

eAppendix 1

Definition of the exposure-lag-response risk surfaces in the four scenarios

The four scenarios of the simulation studies are defined by different exposure-lag-response risk surfaces, expressed by the bi-dimensional function $f \cdot w(x, \ell)$. The surfaces are constructed using the same marginal exposure-response function $f(x)$, and different marginal lag-response function $w(\ell)$.

The function $f(x)$ was defined as the simple untransformed x in the first two scenarios illustrating linear exposure-response relationships between ozone and mortality. In the other two scenarios, the non-linear exposure-response function $f(x)$ modelling the association between temperature and mortality was generated in the range $[-20,35]$ of temperature ($^{\circ}\text{C}$) as:

$$f(x) = \begin{cases} [(x - 20)/2.4]^{2.5}/450, & x > 20 \\ [(20 - x)/200]^{1.5}, & x \leq 20 \end{cases}$$

The function $w(\ell)$ was defined in the range $[0,20]$ of lag (days) in the different ways depending on the scenario. In the short-lag scenario for both linear and non-linear relationships, it was defined as:

$$w(\ell) = e^{-\ell/0.7}$$

In the linear long-lag scenario was defined as:

$$w(\ell) = 5 \cdot \Phi_{2,5}$$

where $\Phi_{m,d}$ is the Gaussian density function with mean m and standard deviation d . In the non-linear long-lag scenario, the function was defined as:

$$w(\ell) = \begin{cases} e^{-\ell/0.7}, & x > 20 \\ 4 \cdot \chi_6(\ell), & x \leq 20 \end{cases}$$

where χ_d is a function representing the chi-squared distribution with d degrees of freedom. The reader can refer to the R scripts available at www.ag-myresearch.com for more details.

eAppendix 2

Definition of bias, coverage and root mean square error (RMSE)

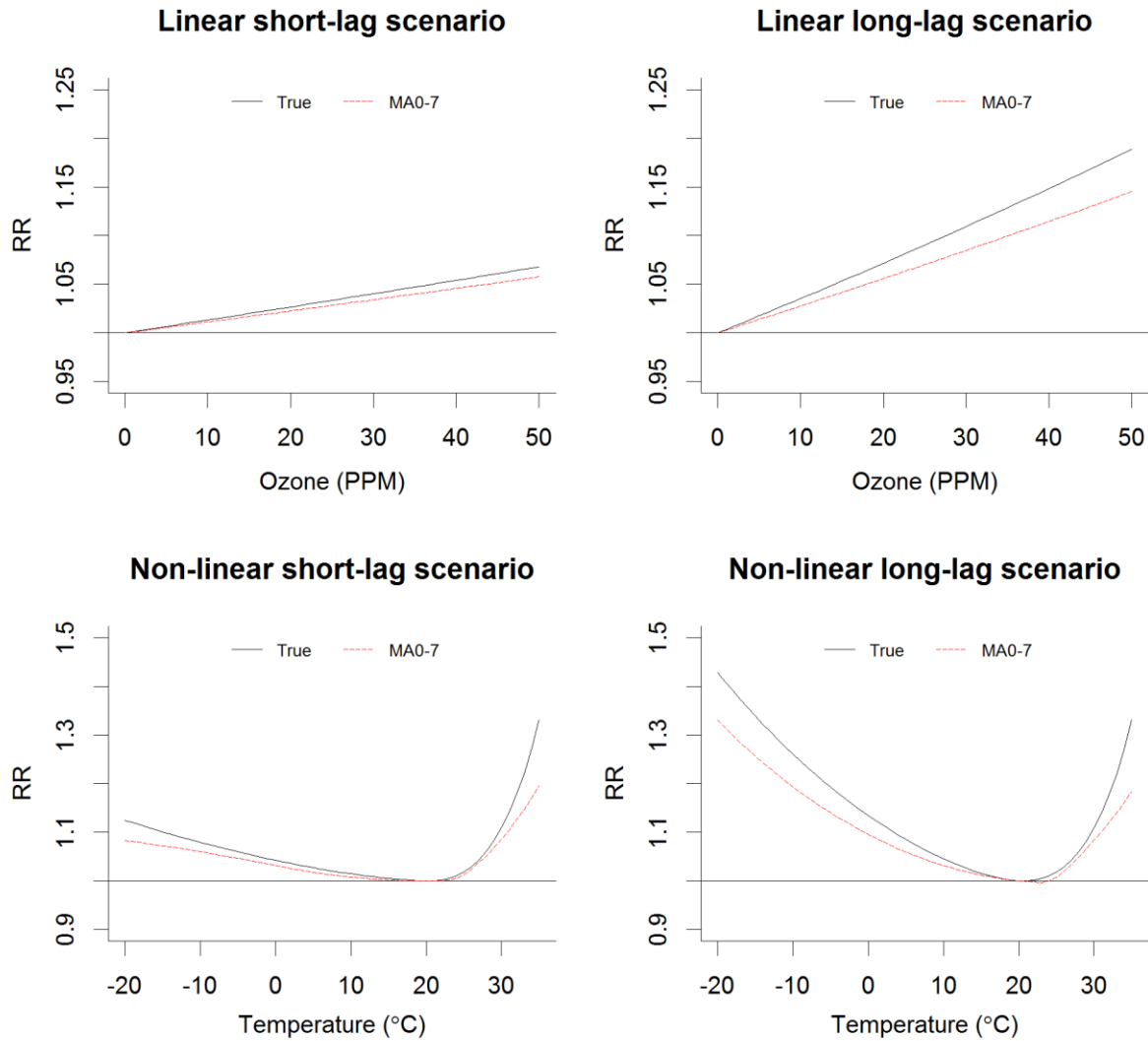
These statistics are computed as the average across the curve representing the overall cumulative exposure-response association, represented in the relative risk (RR) scale. First, let's define β_j as the true simulated overall cumulative log-relative risk, and $\hat{\beta}_{ji}$ and $V(\hat{\beta}_{ji})$ as the corresponding point estimates and variance at the i^{th} iteration of the simulations. Here $j = 1, \dots, p$ corresponds to integers within the ranges 0 to 50 PPB for ozone (in the first two scenarios) and -20°C and 35°C for temperature (in the last two scenarios), while $i = 1, \dots, n$, with $n = 5000$.

The three statistics are computed as:

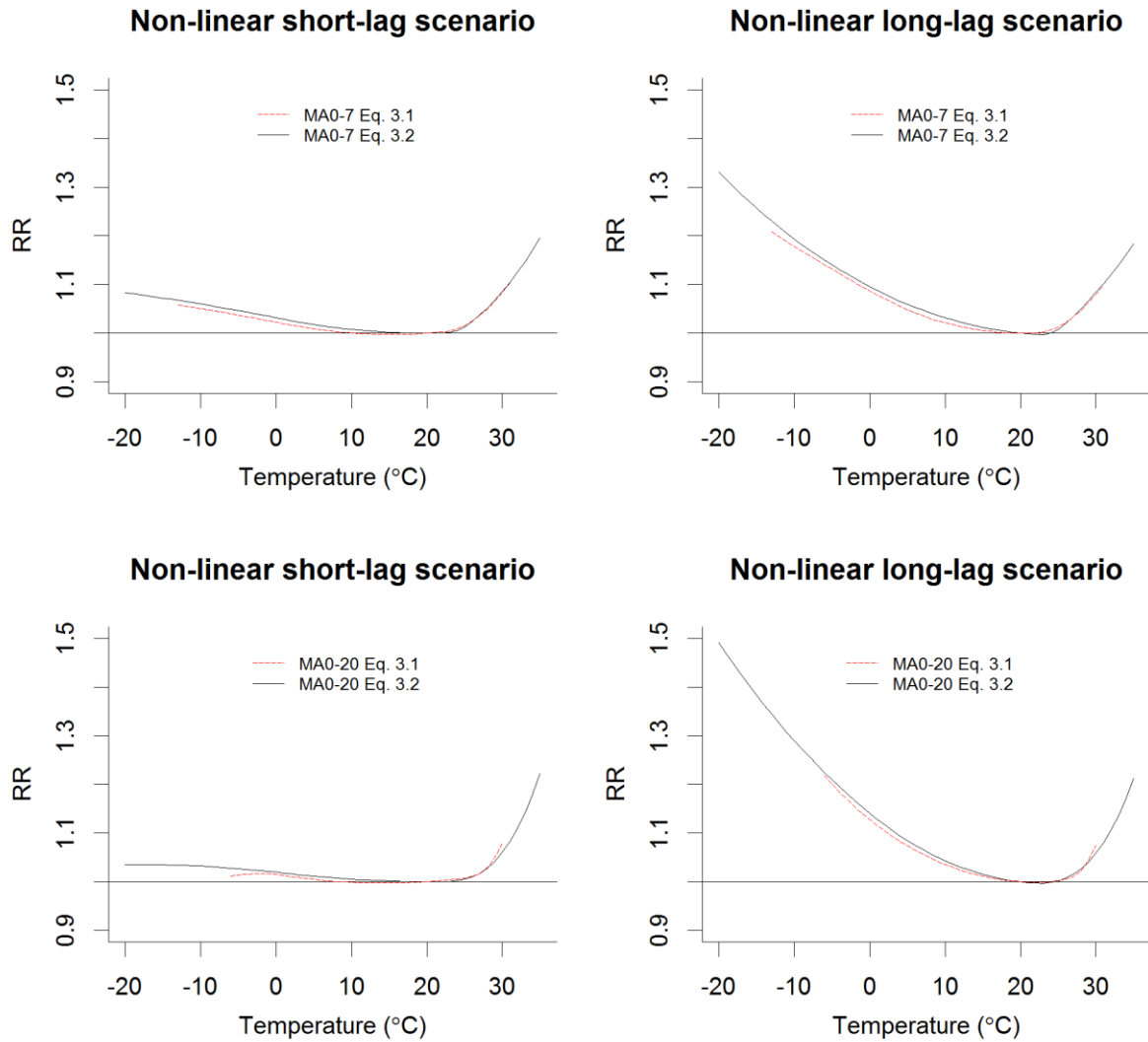
$$\begin{aligned} bias (x100) &= \sum_j^p \frac{|\sum_i \hat{\beta}_{ji} / n - \beta_j|}{p} \cdot 100 \\ coverage &= \sum_j^p \frac{\sum_i I\left(|\hat{\beta}_{ji} - \beta_j| \leq \Phi_{0,1}^{-1}(1 - \alpha/2) \cdot \sqrt{V(\hat{\beta}_{ji})}\right) / n}{p} \\ RMSE (x100) &= \sum_j^p \frac{\sqrt{\sum_i (\hat{\beta}_{ji} - \beta_j)^2 / n}}{p} \cdot 100 \end{aligned}$$

with $\Phi_{0,1}^{-1}(1 - \alpha/2)$ as the quantile function of the cumulative normal distribution related to probability $1 - \alpha/2$, with $\alpha = 0.05$ (approximately 1.96).

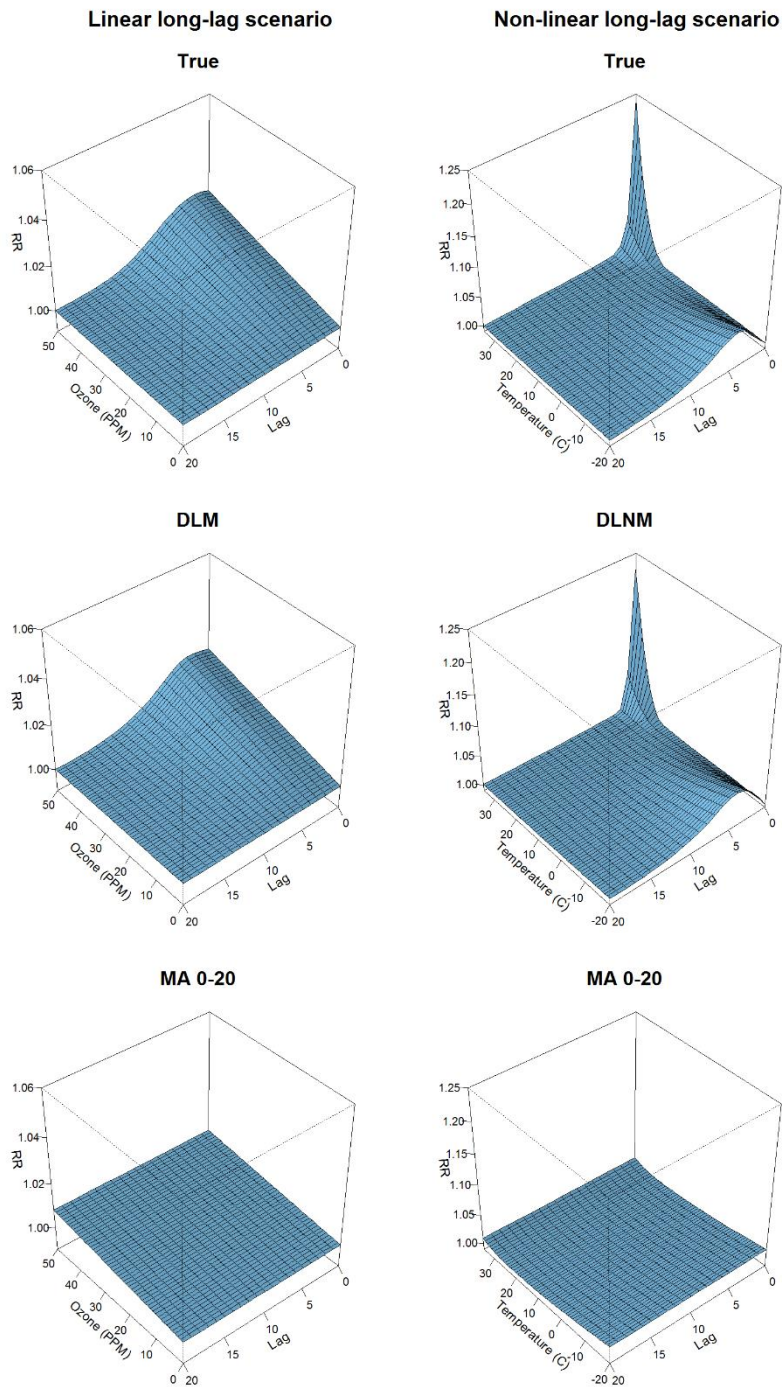
eFigure 1. Overall cumulative exposure response relationships as RR estimated by the moving average model with lag 0-7 (MA0-7). The graphs represent the linear association with ozone (top panels) and the non-linear association with temperature (bottom panels) in the short-lag (left panels) and long-lag (right panels) scenarios. The slopes represent the real simulated relationship (continuous black lines) and the average of the estimated relationship across 5000 replicates (dashed red lines).



eFigure 2. Overall cumulative exposure response relationships as RR estimated by the moving average models with lag 0-7 (MA0-7, top panels) or lag 0-20 (MA0-20, bottom panels) in the non-linear short-lag (left panels) and non-linear long-lag (right panels) scenarios. The curves represent the average of the estimated relationship across 5000 replicates with two different definitions of moving average models, following Eq. (3.2) (continuous black lines) Eq. 3.1 (dashed red lines), respectively.



eFigure 3. Exposure-lag-response surfaces as RR, for ozone-mortality relationship in the linear long-lag scenario (left panels) and for temperature-mortality relationship in the non-linear long-lag scenario (right panels). The surfaces represent the true simulated relationship (top panels) and the average of the estimated relationship across 5000 replicates for the distributed lag models (DLM and DLNM, mid panels) and moving average model with lag 0-20 (MA0-20, bottom panels) models.



eFigure 4. Overall cumulative exposure-response relationships as RR estimated by the distributed lag models (DLM and DLNM) with alternative specifications in sensitivity analyses. The graphs represent the linear association with ozone (top left panel) and the non-linear association with temperature (other panels) in various scenarios. The curves represent the real simulated relationship (continuous black lines) and the average of the estimated relationship across 5000 replicates (dashed lines, with different colours and patterns depending on the model).

