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Towards a threshold climate for emergency lower respiratory hospital admissions

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Abstract

Identification of 'cut-points' or thresholds of climate factors would play a crucial role in alerting risks of climate change and providing guidance to policymakers. This study investigated

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a 'Climate Threshold' for emergency hospital admissions of chronic lower respiratory diseases by using a distributed lag non-linear model (DLNM). We analysed a unique longitudinal dataset (10 years, 2000-2009) on emergency hospital admissions, climate, and pollution factors for the Greater London. Our study extends existing work on this topic by considering non-linearity, lag effects between climate factors and disease exposure within the DLNM model considering B-spline as smoothing technique. The final model also considered natural cubic splines of time since exposure and 'day of the week' as confounding factors. The results of DLNM indicated a significant improvement in model fitting compared to a typical GLM model. The final model identified the thresholds of several climate factors including: high temperature ($\geq 27^0$C), low relative humidity ($\leq 40\%$), high Pm10 level (≥ 70-μg/m^3), low wind speed (≤ 2 knots) and high rainfall (≥ 30mm). Beyond the threshold values, a significantly higher number of emergency admissions due to lower respiratory problems would be expected within the following 2-3 days after the climate shift in the Greater London. The approach will be useful to initiate 'region and disease specific' climate mitigation plans. It will help identify spatial hot spots and the most sensitive areas and population due to climate change, and will eventually lead towards a diversified health warning system tailored to specific climate zones and populations.

Keywords: Climate Change; Threshold; Delayed model; Emergency hospital admissions; Air pollution; Health warning System.

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1. Introduction

Climate is changing at an unprecedented alarming rate. Thirteen of the 14 warmest years on record have all occurred in the 15 years since 1997 (WMO, 2011; WMO, 2014). The world experienced unprecedented high-impact climate extremes between 2001 and 2010, which was the warmest decade since the start of modern measurements in 1850 (WMO, 2011). There has been an increasing interest in the impact assessment of any sudden changes in climate factors on health. Scientific consensuses alerted that climate change is already adversely affecting human health (WHO, 2008). According to WHO, a one-degree increase of temperature may trigger mortality by 1-4% in Europe. Given an expected rise in global mean temperature of 30^0C by 2071-2100, extra deaths of 86,000 are projected every year, (Menne et al., 2008). Other climate factors are found to be affecting various disease categories, including rainfall with Diarrhoea (Hashizume et al., 2007); humidity with heart disease (Schwartz et al., 2004) and influenza (Barreca and Shimshack, 2012); COPD with wind speed (Ferrari et al., 2012). Air pollution also plays as a triggering factor in the detrimental role of climate fluctuations (Carson et al., 2006; World Health Organisation (WHO), 2006). The frequency and severity of extreme weather events (e.g., heat waves, flooding and cold winters) are also increasing as an indirect effect of climate change. There were high numbers of excess deaths associated with the European heat wave during August 2003 (Fouillet et al., 2006; Johnson et al., 2004). Heat-related mortality is projected to experience a steep increase in the UK in the 21st century. Compared to the baseline figure of about 2,000 premature death in the 2000s, the projection to increase by 70% (in year 2020s) , 260% (in 2050s) and 540% (in 2080s) (Vardoulakis and Heaviside, 2012). Climate

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fluctuations are indirectly linked to many prevalent poor human health outcomes from cardiovascular mortality and respiratory illnesses due to heat waves, to altered transmission of infectious diseases, increased food poisoning and malnutrition from crop failures (Patz et al., 2005). Respiratory diseases are the most climate affected diseases and among the leading causes of death worldwide (Muggeo and Hajat, 2009; Schwartz et al., 2004). Beside health, climate change also effects the environment and the global economy to a great extent (Luo and Wu, 2016). According to the British Thoracic Society, respiratory diseases kill one in five people in the UK and cost the NHS over £6 billion (Society, 2006). Under such circumstances, a challenge for policy makers and health managers is how well the health service will be able to respond to sudden extreme changes in climate factors.

Wu et al. (2014) suggest that risks may be studied from a multidisciplinary perspective (e.g. financial risk, environmental risk due to human endeavours) and one of the effective ways to cope with risks is to adopt an integrated approach specific to any area or organisation (Wu et al., 2015). Irrespective of the areas, the interconnection and dependence of the risks deals with correlation among the risk factors e.g. temperature, wind speed as risk factors in climate change; and one of the initial step of risk management is the process of identification of these factors. They also addressed the importance of early warning system as to control the risk and explored various models in different other areas of risk.

An efficient health alert system based on a precise methodology to reduce the risk of morbidity and (or) mortality can play a crucial role in tackling this challenge. Such an alert system will help hospital and healthcare managers planning necessary precautionary measures

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during extreme climate events (Dolney and Sheridan, 2006; Fouillet et al., 2007; McGeehin and Mirabelli, 2001; Tan et al., 2007). The implications of climate variability will vary according to geographical latitudes, disease categories, socio-economic and population characteristics (Hess et al., 2012; WHO, 2008). So such health alert system would be more efficient if it is location specific and targets homogenous population.

Threshold temperature is defined by the temperature at which mortality/morbidity rates are the lowest (Kalkstein and Davis, 2005). Populations with a temperate climate generally show non-linear U, V, N or J shaped with disease frequencies (Braga et al., 2002; Muggeo and Hajat, 2009; Pattenden et al., 2003; Pauli and Rizzi, 2008). The lowest point of these curves (e.g. temperature vs disease frequencies) can be considered as the optimum temperature value beyond which the events increases (e.g. disease frequencies, hospital admissions) (Curriero et al., 2002). This is the basis of our approach for calculating the threshold point of climate factors for lower respiratory (LR) hospital admissions. Such threshold of climate factors for any specific disease exposure would play a positive role for developing an improved health alert system.

The time between the day of disease onset (or mortality) and meteorological exposure is generally termed as the lag or delayed period (Hu et al., 2010). Hospital admissions predominantly occur within a few days after the exposure to high temperature (Fernández-Raga et al., 2010; Schwartz et al., 2004). Apparently hot weather has a quicker impact on health than cold weather (Bhaskaran et al., 2010; Braga et al., 2002; Hajat et al., 2005; Muggeo and Hajat, 2009; Nastos and Matzarakis, 2006; Pattenden et al., 2003). The susceptibility rate of a

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population varies according to disease and geographical location and exhibits different delayed effects depending on the season of the year (Pudpong and Hajat, 2011).

The main objective of this paper is to derive an accurate threshold-climate for emergency hospital admissions of chronic lower respiratory diseases (e.g. asthma, COPD) for the Greater London. For the first time, three unique administrative datasets are linked for this purpose: Hospital Episode Statistics, Met office observational data and London Air Quality Network data. We develop a distributed lag non-linear model (DLNM) with the climate and air pollutions factors, explicitly considering their non-linear relationships with the daily hospital admissions along with their respective delayed effects. We incorporate natural cubic splines of time (days) and 'day of the week' as confounding factors to control the confounding affects by seasonally varying factors other than the climate or pollution factors in the model. This final model is applied to this unique dataset. A disease and region specific heath alert system emerging from such threshold climate could lead to a more robust health care system and play an important role in the event of any sudden changes in climate factors (Laaidi et al., 2006).

2. Material and methods

2.1 Data

Our primary data was the national Hospital Episode Statistics for emergency inpatient hospital admissions for the Greater London (HES; http://www.hscic.gov.uk/hes). We used datasets from the two Met office (http://www.metoffice.gov.uk) observational stations (Heathrow airport and London Saint James Park) for meteorological factors and air quality data

from the London AIR Quality Network (LAQN; www.londonair.org.uk). The LAQN covers a group of air quality monitoring stations in the 33 Boroughs of London, Essex, Kent and Surrey. These three datasets were covering 10 years from 1 January 2000 to 31 December 2009 and linked into one platform for the purpose of this study.

We choose chronic lower respiratory disease (ICD-10, J40-J47), because it is one of the most climate affected disease category (D'Amato et al., 2014). The reasons for choosing Greater London as the study site are population density, number of hospital admissions and London's vulnerability to air pollution (Authority, 2014). We collected daily observational data for temperature (maximum, minimum and mean), rainfall, mean wind speed, sun hours, radiation, relative humidity and mean pressure. These climate factors were selected on the basis of their reported relationships to morbidity (Barreca and Shimshack, 2012; Bhaskaran et al., 2010; Hashizume et al., 2007; Schwartz et al., 2004). Air pollution is known to have a significant role in some disease exposures that compound the effect of sudden changes in climate factors on health (World Health Organisation (WHO), 2006). Therefore, we assumed that the level of air pollutants would show some confounding effects in our model and collected data on levels of Ozone and PM10 (Particulate matters diameter of 10 micrometres or less).

We created a MySQL database and populated it with HES data to build a longitudinal dataset (2000-2009), where meteorological and air pollution data were linked for each inpatient admission using a deterministic record linkage approach based on patient's partial postcode and admission date. There were 1,055,355 hospital admission episodes in the raw data for the Greater London (2000-2009) including all diseases categories, admissions methods and age groups.

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Among them there were 31,599 emergency admissions due to LR diseases. We created some new variables for the daily emergency hospital admissions due to LR disease, day of the month, day of the week, day of the year and a variable representing geographical location of the patient. We used the **AIRGENE** algorithm to combine the climate data from the two stations and to clean missing values (Bhaskaran et al., 2010). Finally, the mean imputation method was used to replace missing values in the air pollutants (Ozone and PM 10) data.

2.2 Statistical analysis:

We first explored the relationships between climate and pollution factors and daily hospital emergency admission counts for LR disease by using a scatter plot matrix. The scatter plot matrix (Figure 1) explains the relationships between each of the climate and pollution factors with daily LR admission counts along with their histograms, kernel density overlays, absolute correlations and corresponding p-values of significance.

The DLNM model used to calculate the 'Threshold Climate' for LR emergency hospital admissions considers both the non-linearity (between the climate and pollution factors with emergency admissions count) and the respective delayed effects of the climate and pollution factors. The 'Threshold Climate' was calculated as a by-product of this DLNM model.

The framework of the DLNM model is based on the concept of cross-basis. The cross-basis can be imagined as a bi-dimensional space of functions describing the shape of the relationship and the distributed lag effects both at the same time (Gasparrini et al., 2010). Choosing a cross-basis is based on two sets of basis functions, which have been combined to generate the cross-basis functions. The choice of the two sets for each space is perfectly independent and should be

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based on a-priori assumptions or on a compromise between complexity and generalisability. In this study, the nonlinear relationships between the hospital admissions and each of the factors of climate and pollution represented one basis, while the other basis was the delayed effects of these climate and pollution factors on the hospital admissions. For the first basis, we used a B-Spline smoothing technique for dealing with the nonlinearity. For the second, we used different lag structures (delayed effects) between the rate of hospital admissions and each of the climate or pollution factors which emerged from the literature review. Mathematically, we can express our final DLNM model as follows after adding two more terms of 'natural cubic terms of time' and 'day of the week (DOW)':

$$
g(\mu_t) = \sum_{j=1}^{v_{x=t}} \sum_{k=1}^{v_{l(L=30)}} r_{tj.}^T c_{.k} \eta_{jk} + \sum_{j=1}^{v_{x=Rai}} \sum_{k=1}^{v_{l(L=15)}} r_{tj.}^T c_{.k} \eta_{jk} + \sum_{j=1}^{v_{x=Wind\ speed}} \sum_{k=1}^{v_{l(L=2)}} r_{tj.}^T c_{.k} \eta_{jk}
$$

$$
+ \sum_{j=1}^{v_{x=Sun\ hou}} \sum_{k=1}^{v_{l(L=20)}} r_{tj.}^T c_{.k} \eta_{jk} + \sum_{j=1}^{v_{x=R.Humidity}} \sum_{k=1}^{v_{l(L=20)}} r_{tj.}^T c_{.k} \eta_{jk}
$$

$$
+ \sum_{j=1}^{v_{x=Pressure}} \sum_{k=1}^{v_{l(L=1)}} r_{tj.}^T c_{.k} \eta_{jk} + \sum_{j=1}^{v_{x=Ozone}} \sum_{k=1}^{v_{l(L=30)}} r_{tj.}^T c_{.k} \eta_{jk}
$$

$$
+ \sum_{j=1}^{v_{x=PM1}} \sum_{k=1}^{v_{l(L=30)}} r_{tj.}^T c_{.k} \eta_{jk} + S_{ns}(Time) + DOW
$$

(1)

In this equation, $\mu \equiv E(Y)$, g is a monotonic link function, Y (LR disease hospital admissions rate in our model) is assumed to follow the exponential family of distribution, $r_{tj.}$ is

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the vector of lagged exposures for the time t transformed through the basis function j, T is the transpose in matrix notations, C is defined as a series of polynomial or spline functions of l describing the effect as a smoothed curve along lags, x is the exposure variable specific to any of the climate or pollution factors (e.g. daily mean temperature), η is a vector of the unknown parameters. The vector $w_{t.}$ is obtained by applying the $v_x . v_l$ cross-basis functions to x_t. The natural cubic splines of time (with 7 degrees of freedom) was added to control any additional confounding affects due to seasonally varying factors other than the selected climate and pollution factors in the model. For the similar type of confounding factor due to any particular day of a week, we included 'day of the week' (DOW) in the model.

The lag periods presented in the equation (1) were identified based on the literature review and represent the maximum plausible days to improve the precision of the DLNM model. For example, lower temperature normally shows longer impacts on disease outcome than higher temperature (Bhaskaran et al., 2010; Hajat et al., 2005; Muggeo and Hajat, 2009). Thus, we adopted a longer 30 days lag period in the model, to cover both the effect of high and low temperature. In general, the choices of the lag period and smoothing techniques (spline function) are mainly motivated by several methodological and substantive papers on time series analyses in similar applications (Armstrong, 2006; Gasparrini, 2011; Gasparrini et al., 2010).

As smoothing techniques, we used a B-spline basis for all the variables due to its data driven characteristics (for our case the relationships between the climate factors and daily hospital admissions) and works well after the boundary knots. The degree of the polynomial and degrees of freedom for all the variable basis and lag basis were selected based on the results of

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exploratory data analysis, previous studies and also the Akaike and Bayes Information Criteria (AIC/BIC) tested under various values of degrees of freedom and polynomials (Hastie and Tibshirani, 1990; Wood, 2006).

3. Results

The scatter plot matrix (Figure 1) shows that the variables are skewed or non-normal and that LR emergency admission counts are over-dispersed. The kernel density overlays for LR hospital admission counts exhibit non-linearity with all climate and pollution factors. From the scatter plot matrix, it is evident that lower-respiratory hospital admissions counts do not vary by seasons. The first scatter plot (top left) shows the relationships between temperature and rain where the X-axis indicates 'the daily average rain' and the Y-axis indicates the 'the daily average temperature'. Similarly, the other scatter plots show relationships between the rest of climate and pollution factors. We can see that most of the correlation coefficients are significantly high. For this reason, we have investigated whether any multi-collinearity exists that may violate the assumptions in the final model and found that there is multi-collinearity between Sun hours and radiation. The correlation was very high (r=0.82) and the variation inflation factor (VIF) for radiation was 6.97. Thus, Radiation was excluded from our final model.

Figure 1 will be here

Figure 2 will be here

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Figure 2 depicts the effect of **temperature** on LR diseases admissions. It is illustrated by a 3-D image and corresponding contour plot of the relative risk (RR) of emergency hospital admissions along the mean temperature (here 12^0C) as reference and lags. The plot shows a very strong immediate positive effect (lag period of 0-2 days) of the higher temperature above around 27^0C, indicating that a high number of emergency admissions due to LR disease can be expected within the first 0-2 days of any hot spell crossing the temperature of 27^0C. Higher temperature also seems to have a moderate positive effect on emergency LR admissions at around 10-15 days lag period. Lower temperature (e.g. 0^0C) seems to have a moderate effect at around 10-25 days lag period.

Figure 3 will be here

Figure 3 illustrate the overall relationship of **relative humidity** with emergency LR disease admissions. Both higher and lower humidity levels show a shorter lag period effect. The 3-D graph and corresponding contour plot of the relative risk (RR) of emergency hospital admissions along the reference relative humidity of 75.8% show a very strong immediate positive effect of the lower relative humidity at around 40% and a lag period of 0-3 days. Similarly, a higher relative humidity (90% or more) seems to have a moderate positive effect on the admissions at short lag period of 0-2 days. However, there seems to be strong negative relationship between 12-20 days of lower relative humidity (around 40%) and hospital emergency admissions. That is, the hospital admission rate is expected to decrease with 12-20 days of lower relative humidity (40%).

Figure 4 will be here

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The higher **PM10** shows both longer and shorter lag effects on the emergency LR hospital admissions. The 3-D graph and corresponding contour plot (**Figure 4**) of the relative risk (RR) along PM10 and lags compared with a reference value of $28\mu g/m^3$ show a strong positive effect of higher PM10 around $70\text{-}\mu g/m^3$ or higher, and longer lag period of 15-20 days. It also shows some immediate short-term positive effects of 0-3 days lag period.

The relative risk (RR) of **wind speed** and lags compared with a reference value of 7.7 knots indicates a strong positive effect of wind speed around 25 knots or higher and longer lag period of 8-15 days. At the same time, it shows moderate (positive) effect for a shorter lag period of 0-3 days for lower wind speed (approximately 2 knots). We can also see some shorter lag period (0-2 days) but negative effect when the wind speed is higher than around 25 knots (with respect to the reference speed of 7.7 knots). This is shown in the 3-D graph and the corresponding contour plot of wind speed in **Figure 5**. Table 1 summarizes the results of climate thresholds obtained from the final model.

Figure 5 will be here

Table 1 will be here

Rainfall also shows a significant effect on LR hospital admissions. High amount of daily rainfall (≥30mm) have lag period of short term (0-2 days) and long term (8-10 days) with a strong positive effect on the daily LR admissions. Extreme amount of rainfall (≥33mm) also shows longer lag period (13-15 days) but a strong negative relationship with the LR admissions. Sun-

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hours did not reveal any significant relationship (except otherwise at 10% level of statistical significance). The corresponding figures for both rainfall and sun-hours can be found in the supplementary part of the article.

The significance of the climate and the pollution factors and the goodness of fit of the final DLNM model were compared to those obtained from a GLM version of the model using QAIC (Quasi Akaike Information Criterion), QBIC (Quasi Bayesian information criterion) and Nagelkerke R-square (**Table 1**) (Hastie and Tibshirani, 1990; Wood, 2006). The Nagelkerke R-square of the final DLNM model was significantly higher than that of the GLM model (98.91% vs. 59.14%). The GLM model also indicated fewer significant determinants, including the daily mean temperature, relative humidity, PM10, wind speed and rainfall.

4. Discussion

The model developed under this study extends the past "threshold identification models" (e.g. hockey stick model) (Hansen et al., 2008) in several ways. First, we investigated the impact of several climate factors that were not examined in previous studies. In particular, our study demonstrated climate factors such as wind speed and humidity should be included along temperature. In the case of the LR emergency admission outcomes, we have found some relationships between climatic and pollution factors. However, only the relationships of radiation with the sun hours seems to be strongest which also raised the issue of multicollinearity in the final model and therefore neglected in the final model. From the results of the final model, humidity and wind speed were found to play a significant (and compound) role. It is equally

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important to include pollution and other environmental factors to more accurately model the impact of climate change on health.

This study also explicitly modelled non-linearity and delayed effects of climate factors. In terms of methodology, our study revealed that lag effect and nonlinearity play essential roles in improving the statistical model (e.g. typical time series, generalized linear model) and explored the B-spline smoothing technique in this context. In our final DLNM model, all climate and pollution factors included in the model presented various delayed effects on LR emergency hospital admissions. In summary, our study suggests that we can expect a significantly higher number of emergency lower respiratory disease hospital admissions within 2-3 days after high temperature ($\geq 27^0$C), low relative humidity ($\leq 40\%$), high Pm10 level (≥ 70-$\mu g/m^3$), low wind speed (≤ 3 knots), or high rainfall (≥ 30mm) day. We believe that the 'Threshold climate' presented here is more efficient as it captures both the non-linear nature of the data and the delayed effect of climate factors.

Lastly, we applied this model to a unique comprehensive dataset that integrated three large (HES, MET office and LAQN) administrative datasets into one platform. The successful application of our model to this unique data reinforces the usefulness of the administrative data in climate epidemiological research.

4.1 Limitations of the study

We recognize that the findings presented here are based on the data between 2000 and 2009 and does not include the most recent years. This limitation is primarily due to administrative burden in accessing to different levels of data from multiple sources and the challenges

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associated with merging the data. The weakness is common and inherent to many empirical analyses that are similar to the work presented here [1]. Specifically, we obtained, cleaned and merged data from three different levels and sources (HES, climate and pollution data). These data are administered by different agencies and hence are not necessarily available for the same period and/or at the same level. This type of data integration is known to be one of the significant challenges for empirical researchers [2]. Moreover, accessing to the patient level pseudonymised HES dataset entails a long complex process and requires very stringent information governance policies in place. This new process has led many academics to wait for over a year for this to be approved [3].

As an additional limitation, we would like to note that our contributions lie predominantly in the area of empirical research. While our theoretical contribution may be limited, the focus of our study was to demonstrate practical contributions of a quantitative model in climate change research. Empirically, our main contributions were the incorporation of the delayed effect of climate and the use of a natural spline function to better predict the health impact. The decade long data we analysed captured sufficient climate variations to adequately examine these aspects. Finally, the formula and the model we have derived in the present study is rather demonstrative and preliminary and has room for future research. For instance, the predictive power of the model can be checked by using more up to date decade long data.

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5. Conclusions

A better health alert system specifically for vulnerable and elderly people is indispensable in this era of changing climate (IPCC, 2007). However, almost all the health alert systems are currently based on temperature only. Such systems may not be effective in predicting the demands placed on a health system as other factors such as humidity, wind speed, and rainfall also have compounded impact on health and disease frequency. The non-linear model developed and disease specific thresholds calculated in this study provide insights towards an efficient and robust health alert system by considering the compound effect of all the climate and pollution factors. It will add valuable information for policy makers and hospital managers to understand and predict patient flow due to certain diseases and conditions under the changing climate. The government will be able to adopt proactive and dynamic precautionary measures, develop appropriate public health intervention strategies to prevent and mitigate the impact of climate change, and empower climate adaptation in healthcare.

We hope that this study will also create opportunities to calculate threshold levels for various climate or pollution factors for any specific region or disease. Such "threshold levels" will be helpful for policymakers to initiate 'region and disease specific' climate mitigation plans (Laaidi et al., 2006). For the same reason, it will be also possible to identify spatial hot spots and the areas and population most sensitive climate change, eventually leading towards a diversified health warning system tailored to specific climate zones and populations.

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Conflict of interest statement

The authors have no conflicts of interest to disclose

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