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## Introduction

- Understanding the effect of environmental stressors on human mortality can be done using **statistical modelling** of relevant data.
- E.g., **daily mortality counts**  $M_t$  (for day  $t$ ) and max daily **apparent temperature**  $T_t$ .
- To allow for the **aggregated effect** of environmental stress **over a period of time**, regression models called Distributed Lag Models (DLMs) have been proposed:

$$M_t \sim \text{Poisson}(\mu_t)$$

$$\log(\mu_t) = \alpha + \beta_0 T_t + \beta_1 T_{t-1} + \beta_2 T_{t-2} + \dots + \beta_L T_{t-L} \quad (1)$$

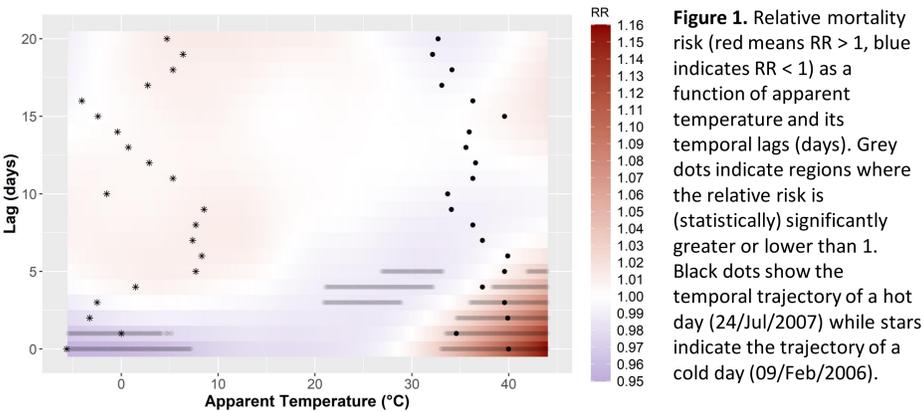
- where the coefficients  $\beta_{t-l}$  are the contribution to mean mortality count  $\mu_t$ , from temperature  $T_{t-l}$  on day  $t-l$  ( $t$  being “today”). Extension to **Distributed Lag Non-Linear Models** or DLNMs (Gasparrini, 2010) allows a non-linear effect from  $T_{t-l}$ :

$$\log(\mu_t) = \alpha + f(T_t, 0) + f(T_{t-1}, 1) + f(T_{t-2}, 2) + \dots + f(T_{t-L}, L). \quad (2)$$

- The expression  $\exp\{f(T_{t-l}, l)\}$  is interpreted as the **relative risk** (RR) interpreted as
  - RR = 1 means that mortality risk is equal to the mean mortality count,  $\exp\{\alpha\}$ ;
  - RR > 1 or RR < 1 means higher or lower risk than average respectively.

## Methodology

- Implementing DLNMs as **Generalized Additive Models** or GAMs (Wood 2011, 2017) enables optimal estimation and straightforward interpretation. Figure 1 shows the RR for the city of Thessaloniki, Greece, based on observational data in the period 2006–2016 (mortality counts and weather station observations).



**Figure 1.** Relative mortality risk (red means RR > 1, blue indicates RR < 1) as a function of apparent temperature and its temporal lags (days). Grey dots indicate regions where the relative risk is (statistically) significantly greater or lower than 1. Black dots show the temporal trajectory of a hot day (24/Jul/2007) while stars indicate the trajectory of a cold day (09/Feb/2006).

- Apparent temperature quantifies the stress from both temperature and humidity (see Figure 2), so the peak around 40°C for lags of 0-5 days indicates **increased mortality risk during extreme hot-and-humid periods**.

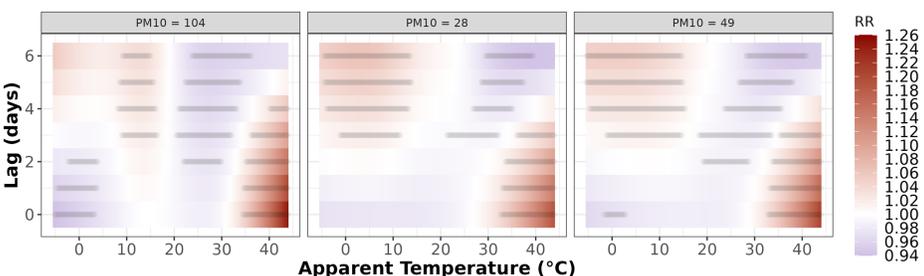
Relative Humidity %	21	24	27	29	32	35	38	41	43	46	49
0	18	21	23	26	28	31	33	35	37	39	42
10	18	21	24	27	29	32	35	38	41	44	47
20	19	22	25	28	31	34	37	41	44	49	53
30	19	23	26	29	32	36	40	45	51	57	64
40	20	23	26	30	34	38	43	51	58	66	74
50	21	24	27	31	36	42	49	57	66	76	86
60	21	24	28	32	38	45	53	63	74	86	98
70	21	25	29	34	41	51	62	74	87	100	113
80	22	26	30	36	45	56	68	81	95	110	125
90	22	26	31	38	48	60	74	89	105	122	140
100	22	27	33	42	53	66	81	97	115	134	154

**Figure 2.** Apparent temperature as a function of air temperature and relative humidity. **Image source:** Diffey (2018)

- GAMs readily allow inclusion of other stressors such as air pollution, say  $A_t$ , by extending the function  $f(T_{t-l}, l)$  to  $f(T_{t-l}, A_{t-l}, l)$  in Equation (2).

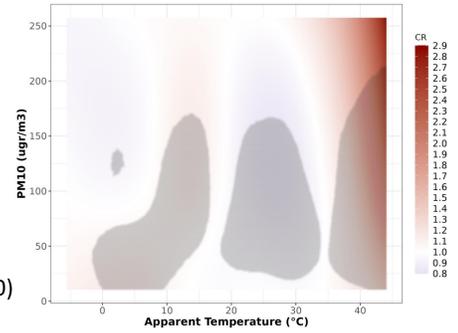
## Compound effect from heat and air pollution

- For  $A_t$  being PM10 (coarse particulate matter which if >40 is considered a health risk), we now have different temperature-lag surfaces for different PM10 values (Figure 3). For Thessaloniki, **the increased risk at hot-and-humid conditions is clearly exacerbated by high PM10 levels**.



**Figure 3.** Relative mortality risk as a function of apparent temperature and its temporal lags (days), for decreasing (right to left) values of PM10.

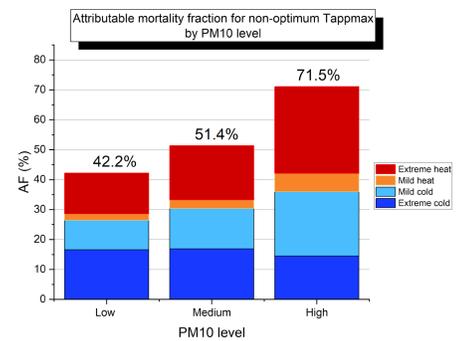
- To better understand the synergy between exposures, the lag dimension can be “integrated out” by summing the risk along lags, for different exposure combinations.



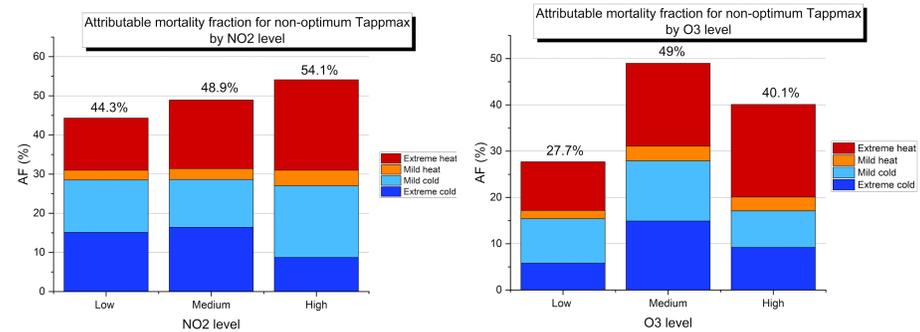
**Figure 4.** Cumulative risk for various apparent temperature and PM10 combinations.

- Figure 4 shows the corresponding **cumulative risk surface** for apparent temperature and particulate matter (PM10) for Thessaloniki, where hot-and-humid weather combined with high PM10 results in enhanced risk.

- To interpret the estimated risk in terms of observed mortality we compute the **Attributable Fraction** – defined as the proportion of death counts that are attributed to the exposures.

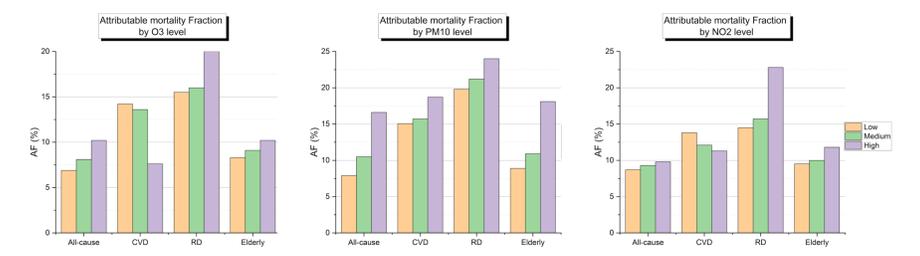


- Figure 5 shows the Attributable Fraction for 3 pollutants: PM10, Ozone (O3) and Nitrogen Dioxide (NO2).



**Figure 5.** Attributable mortality fraction stratified by apparent temperature and PM10/NO2/O3 levels.

- We have also quantified the attributable mortality fraction by **cause-of-death** (cardiovascular disease (CVD), respiratory disease (RD) and elderly mortality (>65 years)). Figure 6 shows this for apparent temperature being between the 75<sup>th</sup> and 99<sup>th</sup> sample quantile, for increasing levels of the 3 pollutants from Figure 5.



**Figure 6.** Cause-specific attributable mortality fraction for different levels for PM10/NO2/O3.

## Conclusions

- This is the first time that the lagged effects of heat-stress and air pollution synergy was studied explicitly at daily temporal resolution.
- Our study confirms the hypothesis that mortality risk due to **heat-stress is compounded by air pollution** – for the city of Thessaloniki, one of the most polluted cities in Europe.
- During hot-and-humid conditions: **respiratory disease mortality is exacerbated for high Ozone and NO2 pollution, while elderly mortality is heightened by high PM10 levels**.
- Further analysis is needed to also allow for the interactions between pollutants.

## References

- Diffey, B. L. (2018). “Time and Place as Modifiers of Personal UV Exposure”. International Journal of Environmental Research and Public Health. <https://doi.org/10.3390/ijerph15061112>.
- Wood, S. (2017). “Generalized Additive Models, 2<sup>nd</sup> edition”. doi = 10.1201/9781315370279.
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