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Building a Multivariate model to estimate and prospectively monitor excess mortality associated with influenza epidemics and extreme temperature

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Background

Influenza virus circulate every year causing epidemics usually benign for the human population, but that can complicate into other diseases, like pneumonia. Flu epidemics have also been associated with excess mortality from respiratory and cardiovascular diseases. The influenza impact is particularly evident in specific groups that presents higher risk of complications associated with influenza infection leading to death [1, 2, 3]. In Portugal, as in most European countries, winter is usually characterized by increased overall mortality from all causes, in contrast to the summer period that are often associated with low mortality but the effects of high temperatures on excess mortality, can be observed during periods of heat waves [4].

Objectives

a) To develop a multivariate model to estimate and prospectively monitor excess mortality associated with influenza epidemics and extreme temperature.

b) Use this multivariate model to estimate the excess mortality observed in Portugal in the 2011/2012 winter, and describe the contribution two factors that are commonly associated with mortality in winter: cold snaps and influenza epidemics.

Methods

“All causes" mortality time series between weeks 26/2007 and 20/2012 were obtained using the daily mortality surveillance system [5]. Air temperature for each District of the territory (Portugal mainland), is provided by 18 weather stations from the network of the Portuguese Institute for the Ocean and the Atmosphere. Influenza-like illness incidence rates were obtained from the Portuguese General Practitioner Sentinel Network, Rede Médicos-Sentinela [6], and influenza detection and characterization was made by the National Reference Laboratory for Influenza Virus.

Excess mortality periods, during winter 2012, was obtain by building a mortality baseline without the effect of events associated with excess mortality. The aim was to estimate the number of expected deaths for each week in the absence of events associated with excess mortality.

The association between "extreme cold" and "flu epidemic" events and observed mortality was analyzed by fitting a Poisson regression model with identity link function, and considering, among others, these two factors as explanatory factors for mortality. The following model is proposed:

$$y_{tj}=C+b_1t+b_2\sin(2*\pi*t/52)+b_3\sin(2*\pi*t/52)+b_4\sin(4*\pi*t/52)+b_5\sin(4*\pi*t/52)+\sum_{k=1}^{K}(a_{1k}IG_{kt}+a_{2k}IG_{kt-1})+c_1CE_t+c_2CE_{t-1}+d_1FE_t+d_2FE_{t-1}+e_t$$

Parameter	Description
Y_{tj}	Number of deaths observed in week t of the year j, considering offset variable 1/population$_j$.
IG_{kt}	FS (Flu syndrome) incidence rate of t week – FS baseline in week t, if incidence rate above the baseline and week t belongs to the season k
$IG_{kt}=0$	If incidence rate of week t is less than the FS baseline or week t does not belong to the season k
CE_t	Mean maximum temperature in the country – 30ºC, if mean maximum temperature greater than or equal to 30ºC
$CE_t=0$	If mean maximum temperature below 30ºC
FE_t	5ºC - mean minimum temperature in the country, if less than or equal to 5ºC
$FE_t=0$	Mean minimum temperature above 5ºC
b1	Trend slope
b2 and b3	Annual seasonality parameters
b4 and b5	Biannual seasonality parameters
a_{1k} and a_{2k}	Parameters that measure the influence of the influenza epidemics level of the same week and of the previous week, respectively, for the season k (k=07/08...11/12)
c_1 and c_2	Parameters that measure the influence of extreme maximum temperature (above 30ºC) in the same week and in the week before respectively
d_1 and d_2	Parameters which measure the influence of extreme minimum temperatures (below 5ºC) in the same week and in the week before respectively
e_t	Random error

Results

We identified an excess mortality period during week 2 to 11/2012, for this period, and after subtracting the observed deaths to the baseline already adjusted to extreme heat, extreme cold and flu epidemics estimate a total of 3994 deaths were observed. Using the same approach, it is possible to verify that extreme cold and flu epidemic explain about 97% of the excess mortality (i.e., 3968 deaths were associated with these two factors). Regarding the specific contribution of each of the factors, the results indicate that 75% was associated with influenza A(H3) epidemics, 2978 deaths (CI95%: 2773 to 3185). The extreme cold period was associated with 889 deaths (CI95%: 801 to 978), which accounts for 22% of the excess mortality, remaining 3% of unexplained excess (Figure 1 and 2).

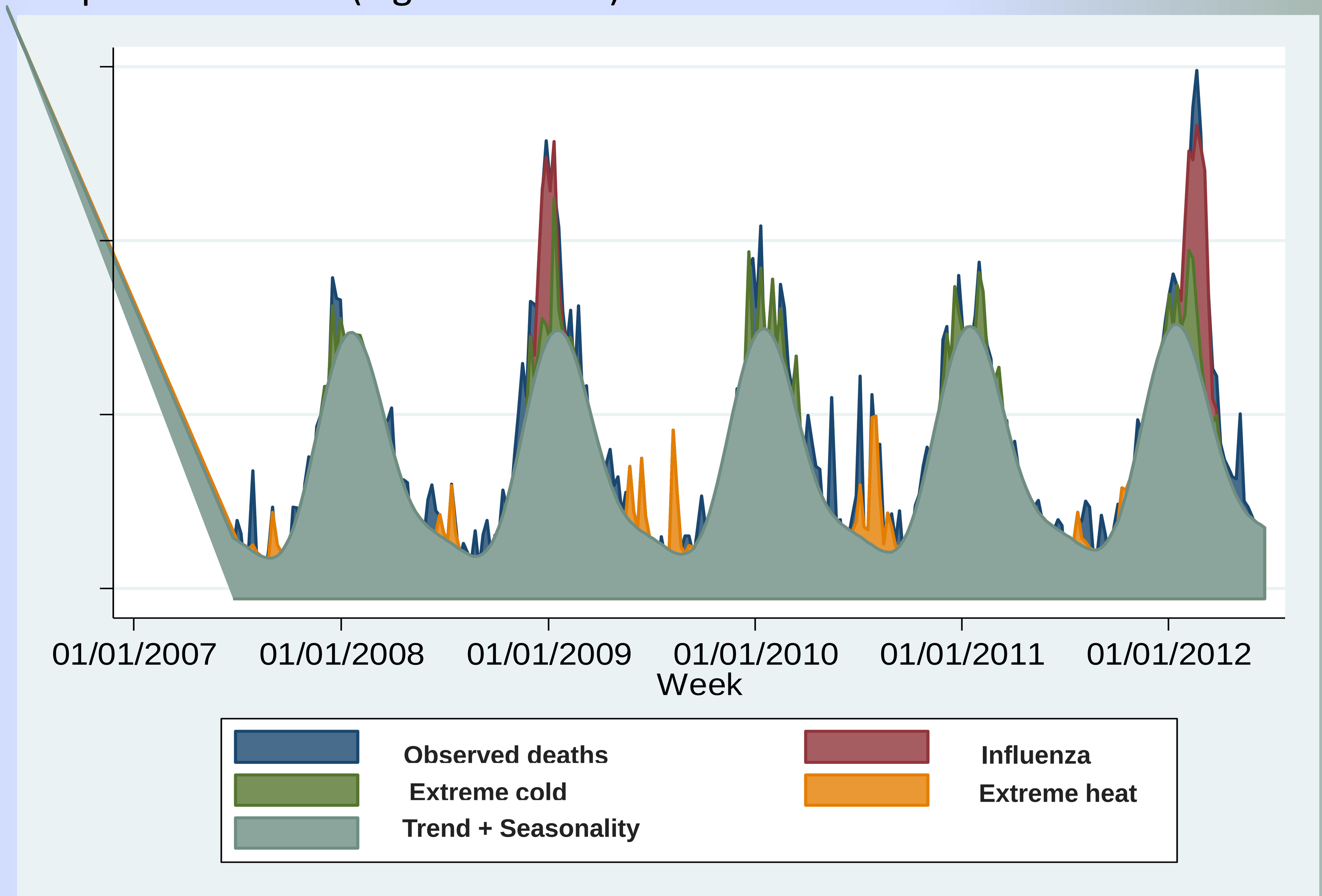

Figure 1: Weekly distribution of observed deaths and components foreseen by the variation of the explanatory factors extreme cold (minimum temperature below 5ºC), extreme heat (maximum temperature above 30ºC) and influenza epidemics (incidence rate of influenza above the baseline).

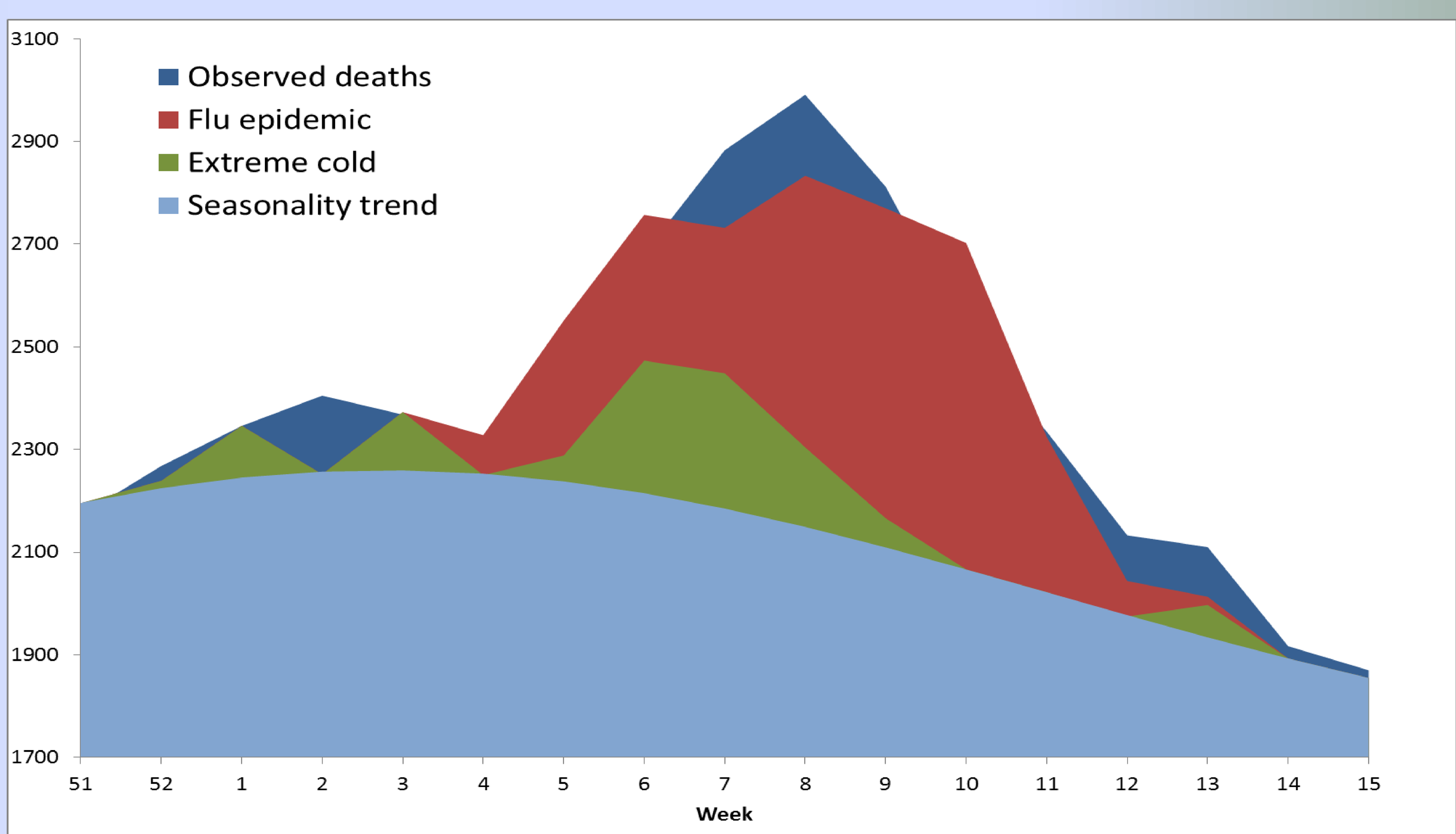

Figure 2: Weekly distribution of observed deaths and components foreseen by the variation of the explanatory factors extreme cold, extreme heat and influenza epidemics (incidence rate of influenza above the baseline) for the 2012 winter.

Conclusions

An excess of 3994 deaths was observed during the 2012 winter, 75% of this excess was associated with influenza epidemic and 22% with extreme cold temperatures. The multivariate model allowed us to estimate excess mortality associated with different events and also to project a baseline for mortality monitoring. Results showed that the multivariate model can be used to prospectively monitor excess mortality, by setting the extreme temperatures and influenza epidemics covariates at zero and projecting the baseline. This approach may be a more suitable method to build baselines to prospectively detect excess mortality since no data is removed from the mortality time series. The ecological approach used precludes conclusions at individual level so the conclusions should not be applied at the individual level. The availability of results by specific causes of death in this period will eventually clarify the role of other factors on the excess mortality.

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