



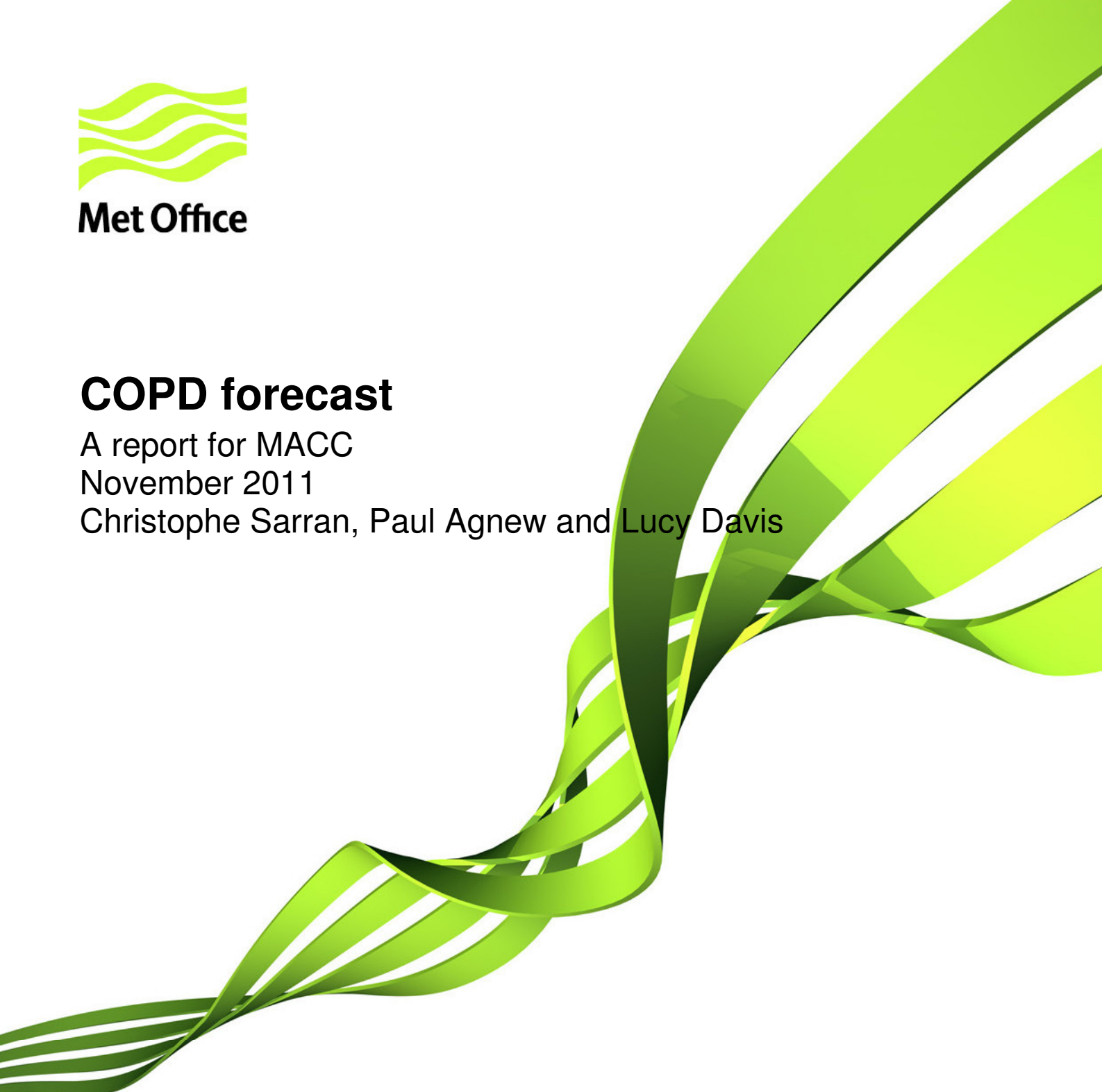
Met Office

COPD forecast

A report for MACC

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Executive summary

The MACC R-Ens forecast PM_{10} concentrations median has been included in the Met Office COPD forecast as a trial to assess the effect of air quality exposure on the health of COPD patients relative to the effect of low air temperature. Preliminary analyses, carried out to support with statistical evidence the inclusion of atmospheric composition in the COPD forecasts, found that: (a) there is a link between the health of COPD patients and air quality, albeit weak; (b) there are important spatial variations in atmospheric composition which makes it difficult to assess patient exposure, in particular in urban areas; (c) it is necessary to adjust the air quality forecasts to account for these spatial variations, as far as is possible.

The following recommendations are made:

1. High resolution air quality forecasts would be optimal for correctly assessing patient exposure (~100 m or less).
2. The new COPD algorithm with air quality has been developed using only 2 years worth of air quality data. Ideally a 10 or more year dataset is recommended to ensure a robust model.

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1. Introduction^a

The incidence of COPD is known to increase during and following period of extremes of temperature and poor air quality. This can result in a significant reduction in patient quality of life and the possible requirement of hospital admission for those worst affected. It has been demonstrated that, given advanced warning of increased risk of the onset of COPD exacerbation, patients are better able to control their symptoms by a combination of medication and environmental/behaviour modifications, and hence reduce the risk of requiring hospital admission. The main objective of this MACC work package is therefore to improve the skill of forecasts of the risk of COPD exacerbation through the inclusion of air quality data.

The incidence of COPD episodes is known to increase during periods of temperature extremes and air quality has also been shown to have an influence. However the previous unavailability of reliable air quality forecasts and the impact of poor air quality episodes on COPD exacerbation have hampered progress in identifying the link between the two. The MACC core services will provide regional air quality forecasts which can be used to clarify and evaluate the role of poor air quality in contributing to COPD exacerbation. The present task will provide this evaluation and investigate ways in which the forecasts can contribute to improved assessments of COPD risk. The main users of COPD forecasts are Primary Care services.

The Met Office has developed a rule-based forecast model of the risk of COPD exacerbations, based on an understanding of how weather and environment affect patients with COPD. The original model was created using data from the UK Hospital Episode Statistics (HES) database. It has two main inputs: an underlying seasonal pattern given by cumulative relative humidity and the cumulative effect of cold weather 1-3 weeks prior to the forecast period. The model output is the percentage above or below the mean annual risk of COPD hospital admission. There has been up to now no air quality dependence and a key output from this work package has been to investigate the role of air quality and incorporate a dependence as appropriate. The numerical model is only one input in the forecasting process. In the current system devised by the Met Office a health forecaster uses additional data to provide more information to users about the factors which might affect COPD, and to quality control the model prediction. These data include: a real-time surveillance data for COPD or total respiratory hospital admissions where available; calls to out-of-hours providers and NHS Direct; GP

^a Agnew, P., and Marno, P., 2009: WP R-Health 1: Improved Chronic Pulmonary (COPD) Disorder forecasting. Exeter, Met Office.

consultations for infectious diseases; and other weather and air quality data. Introducing the ability to focus on air quality would allow a more integrated use of this information into the model itself.

It has been proposed to identify the air quality variables which have the greatest influence on COPD occurrence. Using MACC R-Ens forecasts and data on past COPD hospital admissions the correlation between the latter and poor air quality have been investigated. Identification of a link, isolated from temperature effects, has allowed the development of an improved COPD forecast algorithm incorporating atmospheric composition variables. This has been achieved by including the spatial and temporal variations of fields of temperatures and air quality and differences in the incidence of COPD. In order to carry out this research, MACC R-Ens regional air quality forecasts from the core services have been required. By examining the relative contribution to the overall COPD risk exposure of the weather and air quality components, the value of MACC forecasts have been assessed. Progress with improvements in COPD forecasting has been assessed both quantitatively and qualitatively.

2. The influence of air quality on COPD hospital admissions

MACC models have been used to estimate the air quality exposure experienced by patients in England with Chronic Obstructive Pulmonary Disease (COPD) who are admitted to hospital. In the same way as it is colder on days of COPD hospital admissions, results indicate the air quality is poorer in these days. Concentrations of nitric oxide present the strongest difference, up to 13% higher on 4 cumulative days followed by 8 lag days. Despite possibly linking air quality to COPD admissions statistically, models based on physiological mechanisms are recommended for such epidemiological studies.

2.1 Introduction

Mortality rates in England and concentrations of air pollutants are more strongly linked than previously estimated according to an article by the UK Economic and Social Research Council¹. Chronic Obstructive Pulmonary Disease (COPD) is a debilitating and progressive disease that affects 1% to 2% of the population in England. Particulate Matter (PM) has been extensively studied in relation to respiratory disease, though some have failed to find a link². No significant association between chronic respiratory hospital admissions and PM was found in a study by Van Den Eeden et al.³ (1999). The 2008 guidance document⁴ published in the Journal of Toxicology and Environmental Health lists three studies that fail to link COPD admissions with PM (Ito 2003; Slaughter et al.

2005; Peel et al. 2005) and three studies with positive excess risk estimates (Moolgavkar 2003; Dominici et al. 2006; Chen et al. 2004). Increases in COPD admission risk have been measured between 0.1%/($\mu\text{g}/\text{m}^3$) and 0.3%/($\mu\text{g}/\text{m}^3$) for PM_{10} ^{5,6}. Despite these measurable risks linking PM to COPD hospital admissions, the relationship has been reported as weak⁷. Association of COPD admissions with ozone (O_3), sulphur dioxide (SO_2), carbon monoxide (CO) and nitrogen dioxide (NO_2) have also been found^{3,5,7,8}.

As a first step in using air quality forecasts in a UK health forecast system⁹, air quality in England on days of COPD hospital admission is examined to determine if there are any differences compared to normal air quality in England. The UK Met Office delivers health forecasts to patients with COPD¹⁰ based on weather variables such as daily maximum temperature. The work described here is aimed at investigating the added value air quality forecasts would provide the existing UK health forecast to COPD patients. The air quality model data comes from separate sources: (i) a UK configuration of the NAME model (as used for the UK national air quality forecast); (ii) hindcast runs for 2003¹¹ by the MACC partners using EURAD (RIU), SILAM (FMI) and BOLCHEM (CNR).

2.2 Methods

Determining the relationship between air quality indicators (pollutant concentrations) and COPD admissions is complicated by the correlation between pollutants and many confounders relating to seasonality and weather^{12,13,14}. This is further complicated by the spatial correlation¹⁵ of air quality with confounders, and the difficulty in attributing cases of COPD admission to air quality¹⁶. Indeed, the vast majority of COPD admissions may be caused by other health factors not related to atmospheric conditions or composition.

The data available consist of all COPD admissions for England from April 1997 to March 2007 from Hospital Episodes Statistics¹⁷ (HES). Each case includes the postcode district of residence of the patient, as well as the date of hospital admissions. The latitude-longitude coordinates of the postcode district centroids were computed to match with air quality data. Air pollutant concentrations were estimated by interpolation of model data. Hourly values were estimated for each postcode district in England, and subsequently converted into daily mean and daily maximum values. RIU, CNR and FMI models were available for 2003 and the NAME model for 2005 and 2006. In addition, air quality measurements made by the UK Automatic Air Quality Network (AURN)^{18,19} were matched to postcode districts by taking the closest AURN site to the postcode location within 5 km, again computing daily means and maxima. The distributions of the pollutant

concentrations were examined and compared to the distribution of the concentrations on days of COPD hospital admissions.

The distributions were transformed by taking the square-root of the concentrations so as to render the distributions approximately normal. The mean square-root pollutant concentrations μ_0 were computed and compared to the mean square-roots for days of admissions μ_1 . The statistic $\Delta\mu \equiv (\mu_1 - \mu_0)/\mu_0$ was used to evaluate which pollutant displayed the greatest difference on days of admission compared to the normal mean concentration (using an adapted one-sample hypothesis test of the sample mean²⁰). Lag and cumulative means were also analysed, up to 45 days for both, whereby the pollutant concentrations $[X]$ for each day were defined by

$$[X](t;L;C) = \frac{1}{C} \sum_{t'=t-L-C+1}^{t-L} [X](t')$$

$L \geq 0$ is the number of lag days and $C \geq 1$ is the number of cumulative days.

2.3 Results

The model pollutant concentrations are strongly correlated with each other (c.f. table 1) as has been previously noted for air quality observations¹². Consequently, as a first step it is only necessary to find the pollutant with the strongest link with hospital admissions.

Table 1. Median Pearson correlation coefficients for pollutant concentrations estimated by RIU, FMI and NAME.

	[HCHO]	[NO ₂]	[NO]	[O ₃]	[PM ₁₀]	[SO ₂]
[CO]	0.83	0.90	0.78	-0.47	0.71	0.70
[HCHO]		0.81	0.92	-0.50	0.66	0.71
[NO ₂]			0.67	-0.48	0.71	0.78
[NO]				-0.53	0.59	0.69
[O ₃]					-0.20	-0.38
[PM ₁₀]						0.71

Concentrations of nitric oxide showed the strongest $\Delta\mu$ difference with increased concentrations of nitric oxide on days of COPD hospital admission. This can be seen for all three models, with $\Delta\mu$ values of 0.07, 0.11 and 0.05 for NAME, RIU and FMI, respectively. The difference in $[NO]$ is comparable to the difference in daily mean temperature T_{mean} (figure 1) when it is relatively colder on days of COPD admissions: the mean temperature is 10.7 °C while on days of COPD admission it is 9.3 °C, hence a difference of -1.4 °C. The normal $[NO]$ mean for NAME is $\mu_0^2 = 6.4 \mu\text{g}/\text{m}^3$ while for RIU and FMI it is $3.6 \mu\text{g}/\text{m}^3$ and $3.7 \mu\text{g}/\text{m}^3$, respectively. The difference may be in part due to different biases in the models, but also because the NAME data was for 2005-2006 (figure 2) in contrast to RIU and FMI that were for 2003 (figure 3). Computation of the $\Delta\mu$ statistic for difference numbers of lag and cumulative days show similar characteristics for the RIU and FMI models, with a peak in the difference of mean $[NO]$ with a lag of around $L = 8$ days after averaging over about $C = 4$ days. A very different result is obtained from the NAME model suggesting the importance of annual variation in meteorology.

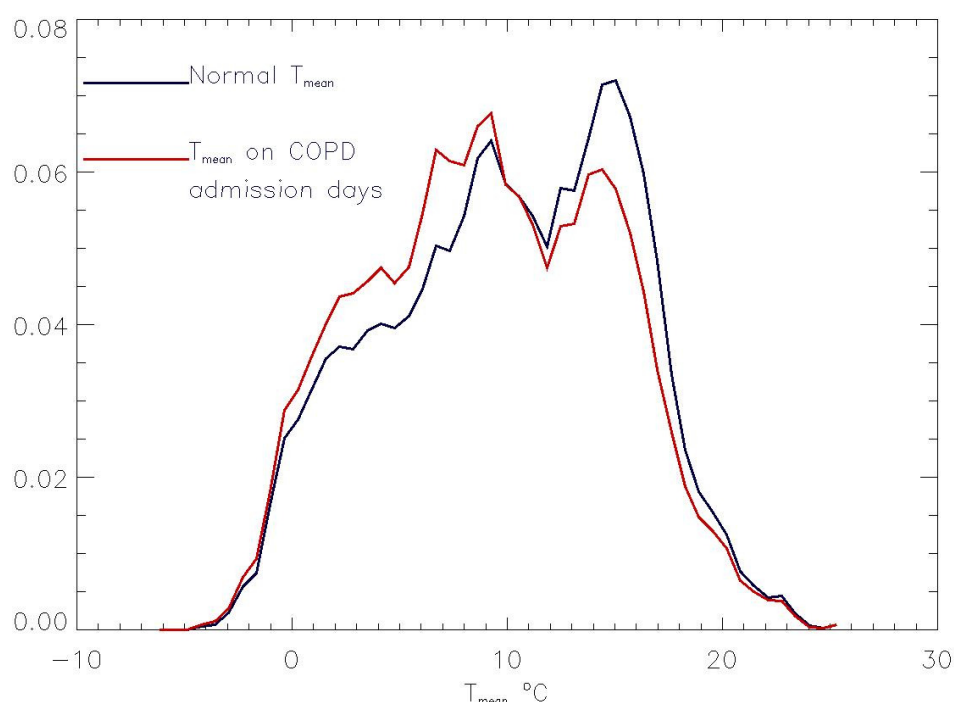


Figure 1. Normalised distributions of daily mean temperature T_{mean} estimated by NAME for 2005-2006.

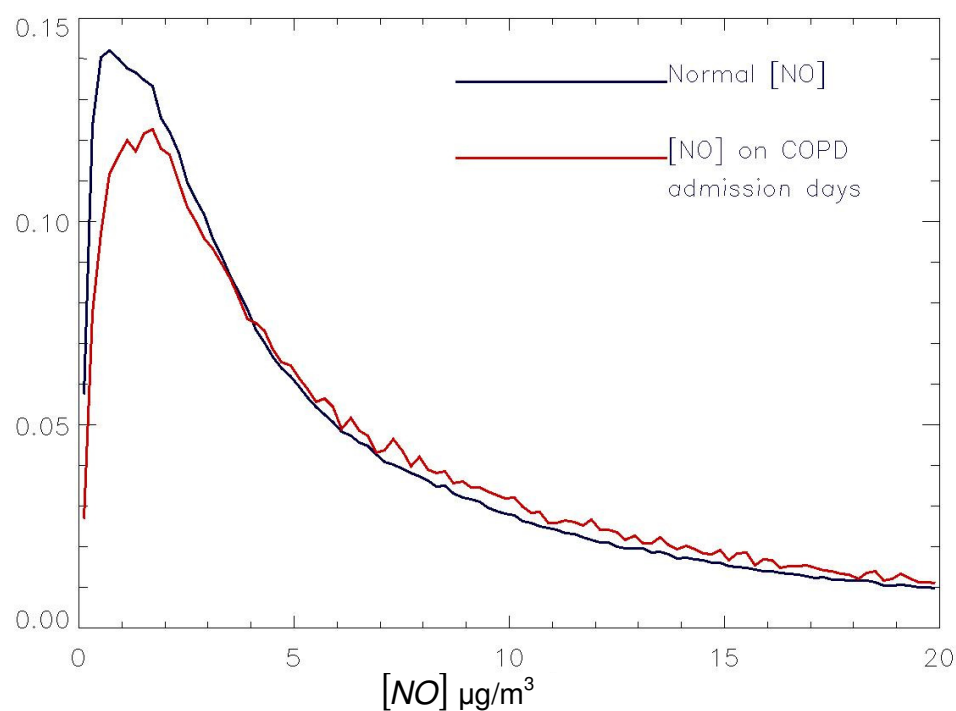


Figure 2. Normalised distributions of $[NO]$ estimated by NAME for 2005-2006.

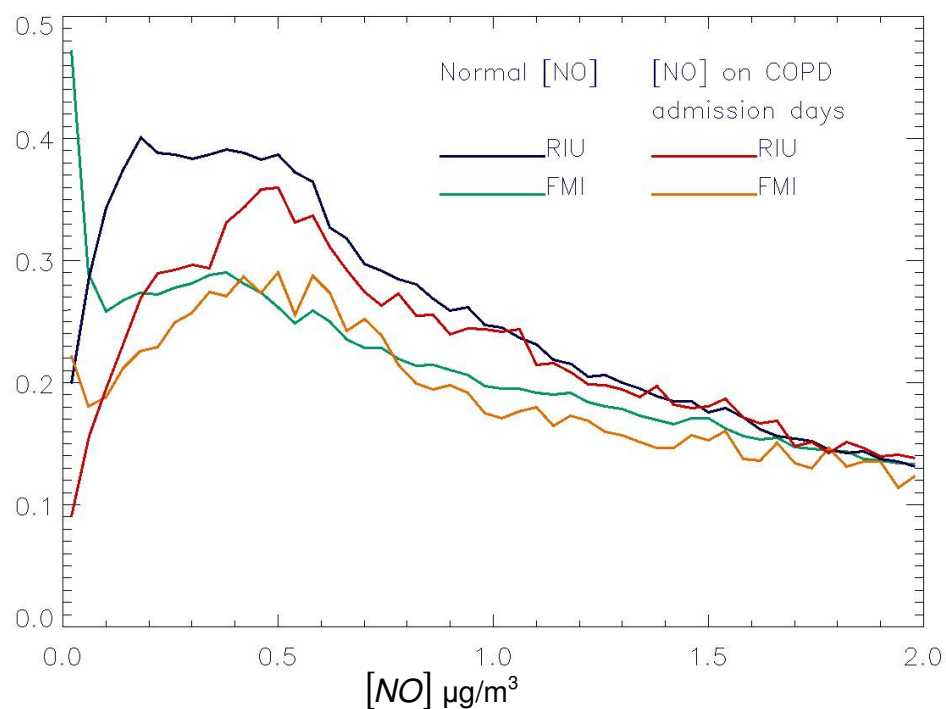


Figure 3. Normalised distributions of $[NO]$ estimated by RIU and FMI for 2003.

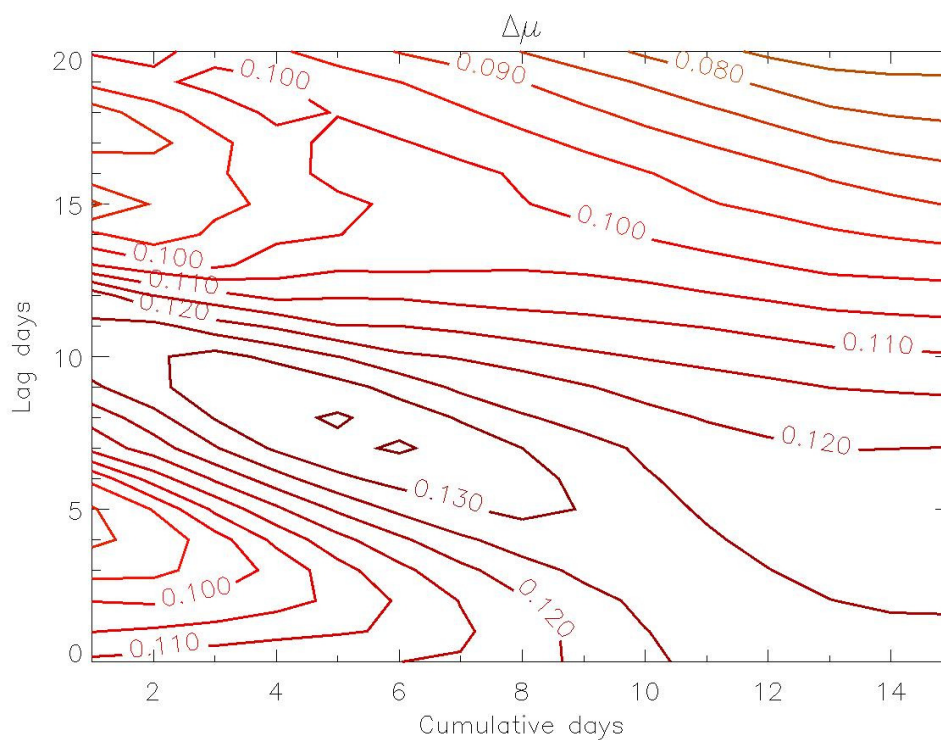


Figure 4. $\Delta\mu$ statistic for COPD hospital admissions for [NO] from the RIU model with lag days $0 \leq L \leq 20$ and cumulative days $1 \leq C \leq 15$.

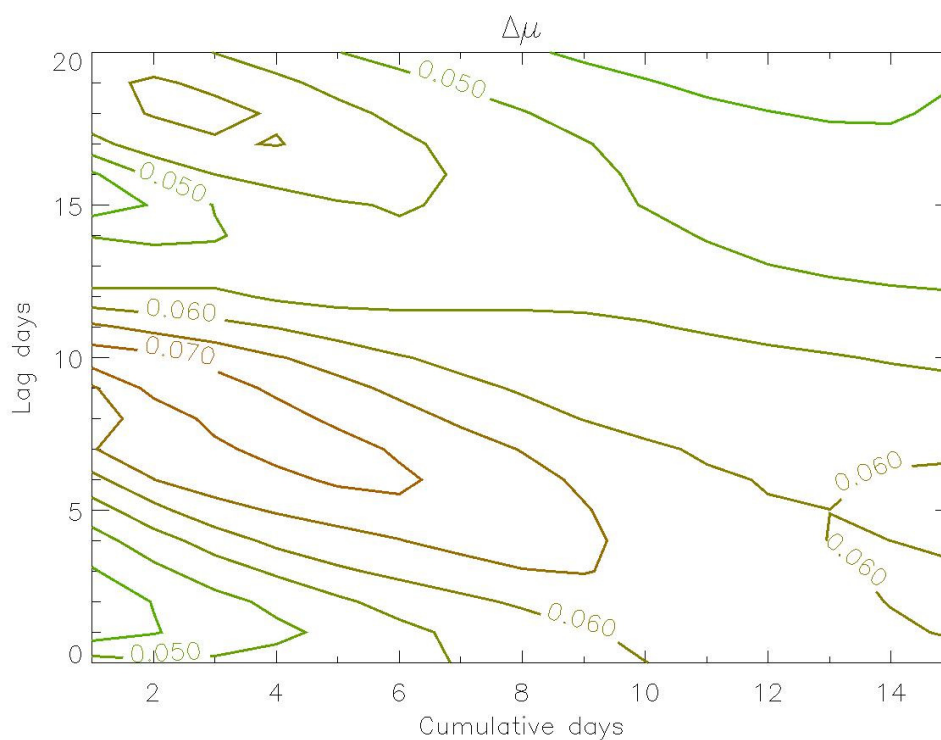


Figure 5. $\Delta\mu$ statistic for COPD hospital admissions for [NO] from the FMI model with lag days $0 \leq L \leq 20$ and cumulative days $1 \leq C \leq 15$.

2.4 Discussion

The magnitude of the effect of air pollution described here ($\Delta\mu > 13\%$ for $[NO]$ from RIU data) is similar to published effects of air pollution on respiratory admissions²¹. The results indicate that air pollution is linked to COPD hospital admission. They do not however show any causal effect of pollutant atmospheric concentrations on COPD admissions. Studies have been carried out to determine the physiological mechanisms of the effect of different pollutants on the lungs^{22,23} and have highlighted the importance of having a biochemical model to avoid erroneously linking confounding factors. In particular, weather is strongly correlated to air quality and separating their effects on COPD admissions statistically is difficult. McGregor et al.²⁴ (1999) have shown the association between weather type and levels of $[PM_{10}]$ and their conclusions support the COPD forecast model used by the UK Met Office¹⁰. The World Health Organization's air quality guidelines for Europe²⁵ contains descriptions of the health effects of $[NO]$ and $[HCHO]$ (formaldehyde), the later being also linked to COPD admissions using NAME model data. Nitric oxide, ozone and nitrogen dioxide are strongly linked by photochemistry²⁶ and the effects of these on health have been described²⁷. It is therefore important to consider frameworks for epidemiological studies using physiological models as described by Mindell and Joffe²⁸ (2004).

2.5 Conclusion

Simple descriptive analyses of distributions of pollutant concentrations provide a means of assessing the impact of air quality on COPD hospital admissions. Nitric oxide, estimated by the RIU, FMI and NAME models, provides the strongest indication of an effect on COPD admissions. However note that we do not suggest a causal link between this pollutant and COPD. The important correlations between pollutants and between weather and pollutants prevent the formulation of a simple statistical model, as do the important confounders and other none meteorological causes of COPD exacerbation.

Hospital admission for COPD symptoms is a relatively extreme outcome and this may be one reason why it is difficult to identify links with air quality in the above analysis. We have therefore conducted a study of COPD symptom exacerbation to investigate links.

3. Air quality and symptoms of COPD in Exeter and Honiton

3.1 Background

Within the scope of a diagnosis of Chronic Obstructive Pulmonary Disease (COPD) there is a heterogeneous range of clinical presentations and disease progression. Two pathological processes contribute to the progressive airflow limitation in COPD: (1) remodelling and narrowing of the small airways; (2) destruction of the lung parenchyma, with consequent destruction of the alveolar attachments of these airways – emphysema. Both the small airway remodelling and narrowing and the emphysema are due to chronic inflammation in the lung periphery²⁹. The key symptoms of COPD are breathlessness (dyspnoea), coughing and purulence of sputum. The triggers of exacerbation of these symptoms are associated with infections caused by bacteria and viruses³⁰, and there is growing evidence for the effect of pollutant upon COPD sufferers who exhibit greater sensitivity. An example of how weather conditions are also likely to contribute to these mechanisms is that in cold weather bronchoconstriction will contribute to reduction in the diameter of the airways, which may lead to increased breathlessness.

3.2 Aim

The object of this study is to investigate the correlation of modelled air quality with variations in the clinical symptoms of COPD reported by a group of patients in their local environment of residence in the Exeter area³¹.

3.3 Methods

During Winter 2008/09 75 patients were recruited to undertake a 16 week study. All received a questionnaire via a Blackberry smartphone and reported the severity of their symptoms daily using the EXACT-PRO³² patient reporting measure. Over the course of the study about 60% of patients experienced exacerbations (figure 6). Most of these exacerbations were not severe enough to require hospitalisation and so this data gives insight into variations of symptoms which are not usually reported. Over the study period, there were two cold periods lasting about a fortnight (figure 7); temperatures were low and relative humidity high, resulting in an elevated risk of COPD exacerbations, as forecast by the existing models used by the Met Office. The risk levels peaked in mid-February and were higher in Honiton than Exeter; this was due to the lower temperatures arising from the higher altitude at Honiton.

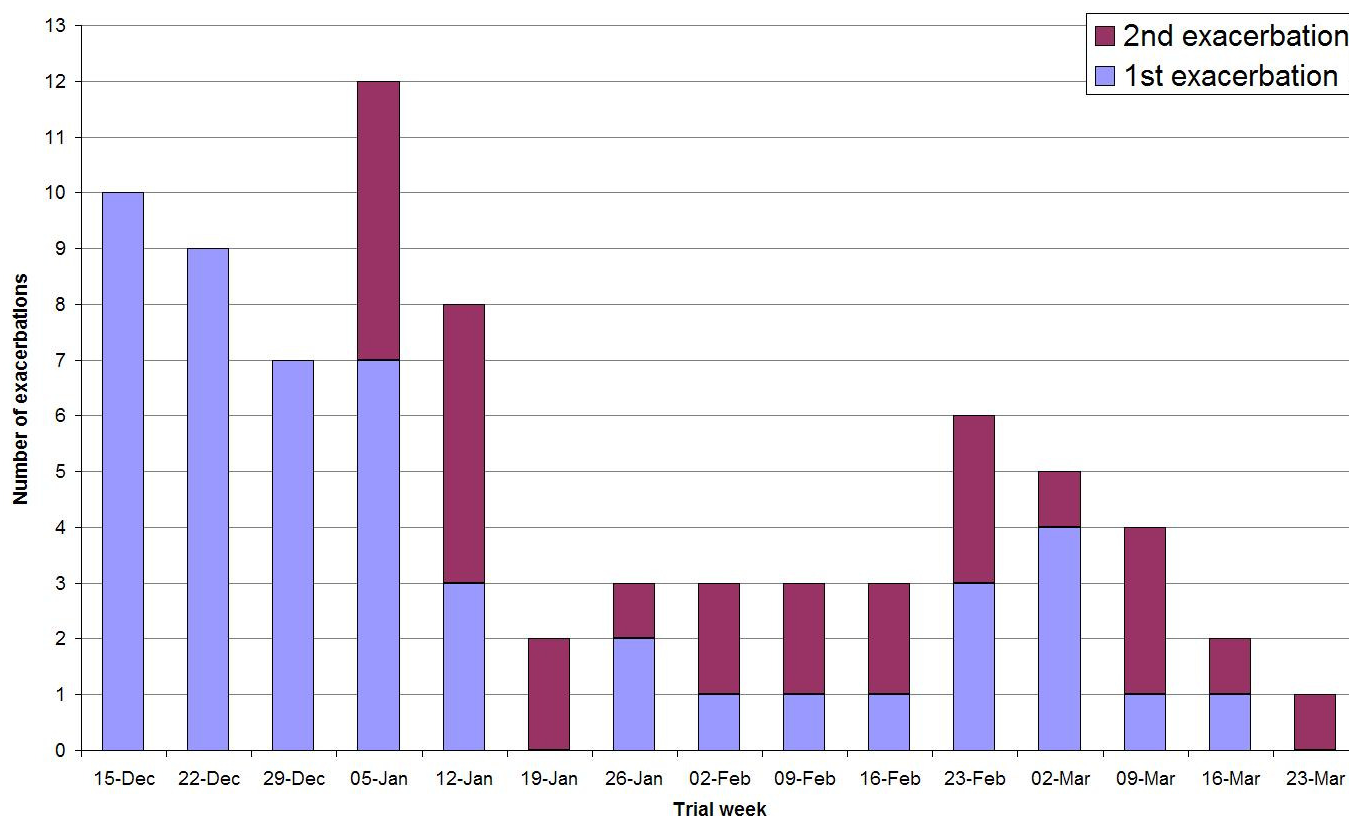


Figure 6. Count by trial week of 1st and 2nd exacerbations suffered.

The air quality simulations carried out for this study used the latest version of the Lagrangian Met Office NAME III model^{33,34}, driven with input from the Met Office Unified Model. The raw emissions inventory data used was drawn from a range of sources: the National Atmospheric Emissions Inventory (NAEI) was used over the UK, while the ENTEC inventory was used for other shipping data and European data was sourced from the European Monitoring and Evaluation Programme (EMEP). Over the UK mainland the emissions inventory was fitted onto a grid of 0.03 degrees in longitude and latitude. Hourly time series of pollutant concentrations levels were output for a range of locations corresponding to the places of residence of the COPD patients (figure 8).

The daily counts of exacerbation data and maximum hourly concentrations of pollutants, along with meteorological data, has been analysed using generalized additive models with the statistical program R³⁵, with the subroutine mgcv³⁶. The technique used³⁷ assumes a log-linear Poisson model where the outcome is a Poisson distribution with mean μ_t such that $\text{Log}(\mu_t)$ is a linear predictor, and where a pollutant might be included in the model with a lag that may range from 0 – 14 days typically. The parameters treated in this way were daily maximum hourly concentrations of the pollutants O₃, NO₂, SO₂ and PM₁₀, as well as the maximum air temperature.

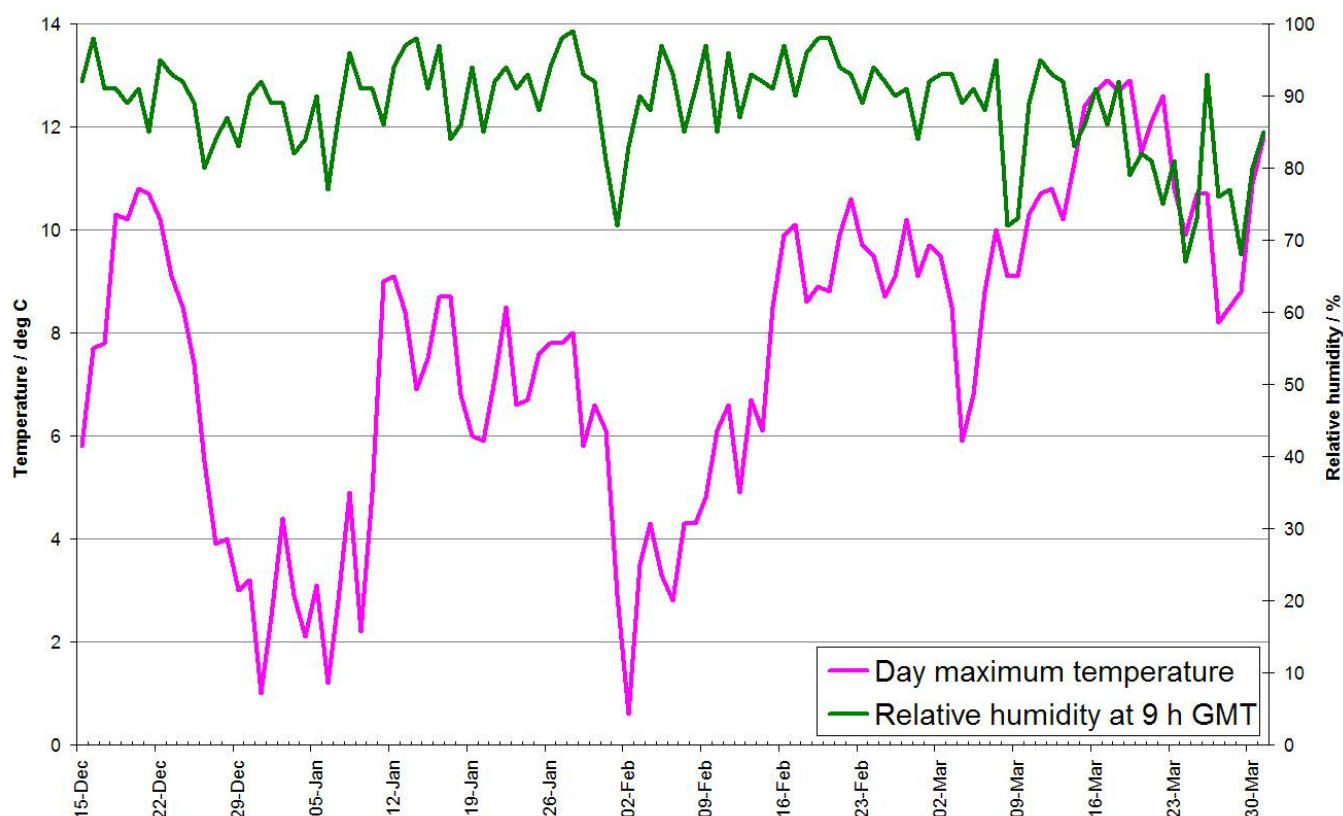


Figure 7. Daily weather parameters at Exeter for the study period 15 December 2008 to 31 March 2009.

3.4 Results

The study data showed that 65% of patients reported an exacerbation over the study period. Study of the home postcodes of patients reporting exacerbations has shown that 75% of those patients in Exeter suffered exacerbations, whereas only 42% living in Honiton and its outlying area reported exacerbations. Due to the variety of different phenotypes seen within COPD sufferers, not all patients are equally susceptible to exacerbations. However, when data from individual patients were analysed, some patients who did not experience significant exacerbations did nevertheless exhibit variations in their symptoms during the study period.

By using the maximum hourly concentration of nitrogen dioxide occurring each day, summed over a 5 day period, a simple generalized additive model was built which accounted for 41% of the daily variability of occurrence of exacerbations (table 2). Use of daily values of maximum PM₁₀ Particulate Matter concentrations accounted for 36% of the variability. These results suggest that ~40% of the deviance in numbers of daily exacerbations can be explained using a model which takes account of peak hourly

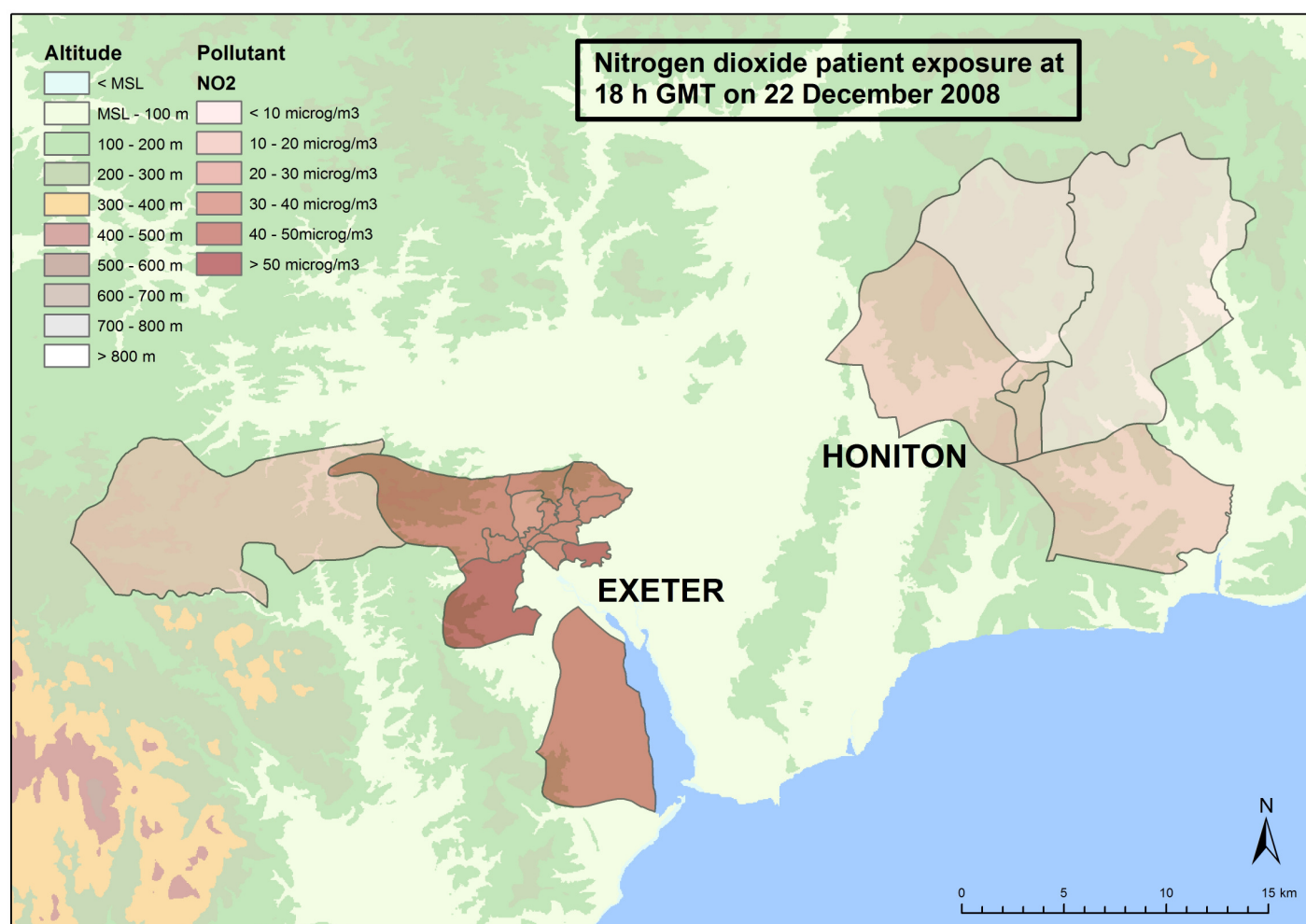


Figure 8. Patient exposure to nitrogen dioxide modelled by NAME by postcode sector of residence of the trial participants.

Table 2. p -values and deviance explained (R^2 -value) for three generalized additive models with time, ozone (O_3), temperature, nitrogen dioxide (NO_2) and particulate matter (PM_{10}); the results depend on the model used: NO_2 is significant in model 1 but not model 2; model 3 was the best model for PM_{10} which was not significant.

Model	1	2	3
Time	0.12	0.05	0.18
O_3 and temperature	0.05	0.06	0.15
NO_2	0.04*	0.13	-
PM_{10}	-	-	0.29
Deviance explained	41%	41.7%	35.6%

* significant parameter with $p < 0.05$

nitrogen dioxide concentrations, fitting time, daily maximum temperatures and ozone concentrations with smoothing functions as well.

The locations of the homes of patients were mapped using ESRI Arcview GIS software in order to understand which patients live within, or close to, the Exeter Air Quality Management Area (AQMA) where traffic on the city's main routes is a major cause of pollution. Analysis of patient data shows that 70% of the patients in Exeter lived within 100m of the AQMA in the lower-lying areas of Exeter where most traffic flows. It is clear that the modelled data fails to capture the peak levels of nitrogen dioxide occurring close to major roads in the AQMA (figure 9). This is to be expected, since the model resolution is around 8 km and is unable to accurately represent the high roadside concentrations of pollutants. The implication is that the concentrations of pollutants near to the homes of patients may be higher than the urban background levels modelled using regional air quality models such as NAME. Furthermore, if patients went outside on the main roads, it is likely that their personal exposure may well have been elevated. A similar observation is made by analysis of the home locations for patients in the Honiton area, where about 50% live close to the town centre which is affected by increased pollution from the nearby A30 and stationary traffic in the town centre.

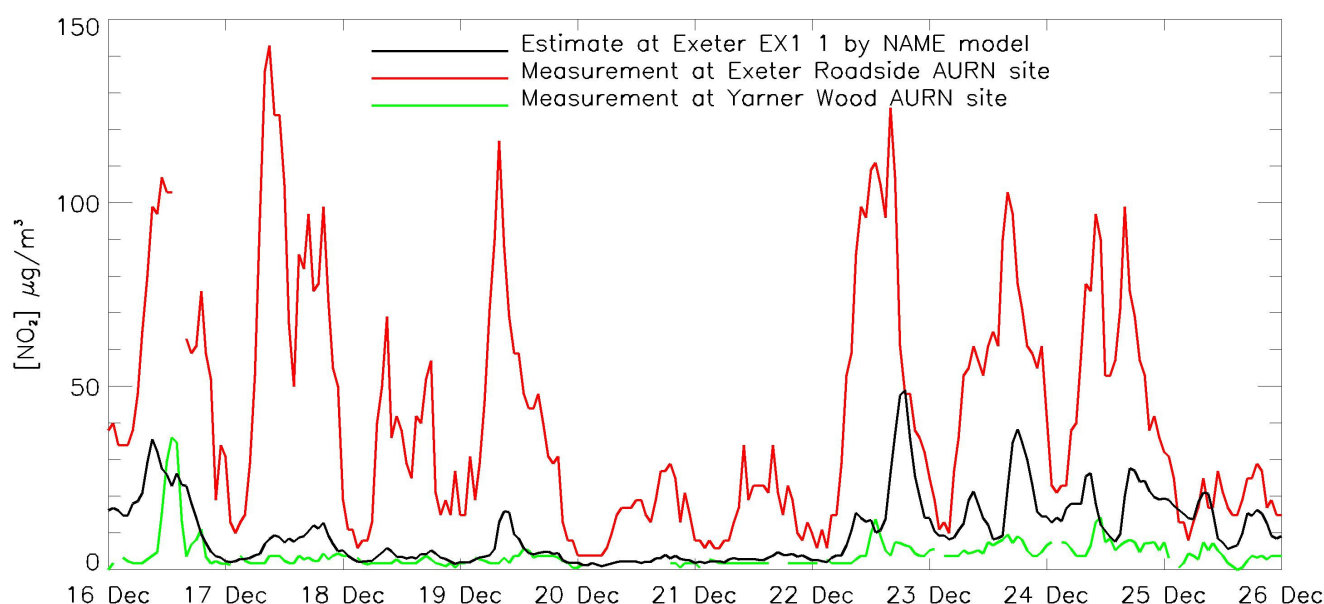


Figure 9. Comparison of modelled NO_2 concentrations in central Exeter with observations at Exeter Roadside (AURN roadside site) and at Yarner Wood (AURN rural site) over the period 16 to 25 December 2008.

3.5 Conclusions

The analysis of the data within this study is strongly suggestive of a relationship with air quality in Winter: 41% of the deviance in exacerbations of a group of COPD patients could be explained by variations in nitrogen dioxide levels that occurred over the short period of this study. There was some evidence of greater occurrence of exacerbations in patients whose home address was likely to be exposed to greater levels of traffic-generated pollution.

4. Improved COPD forecast algorithm incorporating atmospheric composition variables

The Met Office operates the Healthy Outlook service to patients with Chronic Obstructive Pulmonary Disease (COPD). The service consists in a weekly forecast of the risk of exacerbation to COPD patients, and since 2006 alerts have been delivered through automated telephone calls directly to patients. Making use of 11 years worth of hospital admissions data available from the Hospital Episode Statistics (HES) database, a model that predicts the risk to COPD patients due to the weather has been developed. As a result of this analysis, the model algorithm has been adopted as the Healthy Outlook algorithm that predicts the COPD risk attributable to the weather throughout the United Kingdom.

In addition to using weather parameters as predictors of COPD risk, the COPD risk attributable to air quality has been analysed using 2-year long time series of air pollutant levels, hospital admissions and weather elements. The results from this analysis was used to produce a new air quality dependent COPD model algorithm that was trialled using the MACC R-Ens median PM₁₀ forecasts over the period 15 June to 30 September 2011.

4.1 Introduction

Initial descriptive analyses of COPD emergency hospital admissions in the United Kingdom (UK) using the EURAD (RIU) and SILAM (FMI) air quality models, as well as the Met Office NAME, found that there was a link between risk of hospitalisation for COPD and air quality, with nitric oxide concentrations being the strongest predictor. Follow-on analyses of modelled air quality indicators against measured COPD exacerbation events using generalised additive models found the concentrations of nitrogen dioxide were a significant predictor of exacerbation events. It was therefore

proposed to repeat the COPD algorithm development analysis using atmospheric composition parameters as well as meteorological ones.

4.2 Hypotheses of the current weather-only model

One of the primary causes of COPD exacerbations is circulating Influenza-Like Illnesses (ILI). The greater the ILI rate, the greater the number of patients that will be ill and as a consequence suffer an exacerbation. This is evidenced by the close relationship between the ILI rate and the rate of COPD hospital admissions

The emergence of the flu virus and its subsequent build up in numbers through transmissions occurs over a period of months before patients suffer from ILI. Other research^b has also suggested that particular conditions in the Autumn months (cold/damp) cause greater ILI rates in the Winter. This seasonal emergence and transmission of ILI viruses suggests lags of up to 3 months between weather factors and impact on COPD patients' health.

Hence a component of the COPD model accounts for the long term (~months) hypothesis that weather promotes the emergence of Influenza-Like Illnesses (ILI).

It is not sufficient for there to be high rates of circulating viruses before there is an impact on COPD patients' health. It is also necessary for the patient's immune system to be stressed by other factors, including the weather. It is thought that stress of the immune system from heat loss occurs over a period of weeks which suggests lags of up to 1 month of the effect of weather on the patient's health. Indeed, research has demonstrated that peaks in COPD hospital admissions happen 10 to 12 days after a period of cold weather.

A second component of the COPD model accounts for the short term (~weeks) hypothesis that weather affects the COPD patient's immune system.

Despite the mechanisms concerning the emergence and transmission of ILI viruses and stress of the immune system, there remain important factors that affect the final risk that COPD patients will incur. Not least is the effect of acclimatisation that will mean that patients in the north of Scotland may better endure cold weather than patients in the south of England. Acclimatisation here means physiologic and social adaptation. In addition to these possible physiologic differences between populations of different regions, behaviour is an important confounder. It is likely that a population in a region with a cold climate will be adapted behaviourally and will have better insulation, both in

^b Personal communication, Oregon State University.

terms of what they wear as well as for their dwellings. However, there are also important differences in behaviour dependent on socio-economic factors and cultural factors. The heterogeneity of the UK population, and the important migrations both internally as well as immigration and emigration, mean that it is very difficult to examine the impact of the weather on COPD patients' health by including socio-economic and cultural behavioural characteristics of each geographical area. It is also beyond the scope of the COPD model to attempt to separate out the purely physiologic acclimatisation from the behavioural effects. Hence behavioural and acclimatisation effects are not included.

Excluding these population characteristics from the model has the significant advantage of allowing the development of a COPD algorithm that is purely weather dependent (and so draws on the Met Office's key expertise). It also means that the COPD risk calculation is homogeneous over the whole of the UK. This risk can be interpreted by the individual patient with full knowledge of their own socio-economic, cultural and ethnic circumstances rather than the risk being adjusted for some mean characteristics of the local population.

4.3 Preparation of health data

The Quality and Outcomes Framework (QOF) provides the number of registered patients and the number of patients with COPD for each family doctor (GP) in the United Kingdom, available at www.gpcontract.co.uk. Data for 2008 has been uploaded from QOF to be used in the development of the COPD model. All 10167 GP surgeries in the United Kingdom have been grouped in to clusters according to their postcode districts to obtain the number of patients with COPD and the total number of registered patients for each cluster. However, some postcode districts contained no GP surgeries while there may be resident COPD patients registered at a GP of a neighbouring district. Therefore the numbers of registered patients have to be distributed and the COPD prevalence interpolated to provide values for the few postcode districts with no GP.

First, the COPD prevalence for each surgery cluster is calculated as the weighted average of the COPD prevalence values from each GP surgery in the cluster. Next, the prevalence at a postcode district with no GP is obtained from inverse-distance interpolation. Finally, the number of registered COPD patients in each postcode district is estimated by mapping the total GP registered population according to the known UK population distribution and using the prevalence to obtain the number of COPD patients for each district (figure 10).

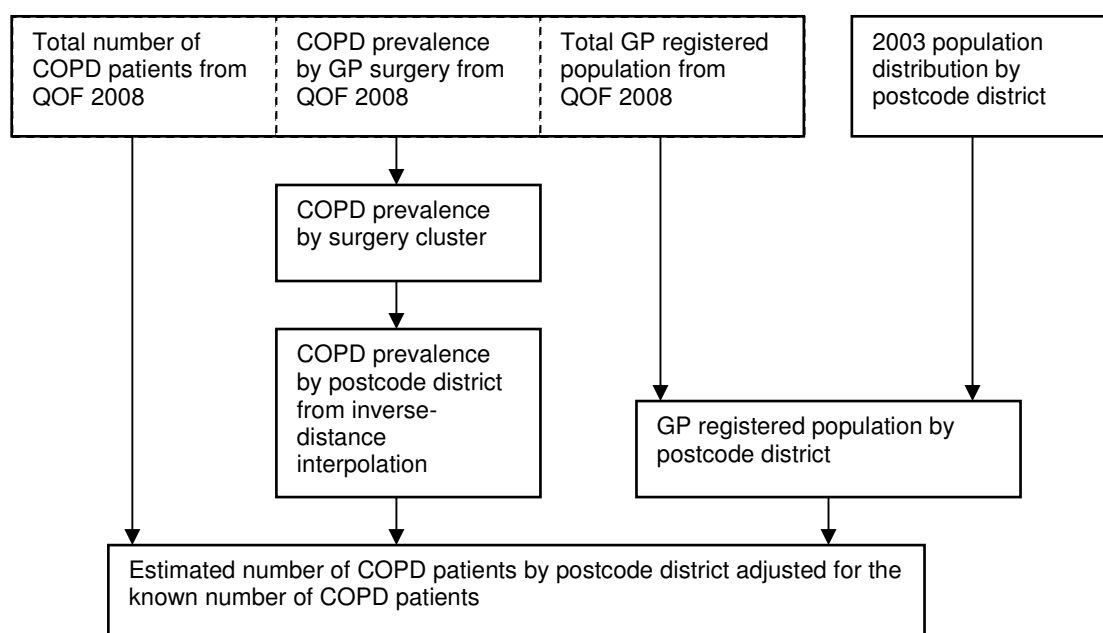


Figure 10. Processing the QOF 2008 data and the 2003 population census figures to obtain the estimated number of COPD patients by postcode district.

While the COPD prevalence values for postcode districts are estimates, these have been compared qualitatively to the original surgery cluster prevalence values. There were no observable significant differences except where the interpolation has estimated for districts with no GP.

The HES (Hospital Episode Statistics) database consists of records of individual hospital admissions in England. Emergency COPD admissions have been extracted from the database, i.e. admissions with the primary diagnosis codes J40 to J44 (ICD-10^c) detailed in table 3. Counts of emergency COPD hospital admissions have then been summed for each day and postcode district.

Table 3. Chronic lower respiratory diseases selected as COPD primary diagnoses.

ICD-10	Diagnosis definition
J40	Bronchitis, not specified as acute or chronic
J41	Simple and mucopurulent chronic bronchitis
J42	Unspecified chronic bronchitis
J43	Emphysema
J44	Other chronic obstructive pulmonary disease

^c apps.who.int/classifications/apps/icd/icd10online

The COPD risk is measured as the rate per annum of COPD admissions in each district and for each day, calculated from the time interval between admissions (i.e. the frequency or number of admissions) and the number of COPD patients estimated from QOF for 2008.

4.4 UK air quality exposure assessment

For several pollutants, it has been found that there is a model bias (systematic measured difference from model) that relates to urbanisation. Air quality forecasts have been adjusted according to how urbanised the vicinity of a place of residence is. This adjustment provides a better estimate of population exposure to different atmospheric pollutants. This is illustrated by figure 11.

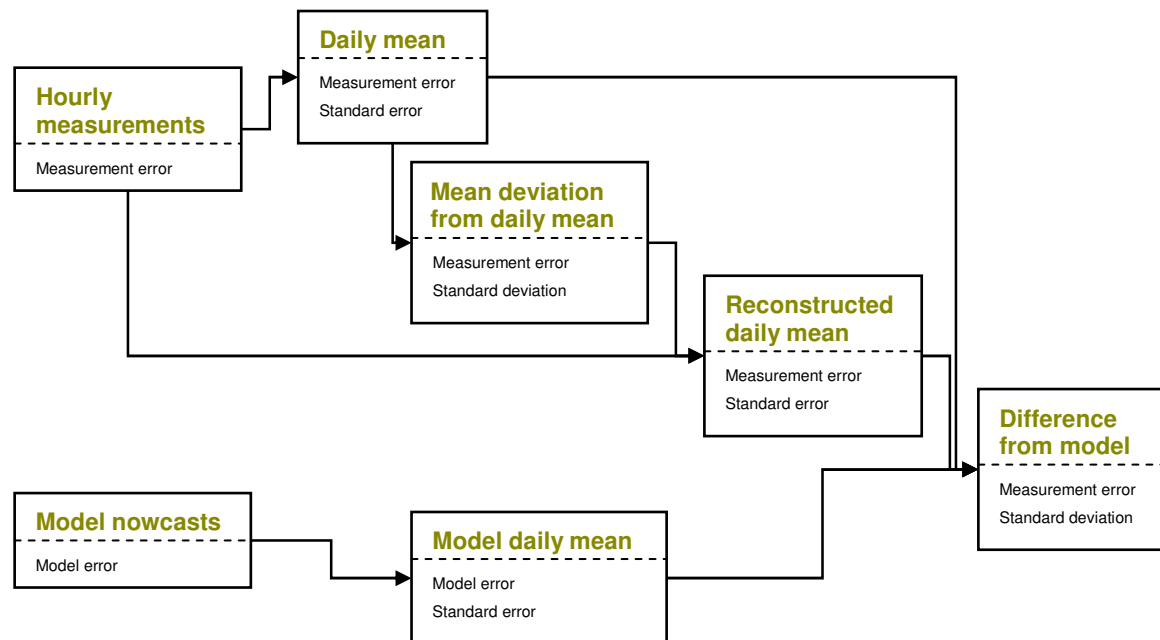


Figure 11. Comparative analysis of AURN measurements and model nowcasts and forecasts.

Given hourly measurements of pollutant X expressed with their error as $[X]_h \pm e_{h;X}$, the mean measurement for the day is:

$$\ln[X]_d = \frac{1}{24} \sum_{h=1}^{24} \ln[X]_h$$

and the associate total square error for the mean for the day is:

$$E_{d;X}^2 = \underbrace{\frac{1}{24^2} \sum_{h=1}^{24} \frac{e_{h;X}^2}{[X]_h^2}}_{\text{measurement square error}} + \underbrace{\frac{1}{24 \times 23} \sum_{h=1}^{24} (\ln[X]_d - \ln[X]_h)^2}_{\text{standard square error}}$$

For each hour of the day, the mean deviation from the daily mean is:

$$\bar{\Delta}_{h;X} = \sum_{d=1}^n \frac{\ln[X]_h - \ln[X]_d}{E_{d;X}^2} \bigg/ \sum_{d=1}^n \frac{1}{E_{d;X}^2}$$

and the associated total variance for the mean deviation from the daily mean is:

$$s_{h;X}^2 = \underbrace{\left(\sum_{d=1}^n \frac{e_{h;X}^2}{[X]_h^2 E_{d;X}^4} + \sum_{d=1}^n \frac{1}{E_{d;X}^2} \right)}_{\text{measurement square error}} \bigg/ \left(\sum_{d=1}^n \frac{1}{E_{d;X}^2} \right)^2 + \underbrace{\frac{n}{n-1} \sum_{d=1}^n \frac{(\bar{\Delta}_{h;X} - \ln[X]_h + \ln[X]_d)^2}{E_{d;X}^2}}_{\text{variance}} \bigg/ \sum_{d=1}^n \frac{1}{E_{d;X}^2}$$

Air quality monitoring often returns hourly measurements for a day with missing values. The daily mean can be established by the reconstructed mean for the day given as:

$$\ln[X]_d = \sum_{h=h_1}^{h_n} \frac{\ln[X]_h - \bar{\Delta}_{h;X}}{s_{h;X}^2} \bigg/ \sum_{h=h_1}^{h_n} \frac{1}{s_{h;X}^2}$$

with associated total square error for the reconstructed mean for the day given as:

$$E_{d;X}^2 = \underbrace{\left(\sum_{h=h_1}^{h_n} \frac{e_{h;X}^2}{[X]_h^2 s_{h;X}^4} + \sum_{h=h_1}^{h_n} \frac{1}{s_{h;X}^2} \right)}_{\text{measurement square error}} \bigg/ \left(\sum_{h=h_1}^{h_n} \frac{1}{s_{h;X}^2} \right)^2 + \underbrace{\frac{1}{n-1} \sum_{h=h_1}^{h_n} \frac{(\ln[X]_d - \ln[X]_h + \bar{\Delta}_{h;X})^2}{s_{h;X}^2}}_{\text{standard square error}} \bigg/ \sum_{h=h_1}^{h_n} \frac{1}{s_{h;X}^2}$$

If the model casts of pollutant X are expressed as $[X]_h \pm e'_{h;X}$, then the model mean for the day is (given 8 casts per day):

$$\ln[X]_d' = \frac{1}{8} \sum_{h \in \{3 \bmod 3\} \cap [0;24]} \ln[X]_h'$$

and the associated total square error for the model mean for the day is:

$$E_{d;X}'^2 = \underbrace{\frac{1}{8^2} \sum_h \frac{e_{h;X}'^2}{[X]_h'^2}}_{\text{model square error}} + \underbrace{\frac{1}{8 \times 7} \sum_h \left(\ln[X]_d' - \ln[X]_h' \right)^2}_{\text{standard square error}}$$

The measured difference from the model (which is the exact opposite of the model bias) is given as:

$$\Delta \ln[X] = \sum_{d=1}^n \frac{\ln[X]_d - \ln[X]_d'}{E_{d;X}^2} \bigg/ \sum_{d=1}^n \frac{1}{E_{d;X}^2}$$

with associated total variance for the difference from the model given as:

$$s^2_{\Delta \ln[X]} = \underbrace{\left(\sum_{d=1}^n \frac{1}{E_{d;X}^2} + \sum_{d=1}^n \frac{E_{d;X}'^2}{E_{d;X}^4} \right) / \left(\sum_{d=1}^n \frac{1}{E_{d;X}^2} \right)^2}_{\text{measurement square error}} + \underbrace{\frac{n}{n-1} \sum_{d=1}^n \frac{\left(\Delta \ln[X] - \ln[X]_d + \ln[X]_d' \right)^2}{E_{d;X}^2}}_{\text{variance}} / \sum_{d=1}^n \frac{1}{E_{d;X}^2}$$

The regression of the measured difference from model $\Delta \ln[X]$ against the degree of urbanisation (defined by the proportion that is built up of the surface area of a postcode district) provides an urbanisation dependent adjustment coefficient that better estimates the air quality exposure of the COPD patients residing within the district.

4.5 Method

Following from the reviews of and recommendations from the latest COPD algorithm development (2009), a simple stepwise linear regression method was used to analyse COPD emergency hospital admission rates r against suitably transformed parameters X_i , X_i' , X_i'' of meteorology and atmospheric composition.

The general linear model is:

$$\ln r = B + \underbrace{\sum_i a_i X_i}_{\text{UK}} + \underbrace{\sum_i a_i' X_i'}_{\text{PCA}} + \underbrace{\sum_i a_i'' X_i''}_{\text{PCD}} + \varepsilon$$

where ε is the residual to be minimised, the steps being first to compute coefficients a_i for the UK as a whole, next coefficients a_i' based on rates for postcode areas PCA and finally coefficients a_i'' based on rates for postcode districts PCD, with B a constant.

At each step the coefficient a is selected if it satisfies the t-test $|t| \geq t_{crit}$ for the null hypothesis h_0 with alternative hypothesis h_a such that:

$$\text{I } \begin{cases} h_0 : a = 0 \\ h_a : a \neq 0 \end{cases} \quad \text{II } \begin{cases} h_0 : a = 0 \\ h_a : a \geq 0 \end{cases}$$

The 2-tailed t-test (I) is used for meteorological parameters of temperature, relative humidity and pressure, while the 1-tailed t-test (II) is used for other meteorological parameters and all parameters of atmospheric composition. For this purpose, t_{crit} is calculated to reject h_0 with a $p \leq 0.1$ probability of error using the number of weeks analysed for the degrees of freedom.

4.6 Results

The analysis provides a list of significant parameters that are subsequently used in the COPD algorithm to deliver the Met Office COPD forecasts. These include a lag L , a cumulative period C along with the regression coefficient a . UK results (table 4) are computed on the strength of the measurement of hospitalisation risk over the whole of England, while PCA results (table 5) take into account spatial variations in the hospitalisation risk with respect to spatial variations of weather and air pollution exposure. Analysis using a probability of error of $p \leq 0.05$ returned the three UK weather parameters only (and no PCA parameters) (table 6).

Table 4. UK results with $p \leq 0.1$.

Parameter	Lag L	Cumulative period C	Regression coefficient a
Maximum temperature	5 days	18 days	-0.93
PM ₁₀ particulate matter	0 days	9 days	0.050
Surface pressure	0 days	1 day	-0.0185
Precipitation	57 days	17 days	1240
Nitrogen dioxide	88 days	5 days	0.065
Ozone	33 days	32 days	0.0195

Table 5. PCA results with $p \leq 0.1$.

Parameter	Lag L	Cumulative period C	Regression coefficient a
Maximum temperature	3 days	19 days	-1.61
Mean temperature	0 days	20 days	-3.3
Minimum temperature	0 days	18 days	-6.8
Carbon monoxide	0 days	21 days	10.0
Relative humidity	6 days	91 days	52
Nitrogen dioxide	0 days	91 days	28
Nitric oxide	45 days	91 days	15.0
Wind speed	0 days	40 days	23
Precipitation	21 days	91 days	54×10^4
Sulphur dioxide	22 days	58 days	22

Table 6. Results with $p \leq 0.05$.

Parameter	Lag L	Cumulative period C	Regression coefficient a
Maximum temperature	5 days	18 days	-0.93
Surface pressure	4 days	8 days	0.024
Precipitation	61 days	10 days	850

The UK results show that PM_{10} , NO_2 and O_3 all are predictors of risk to COPD patients. Furthermore, PCA results include CO , NO and SO_2 . It can be seen that more parameters were selected at the higher spatial resolution (PCA) than at UK level. The PCD analysis was not carried out at this stage. These results suggest that, with even higher spatial resolution, the PCD level analysis may yield significant results especially given the argument of the localised effect of atmospheric pollution in urban areas.

For the purpose of delivering the Met Office COPD forecasts, only risks of exposure with lags of up to 1 month were considered. This more selective analysis returned the first three UK parameters (c.f. table 4) followed by maximum, mean and minimum temperatures from the PCD level analysis.

For the purpose of the trial, the COPD forecasts using MACC R-Ens median air quality forecasts for PM_{10} are visualised by (a) plots of the predicted risk of COPD hospital admission for each PCA with the exposure contribution for each parameter in the model, and (b) a map of the predicted change in total exposure risk from the previous week colour-coded by the parameter that contributes most to that exposure risk. Two forecasts are presented here.

18 August 2011. In London, during the preceding week and the following few days, the PM_{10} concentration has been steadily rising from ~ 10 to $\sim 40 \mu g/m^3$ (figures 12 and 13). In contrast, the daily maximum temperature, represented on the same scale of exposure risk, varies some 4 to 5 times more than the exposure risk associated with PM_{10} concentrations. A peak daily maximum temperature of $30^\circ C$ can be seen on 2 August and this drops to $14^\circ C$ on 18 August. (To be noted that the weather parameters used here are health exposure parameters computed from local weather observing sites.) The increase in PM_{10} levels is equivalent to a drop of 2 or $3^\circ C$ in maximum temperature. The predicted COPD hospital admission risk (bold green line) is relatively low on and around 18 August. This is because of the lag between exposure and risk impact: the low impact is due to the warmer weather around 2 August and the lower PM_{10} levels 5 to 9 August.

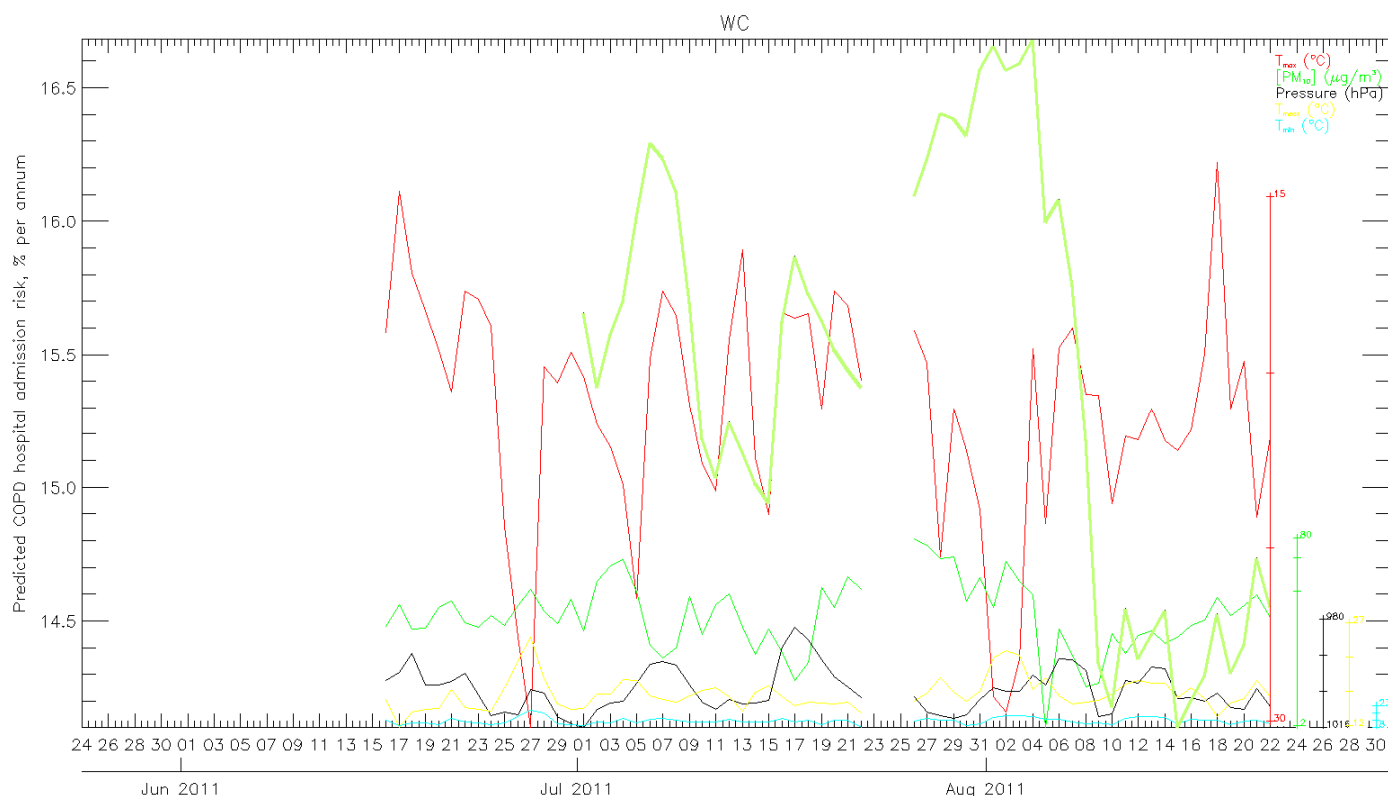


Figure 12. COPD forecast as plot of predicted COPD hospital admission risk for the centre of London (WC) on 18 August 2011 using the Met Office NAME air quality model.

The map representation of exposure (figures 14 and 15) are useful in that they highlight the areas where risk exposure has increased from the previous week. On 18 August the area affected consisted of west of London, the south-central region and the Midlands. The main contributors to the increase in risk are a lowering of maximum temperature and an increase in PM₁₀ levels. Even in the Summer, one of the main contributors to the increase in risk remains drops in temperature with increases in levels of PM₁₀ having an equivalent effect.

26 September 2011. At the end of the trial using the MACC R-Ens PM₁₀ data, there were no increases in risk exposure from the previous week. The maximum temperature in London increased from 16 °C on 18 September to 27 °C as forecast on 30 September (figures 16 and 17). This increase in temperature has by far reduced the total risk exposure when compared to the variations in risk from exposure to PM₁₀ alone. The predicted COPD hospital admission risk is also lower around 26 September compared to earlier in the month, but due to the lag this is attributed to the maximum temperatures in the first half of September that were somewhat higher than those at the end of August.

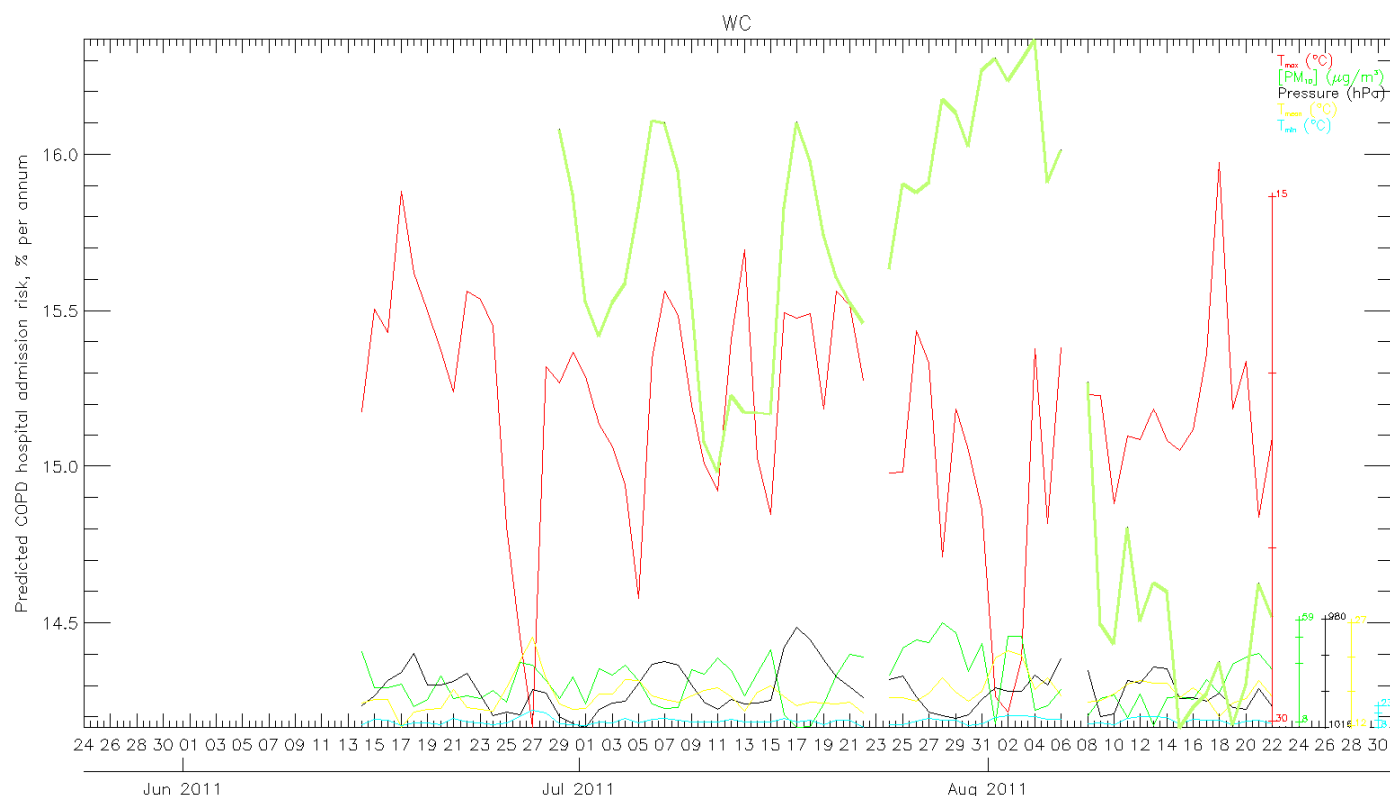


Figure 13. COPD forecast as plot of predicted COPD hospital admission risk for the centre of London (WC) on 18 August 2011 using the MACC R-Ens air quality model median.

This demonstrates how much more dependent the risk of COPD hospital admission is on temperature than on PM₁₀ levels.

5. Conclusion

MACC air quality forecasts have been included in the Met Office COPD forecast service as a trial. While it has been hypothesised that typical variations in atmospheric air quality affects the health of COPD patients, no strong evidence has been found to support this hypothesis. The analysis of several years worth of COPD hospital admissions in England with respect to local air quality has indicated that air quality may have an effect on the health of COPD patients (though not statistically strong). The conclusion from this initial analysis of hospital admissions was that the health impact of air quality may not result in hospital admission, but in the deterioration of COPD patients' health through mild to moderate exacerbations. Therefore, the analysis of exacerbation data of a cohort of 75 patients residing in Exeter and Honiton was carried out with high resolution air quality exposure estimates. This analysis of exacerbations has resulted in a plausible model of the impact of air quality, however the results were still statistically weak mainly

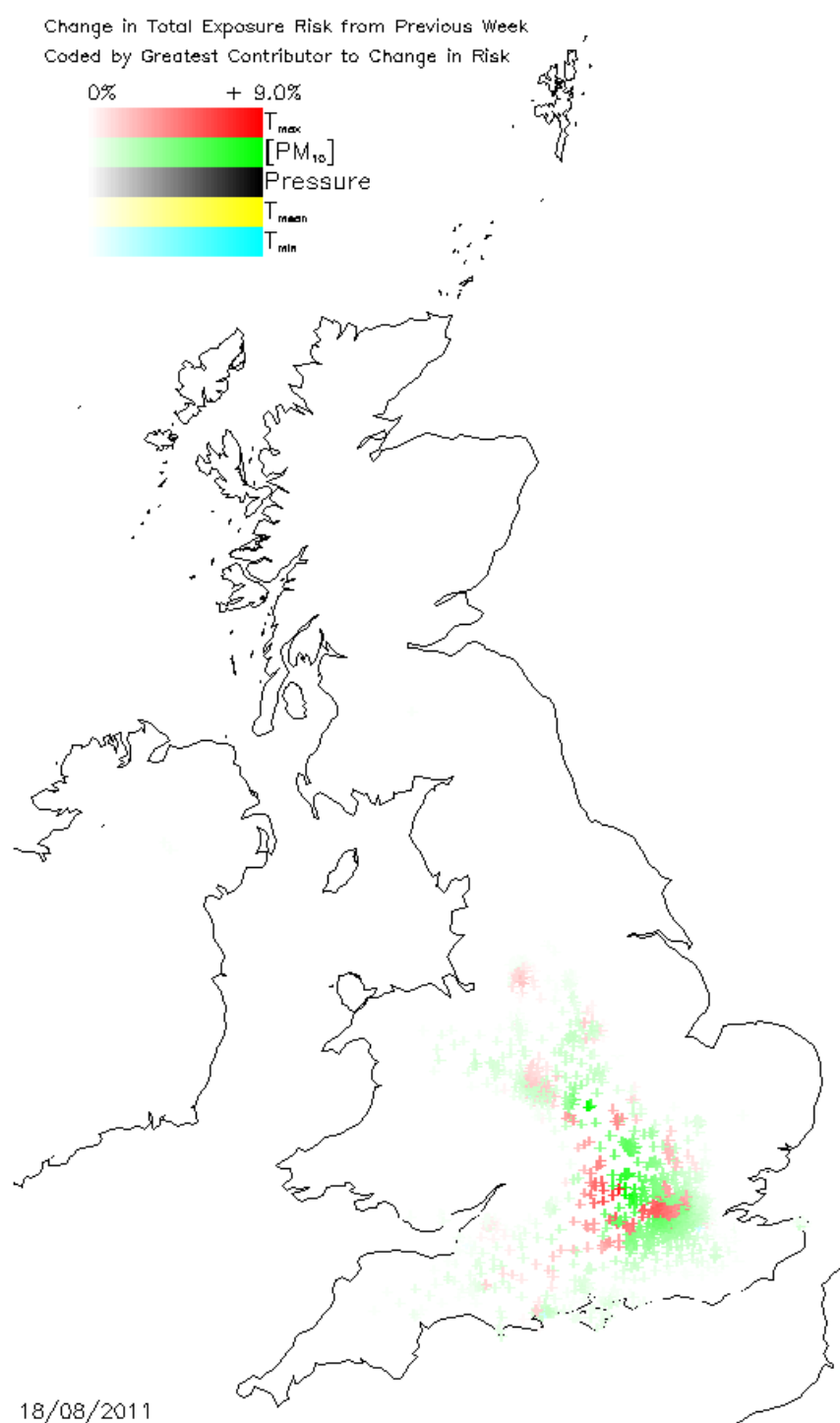


Figure 14. COPD forecast as map of predicted change in total exposure risk from previous week on 18 August 2011 using the Met Office NAME air quality model.

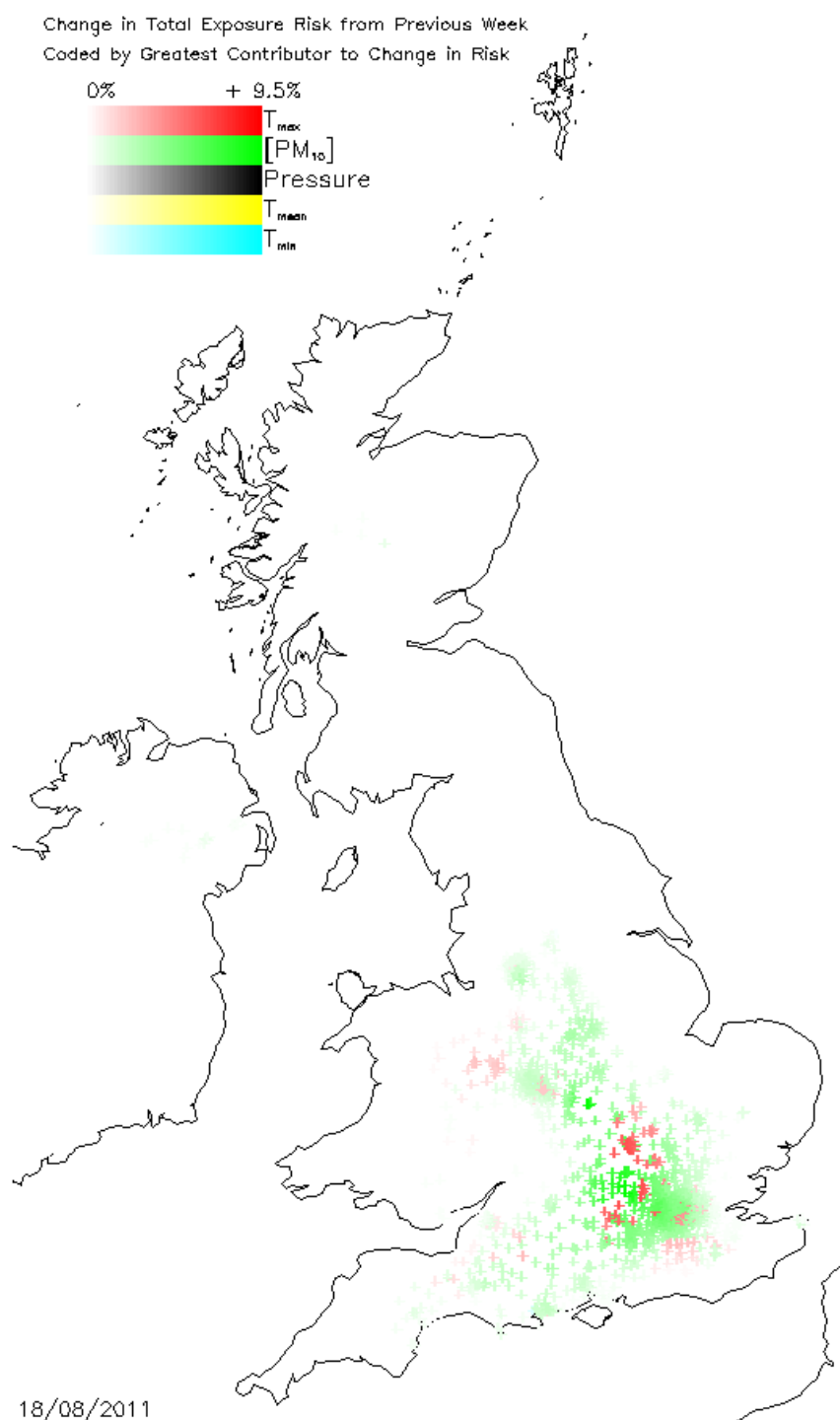


Figure 15. COPD forecast as map of predicted change in total exposure risk from previous week on 18 August 2011 using the MACC R-Ens air quality model median.



Figure 16. COPD forecast as plot of predicted COPD hospital admission risk for the centre of London (WC) on 26 September 2011 using the Met Office NAME air quality model.

because of the small number of patients of the cohort. Strong statistical evidence is required to support a direct-to-patient COPD service. Finally, taking the results from both these analyses into perspective, the analysis that had been carried to develop the existing COPD forecast (dependent on weather factors only) has been repeated with a relaxed selection criterion: weather and air quality parameters have been included in the model if they satisfy rejecting the null hypothesis that the parameter is not a predictor of the residual variation in COPD hospital admission risk with a probability $p \leq 0.1$. This allowed the inclusion of the MACC PM₁₀ forecast R-Ens median as a predictor of COPD risk. Yet, the PM₁₀ concentration is only a small contributor to the total risk of exposure and compared to the risk due to low maximum temperatures. A COPD alert is unlikely to be triggered on the basis of high PM₁₀ concentrations, unless these are exceptionally high or contribute significantly to the risk due to concurrent low temperatures.

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Figure 17. COPD forecast as plot of predicted COPD hospital admission risk for the centre of London (WC) on 26 September 2011 using the MACC R-Ens air quality model median.

quality on COPD hospital admissions') and from Peter Murkin and Drs. Tish Laing-Morton and David Halpin for their analysis and clinical insights for section 3 ('Air quality and symptoms of COPD in Exeter and Honiton').

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