks.James@epa.gov

27

28 Val Garcia:

29 U.S Environmental Protection Agency, Atmospheric Modeling Division

30 U.S. Environmental Protection Agency

31 109 T.W. Alexander Drive

32 Research Triangle Park, NC 27711

33 Garcia.Val@epa.gov

34 **Abstract**

35 We used wavelet analysis and generalized additive models (GAM) to study timescale effects in the
36 acute association between mortality and air-pollution. Daily averages of measured NO₂ concentrations
37 in the metropolitan Paris area are used as surrogates of human exposure from 2000 to 2004. The NO₂
38 time series was decomposed with wavelet analysis to six independent variables representing different
39 durations of population exposure. We used these variables as predictors in a mortality regression model
40 and compared the coefficients estimated for the different timescales. We found a strong dependency of
41 the exposure-response function on the duration of the air-pollution event. In contrast to previous studies
42 that showed a monotone increase in the relationship between exposure to air-pollution and mortality
43 from shorter to longer timescales, our results show a non-linear response suggesting that the overall
44 acute effect consists of two discrete patterns: a short-term response (2 to 15 days) where mortality
45 relative risks decrease to near null values with the duration of the air-pollution event; an intermediate
46 timescale pattern (16 to 55 days) where mortality relative risk climbs back up to positive levels. The
47 revealed pattern shows that the overall acute effect of air-pollution on mortality does not reflect only a
48 short-term mortality displacement in a population already at high death risk due to chronic conditions
49 but also the transition into this pool from the healthy population.

50

51 **Introduction**

52 Epidemiological evidence relating air-pollution to mortality at metropolitan areas [*Katsouyanni et al.*,
53 2001 and *Samet et al.*, 2000] has been widely interpreted as the response in a population of individuals
54 with fragile health, such as the elderly and persons with chronic cardiac or respiratory diseases
55 [*Environmental Protection Agency*, 1996]. This means that part of the epidemiological association
56 reflects the shortening of life expectancy by only a few days. This effect, termed as mortality
57 displacement [*Schimmel and Murawski*, 1976] has been, in some cases, suggested as the only
58 interpretation of the acute association between air-pollution and mortality and has led to reluctance to
59 enhance emission controls [*Lipfert and Wyzga*, 1995]. Such policy implications, stress the need to
60 quantify the shortening of life expectancy implied by acute epidemiological studies.

61 In response to this, the epidemiological research community developed several methods to
62 estimate air pollution-mortality associations at various timescales. If the statistical association between
63 exposure and mortality only reflected a few days shortening in the life expectancy at a population
64 group already at high death risk, the days following the air pollution episode should be marked with
65 mortality below baseline levels [*Zanobetti et al.*, 2002]. However, previous investigations provided
66 counter evidence of this short-term mortality displacement hypothesis by showing that associations
67 between air-pollution and mortality increase with the duration of the exposure [*Dominici et al.*, 2003;
68 *Kelsall et al.*, 1999; *Zeger et al.*, 1999 and *Schwartz*, 2000].

69 Here we extended the methodology of *Dominici et al.* [2003] to study the mortality displacement
70 effect on a five-year dataset (2000-2004) in the metropolitan Paris area. Similarly to *Dominici et al.*,
71 [2003], we used cutoff frequencies in the power spectrum to isolate the temporal variability of the
72 exposure variable corresponding to a set of discrete timescales. Each wavelength specific component
73 was back transformed to the time domain and the complete set of independent variables was used as
74 co-variates in the regression to mortality. Here, we used an orthogonal wavelet decomposition of the
75 exposure variable instead of Fourier analysis [*Dominici et al.*, 2003]. Wavelets preserve local features

76 of the time-series [*Farge*, 1992] and therefore, the decomposed exposure variables contain an
77 additional layer of information compared to the Fourier decomposition on the moment in time when
78 specific frequency events occur. This enhancement in locality is bound to help capturing the transition
79 between a state where short-term mortality displacement is the major component of the
80 epidemiological association to a timescale where refill from the healthy population overcomes the
81 depletion rate of the susceptible pool.

82 **Data**

83 Mortality and Health Predictors

84 We used daily non-accidental mortality (ICD-10 A00-R99) counts for the metropolitan Paris area from
85 2000 to 2004. Data from August 1st 2003 to August 15th 2003 are excluded from the analysis because
86 of the exceptionally high temperatures and pollutant levels (heat wave of summer 2003 over Europe).
87 The approach we followed (see Methods below) relates daily mortality counts to a set of health
88 predictors. Air-pollution predictors were derived from ambient NO₂ measurements at several central
89 monitors in the area on hourly basis. To assure the quality of NO₂ data only monitors with less than
90 25% of missing hourly values were used. Monitors were selected to represent only background air-
91 pollution levels. This was achieved by applying two criteria: (i) coherence between data measured at
92 different monitors (overlap of the interquartiles and differences between mean values lower than
93 15µg/m³) and (ii) sensitivity to the addition of each individual monitor (variability of the mean value
94 less than 15% and correlation coefficient higher than 0.8). Data were spatially aggregated across the
95 selected monitors and temporally averaged over twenty four hours to represent the daily exposure
96 experienced by the mean metropolitan population (see the study of *Host et al.*, [2008] for more details
97 on data).

98 **Methods**

99 Epidemiological model

100 The daily data were analyzed with time-series methods, using generalized additive Poisson regression
 101 models allowing for overdispersion [Wood, 2006]. Possible confounders, including long-term trend,
 102 seasonality, days of the week, holidays, influenza epidemics, minimum temperature of the current day
 103 and maximum temperature of the previous day, were controlled using Air Pollution and Health: A
 104 European Approach 2 (APHEA-2) methodology [Touloumi *et al.*, 2004]. Long-term trend and
 105 seasonality were modeled using a penalised regression spline of time. A large set of basis functions
 106 (equal to 50 per year) was used, and smoothing was used to remove autocorrelation of the model's
 107 residuals (by minimising the absolute value of the sum of the partial autocorrelation function of the
 108 model's residuals) [Touloumi *et al.*, 2006]. Dummy variables for days of the week and holidays were
 109 included as other independent variables. Temperature and influenza terms were modeled using
 110 parametric splines with 3 degrees of freedom. Both minimal and maximal temperatures were taken into
 111 account because other than minimum or maximum temperatures acting alone, their combination has
 112 been also associated with health effects [Samet, 1998]. All analyses were performed using the MGCV
 113 package in R software (R 2.11.1).

114 Spectral analysis and timescale decomposition

115 Using wavelet analysis, the time series of the exposure variable is decomposed into a set of six
 116 independent variables each representing a different timescale of exposure. All six wavelength
 117 components are used as linear mortality co-predictors in the same Poisson regression following the
 118 model developed by Dominici *et al.*, [2003]:

119

$$\log(\mu_t) = \sum_k (X_{kt}\beta_k) + S(time) + confounders \quad (1)$$

120 where k indicates the discrete timescales of wavelet decomposition, t the day index, μ_t the quasi-
 121 poisson mean of the output mortality distribution at day t , X_k the exposure variable representing

122 temporal variations within the k^{th} wavelength range. S and β are determined by the regression and they
123 represent a smooth function of calendar time and the linear coefficients reflecting correlation between
124 mortality and air-pollution respectively.

125 The wavelet transform of the exposure variable for each pollutant returns a two dimensional set
126 of coefficients representing the wavelet power spectrum at each point in time. The clear advantage of
127 this method compared to the Fourier transform is that the power spectrum is computed separately at
128 each point of the time-series. Its computation depends only on a finite window around that point and
129 not on the whole time series, therefore accounting for transient features of periodicity instead of pre-
130 assuming a global pattern [Cazelles *et al.*, 2007]. The time series decomposition consists of two steps:
131 first, the time series is analyzed following a multi-resolution scheme, providing a set of decomposition
132 coefficients at different scales [Farge, 1992]. For this study, we performed a five level analysis using
133 orthogonal Daubechies (order 5) mother functions. In the frequency domain, we discretized the NO_2
134 power spectra into six timescales: <4 , 4 to 8, 9 to 15, 15 to 28, 29 to 55, and > 55 days. Then the
135 coefficients of each discrete time scale are back transformed to the time domain.

136 **Results and discussion**

137 Wavelet power spectra for each timescale are shown in Figure 1. Note that for visualization
138 reasons the power spectrum shown in Figure 1 has been computed using continuous wavelets (Morlet
139 mother functions) instead of the orthogonal Daubechies to obtain a smoother pattern. To respect the
140 Nyquist theorem, and given that the resolution of our data is one day, the highest frequency considered
141 in the analysis is every two days. For the longest wavelength component (i.e. events of duration longer
142 than 55 days) the dominant feature is the annual cycle at 365 days that is distributed across the study
143 period in a near-uniform pattern. At intermediate time scales sporadic weather and air-pollution events
144 are captured, such as particularly cold months (January 2002 and 2003) or the heat-wave of August
145 2003. At the shortest timescales weekly or few days long anomalies are represented. We note here that

146 these transient features would not have been detected with a Fourier analysis that has maximum
147 resolution in the frequency domain but null resolution in the time domain.

148 We applied the back transform separately to each timescale to obtain the six orthogonal exposure
149 variables at the time domain (Figure 2). Used as independent co-predictors in the epidemiological
150 model (Eq 1), these variables are related to mortality through six regression coefficients (Figure 3).
151 Risk-estimates are expressed as percentages of mortality increase due to a 10-unit increase in exposure
152 (%ERR). The analysis provides evidence of a strong time-scale dependency of a highly non-linear
153 pattern. At timescales shorter than 15 days, mortality relative risk decreases with the duration of the air-
154 pollution events, with an ERR close to 0 for the 9 to 15 days time scale. This is consistent with the
155 short-term mortality displacement hypothesis [Schwartz, 2000]. At the 9 to 15 days time scale, the
156 increase in mortality due to air-pollution is counterbalanced by the depletion of the sub-population at
157 high death risk due to chronic conditions, age etc. However at longer time-scales (from 15 to 55 days)
158 risk estimates climb back up to similar and even higher levels than for the short-term. This provides
159 evidence of an impact not only to a susceptible pool of the population but also to the generally healthy
160 individuals that exposed to high levels of air-pollution for sufficient amount of time (more than 15
161 days) may develop chronic conditions and enter the susceptible group. The interpretation of ERR for
162 timescales longer than 55 days is ambiguous, because of confounding effects of seasonality and other
163 long-term trends.

164 Our analysis provides evidence of larger effects at longer time-scales (i.e. one to two months),
165 which is in agreement with previous investigators that studied the epidemiological association between
166 air-pollution and mortality as a function of the time-scale [Schwartz, 2000 and Dominici *et al.*, 2003].
167 This is also consistent with studies focusing on associations between mortality and air-pollution at even
168 longer-term exposures (i.e. several years) [Pope, 2007; Dockery, 2009 and Jerrett *et al.*, 2009]. On the
169 other hand, the pattern of the association across time-scales revealed from our study implies that short
170 term exposure to air-pollution is not only responsible for a few days shortening of life expectancy but

also for the transition from a healthy population in the susceptible group. This is in agreement with many studies highlighting adverse effects of exposure to air-pollution on less severe outcomes than mortality (e.g. hospitalization [*Host et al.*, 2008] or medical visits [*Larrieu et al.*, 2009]), discarding the hypothesis that air pollution effects are limited to the pool of very frail people. However, our results provide evidence of some degree of short-term mortality displacement during the first two weeks following air-pollution events. Similar patterns were observed by [Schwartz, 2000] for acute pneumonia, but not for all causes mortality.

Conclusion

With the present study we find evidence of strong and highly non-linear time-dependencies in the association between exposure to air-pollution and mortality. A low degree of short-term mortality displacement is found for the first couple of weeks after air-pollution events. However, our analysis strongly suggests that the acute impact of air-pollution on mortality does not reflect only the precipitation of deaths that would occur shortly afterwards regardless pollution; larger effects are estimated for longer-term exposures, which is consistent with the hypothesis that air-pollution is responsible for the development of chronic conditions at healthy individuals.

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242 **Figure captions**

243 Figure 1: Wavelet power spectrum (square modulus of wavelet coefficients) of NO₂ daily averaged
 244 concentration time-series measured and spatially aggregated across several central monitors in the city
 245 of Paris from January 1, 2000 to December 31, 2004. Continuous Morlet wavelets are used as mother

246 functions for the decomposition. The spectrum is divided in six sections to isolate variability in the set
247 of the six discrete timescales (top to bottom) 55 days, 29 to 55, 16 to 28, 9 to 15, 4 to 8, <4. The y-axis
248 is the Fourier period (scale) in days and the x-axis is the date in the time domain. The colormap
249 corresponds to the power of the wavelet spectrum. The absolute value of power increases for long
250 periods due to the corresponding wavelet broadening.

251

252 Figure 2: Decomposition into a six-component series of data on NO₂ (µg/m³) for Paris, from January 1,
253 2000 to December 21, 2004. On each plot the overall (i.e. before decomposition) time series is plotted
254 for reference (black line) and on top of it each wavelength component (colored line). Time series 1 to 6
255 (top to bottom) are the timescale decompositions from the longer to the shortest time-scales (> 55 days,
256 29 to 55, 16 to 28, 9 to 15, 4 to 8, <4)

257

258 Figure 3: Estimated % of increase in mortality due to increase of the NO₂ concentration by 10 µg/m³.
259 The point at the left extreme of the plot represents the overall effect (i.e. without spectral analysis) and
260 is added as a reference. Points 1 to 6 (left to right) are the excess relative risks estimated for each
261 timescale component of the orthogonal wavelet decomposition from the shortest to the longest
262 wavelengths.

264 Figure 1: Wavelet power spectrum (square modulus of wavelet coefficients) of NO₂ daily averaged
 265 concentration time-series measured and spatially aggregated across several central monitors in the city
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 267 functions for the decomposition. The spectrum is divided in six sections to isolate variability in the set
 268 of the six discrete timescales (top to bottom) 55 days, 29 to 55, 16 to 28, 9 to 15, 4 to 8, <4. The y-axis
 269 is the Fourier period (scale) in days and the x-axis is the date in the time domain. The colormap
 270 corresponds to the power of the wavelet spectrum. The absolute value of power increases for long
 271 periods due to the corresponding wavelet broadening.

273 Figure 2: Decomposition into a six-component series of data on NO_2 ($\mu\text{g}/\text{m}^3$) for Paris, from January 1,
 274 2000 to December 21, 2004. On each plot the overall (i.e. before decomposition) time series is plotted
 275 for reference (black line) and on top of it each wavelength component (colored line). Time series 1 to 6
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