The Influence of Air Quality on COPD Hospital Admissions

A report for GEMS

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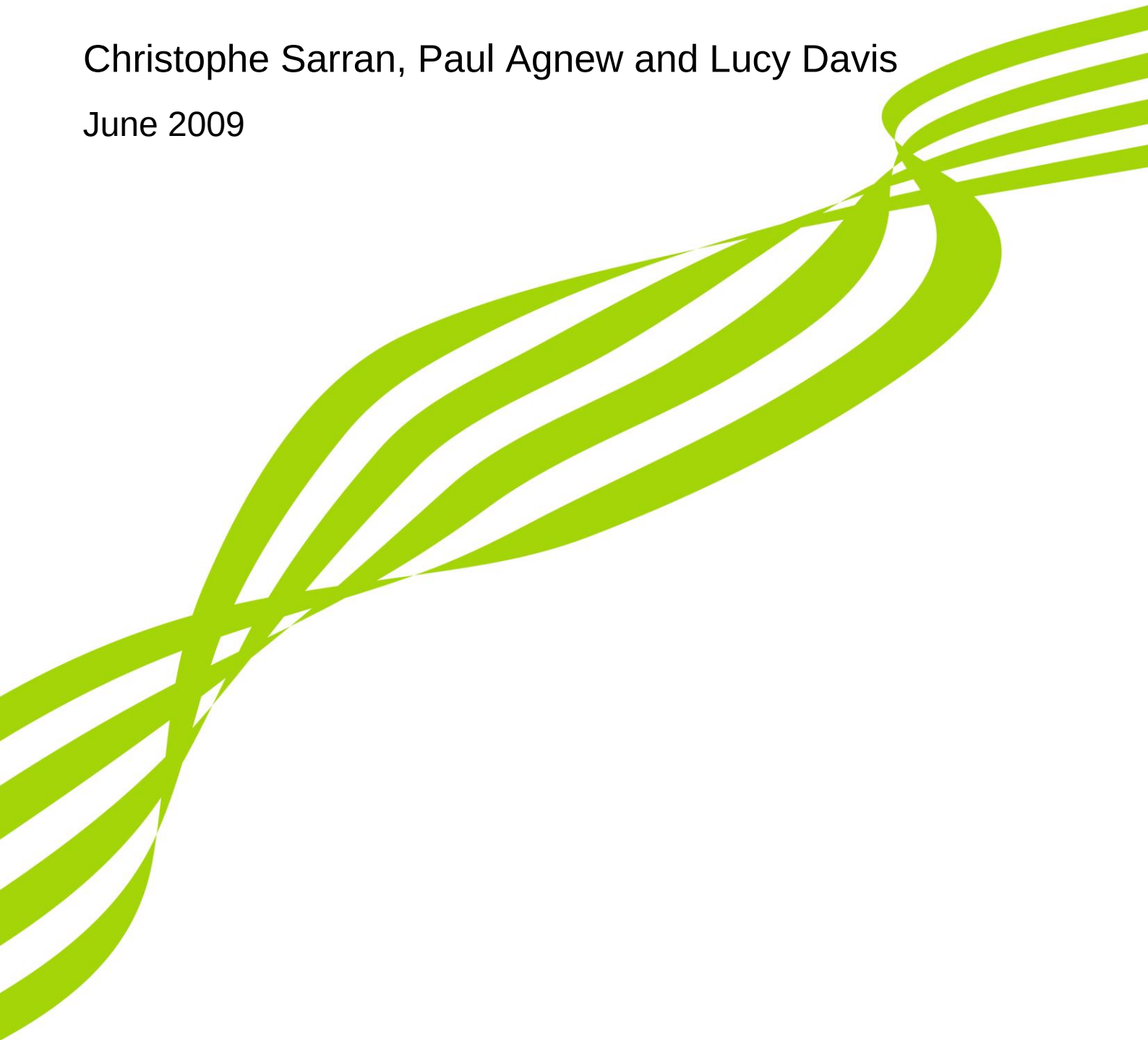

Executive Summary

This report summarises the results of a study investigating the links between air quality and UK hospital admissions for COPD. Air quality observations and hospital admission data have been correlated over the ten year period from April 1997 to February 2007. Air quality model data from two sources has also been used to investigate links with admissions. Data from the UK NAME AQ model (for 2005 and 2006) and two models (SILAM and EURAD) from the GEMS RAQ reanalysis ensemble (for 2003) were used for this analysis. No link was identified between the air quality observation data and COPD hospital admissions. However a link with admissions was found with the model data, with nitric oxide providing the strongest signal as a predictor.

Met Office

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1. Introduction

The Regional Air Quality (RAQ) sub-project of GEMS (Global Earth-System Monitoring using Satellite and in-situ data) has successfully delivered an ensemble of air quality forecasts which are hosted at ECMWF and updated on a daily basis. Eleven models contribute to the ensemble and the ensemble median is also calculated and displayed. Tasks 6.4. and 6.6. of RAQ concern studies into the link between air quality and health, plus an assessment of the value of the GEMS data in forecasting health impacts. In conducting this research we have drawn on the experience within the Met Office of developing a forecast service to anticipate the likelihood of health problems for people suffering from Chronic Obstructive Pulmonary Disease (COPD). The incidence of COPD increases during the winter months and is generally associated with extended periods of low temperature. Exacerbation of symptoms 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.

There are 100 000 COPD related hospital admissions in England and £ 600 million per year is spent by the UK National Health Service (NHS) to provide care to people with COPD. Hence even a small reduction in the proportion of sufferers requiring admission to hospital can have a significant impact on health care requirements at a national scale. The UK Met Office COPD service[1] provides COPD patients an improved quality of care, whilst aiming to reduce hospital admissions. COPD patients are alerted in advance of high risk periods so as to take appropriate self-care measures. Patients are provided with detailed information on how to stay well and the means to monitor the temperature in

their homes. The Met Office provides training to healthcare professionals on the operation of the service including how to maximise the health benefits for their patients. The risk to COPD patients is forecast and an alert for the following calendar week is triggered when a period of elevated risk is predicted. COPD patients are warned of the risk by an automated telephone call while their doctors receive a message informing them of the impending risk. The healthcare professionals can check on their computer systems whether patients have received the telephone call, and patients can contact their doctor if they have any particular concerns and in particular if they require additional medication in anticipation of the high risk period. The service runs every year from October to March.

The Met Office has developed a rule-based forecast model of the risk of COPD exacerbations, based on the understanding of how weather and environment affect patients with COPD. The model was specifically designed to forecast increases and peaks in risk and has several parameters that are altered to make it area specific. The original model was created using data from the Hospital Episode Statistics (HES) database. It has three main inputs: an underlying seasonal pattern, an assessment of whether prevailing conditions are predominantly settled or unsettled, and the cumulative effects of cold weather 1-3 weeks prior to the forecast period. There is currently no dependence in the COPD model of either specific pollutant concentrations or air quality index.

Although many studies have concluded a link between air quality and respiratory health impacts, the picture is complex due to the dominating influence of meteorological factors. In view of this we begin the present report with a review of the existing literature regarding health impacts of air quality. Following this overview we present analyses of the links based on two datasets: (i) measured values; (ii) model values. Both surface measurements and model values have advantages and disadvantages. Whilst measured values purport to represent ‘ground truth’, the measurement network is rather sparse and the high spatial variability of pollutant concentrations means that point measurements are only representative of a small area in the vicinity of the site. Furthermore, measurement techniques for pollutants are imperfect and, in particular for the nitrogen oxides and PM10, subject to significant uncertainties/errors. Model values are generally available on a grid and hence can be generated for any point or time within the domain. However there are many deficiencies in modelling schemes (pollutant emissions, representation of chemistry, meteorology, photolysis plus many others) and these all contribute to an imperfect representation of pollutant concentrations.

Our initial analysis of the link between COPD hospital admissions and air quality uses measured values of pollutant concentrations from the Automated Urban and Rural Network (AURN). Following this we have conducted a similar analysis using model data based on data from the NAME model and two models used in GEMS: EURAD and SILAM. The late availability of GEMS 2003 reanalysis data necessitated restricting the GEMS analysis to these models. However we do intend to extend the analysis to all the available 2003 reanalysis data in the coming months. Following the presentation of our results we conclude with a discussion of the implications for including air quality forecasts in health impacts forecasts.

2. Literature Review

Web of Science and Scopus were used to search for published literature on the topic of Air Quality (AQ) and health. The number of articles published on the topic is significant, even after excluding sub-topics not relevant to outdoor AQ and journals not specifically relevant to outdoor AQ or health. For the last 10 years, Web of Science returned 1614 articles on the topic of air quality and health, excluding the topics 'indoor', 'smoking', 'smoker-' and 'occupation-', and excluding the non-relevant journals. Refining for ozone, O_3, and for Particulate Matter (PM), PM_{10}, returned 257 and 434 articles, respectively. Most weeks there are one or more new articles published on the topic, which makes keeping up to date with the wealth of research in this field challenging.

Scale of AQ effects

The medical profession increasingly requires information on environmental health effects to provide appropriate health care and advice[2,3]. The scale of the difficulty in determining toxicity of the environment in general is illustrated by the 70 000 chemicals used world-wide[4]; this is further confounded by the difficulty in measuring actual individual exposure history, with the University of Toronto's CH^2OPD^2 approach (Community, Home, Hobbies, Occupation, Personal habits, Diet, Drugs) exemplifying the diversity of pollutant sources. While the general practitioner can provide advice to individual patients, it is also found that "*health effects occur even at exposure levels below those stipulated in current air-quality guidelines*"[5]. In the UK, the Economic and Social Research Council describe a "*disturbing picture*" of levels of air pollution and a greater effect on health than previously estimated[6].

Air pollution does not affect only those with specific prevalent respiratory or cardiovascular disease such as asthma, but affects the population as a whole: a study in Bordeaux measured the blood pressure of 2612 residents and found an association between systolic blood pressure and monitored levels of PM_{10}[7]. More worryingly perhaps is the effect of AQ on general life expectancy: a meta-analysis of epidemiological studies to estimate years of life lost found a 5% increase in relative risk of mortality per 10 $\mu g/m^3$ increase in PM_{10}[8]; for Switzerland this corresponds to some 20 000 to 60 000 years of life lost per year.

Results from studies: respiratory and cardiovascular effects

In 2003 the AIRNET/NERAM conference provided suggestions for AQ management policy[9], in particular awareness that "*the moderate and prolonged exposures, rather than peak exposures, are responsible for the majority of human health effects*". It focused on the areas of exposure, toxicology and epidemiology. Results showed that ozone increased lung permeability, and fine PM was linked to blood coagulation which in turn affected cardiac function. Large epidemiologic studies include the European Community Respiratory Health Survey (ECRHS) and the Health Effects of Air Pollution on Susceptible Subpopulations (HEAPSS); the latter study was designed to assess the risk of myocardial infarction. Also of note is the European APHEIS network of traffic-based AQ

monitors, allowing more spatially resolved assessments of the health impact of traffic pollution. One of the purposes of the research is to inform national institutions such as the United States' National Research Committee (NRC) to define AQ standards such as NAAQS (National Ambient Air Quality Standards). The NRC five-stage framework for PM research provides a means to prioritise research topics. J. Samet and D. Krewski have formulated a number of useful research questions for specifying AQ standards[10]. The Global Environmental Monitoring System (GEMS) program set up by the World Health Organization (WHO) provided the tools to measure atmospheric pollution and report the global environmental state[11]. This provided systematic AQ monitoring for many countries, in particular China whose rapidly developing economy led to worsening AQ. Research by J. Fang (1995) based on a sample of nearly 79 million people found that the prevalence for Chronic Obstructive Pulmonary Disease (COPD) was 6%, and respiratory disease at 10%[12]. In Beijing, significant associations between sulphur dioxide (SO_2) have been reported with daily mortality of COPD, pulmonary heart disease and cardiovascular disease. Increased mortality was still found when SO_2 concentrations remained below the WHO Air Quality Guideline. This is in agreement with other studies that have found health effects at AQ levels well below those of the WHO guidelines or the United States' Environment Protection Agency (EPA)[13], e.g. effects on lung function at levels of 100 to 120 $\mu g/m^3$ of [O_3]. A comprehensive review by F.W. Lipfert (1993)[14] specifically on the association of AQ with hospital admissions found some association but concluded that the effects of different pollutants were not always possible to separate and recognised the importance of total exposure (including indoor).

Cardiovascular hospital admissions have been examined in relation to AQ. A study in Tehran found a small but significant relationship between levels of carbon monoxide (CO) and hospitalisations for angina pectoris (admissions increase by 0.9%/(mg/m^3) [CO]), but no significant association with other pollutants (NO_2, O_3, SO_2, PM_{10})[15]. Another time-series study of 4.4 million emergency cardiovascular hospital admissions in Atlanta found significant correlations with nitrogen dioxide (NO_2), CO, $PM_{2.5}$ and oxygenated hydrocarbon[16]. Varying results according to the specific disease (single-pollutant *a priori* models) suggest different mechanism for the effect of AQ: congestive heart failure was associated with increased levels of total $PM_{2.5}$, $PM_{2.5}$ organic carbon and $PM_{2.5}$ elemental carbon but not other PM (such as $PM_{2.5}$ sulfates, $PM_{2.5}$ water soluble metals, etc.); ischemic heart disease was associated with NO_2 and oxygenated hydrocarbons only; peripheral vascular and cerebrovascular disease was linked with NO_2, CO and $PM_{2.5}$.

Mortality

There are still many difficulties in evaluating an acceptable AQ limit for individual pollutants based on evidence from epidemiologic research[17]. However, there is strong evidence that exposure to poor AQ is a cause of mortality. The National Morbidity Mortality Air Pollution Study (NMMAPS)[18] demonstrated that, while AQ had improved in the United States from 1987 to 2000, the effect of PM on health has not changed much over time[19]. Total mortality in Barcelona during 1985-1991, as well as elderly and cardiovascular mortality, was related to black smoke and SO_2[20]; in the summer, respiratory mortality was linked to SO_2, while NO_2 and O_3 were associated with elderly and cardiovascular mortality. A study in the United States for the period 1987-1994

found increases in relative mortality rates of 0.05 and 0.07 %/(µg/m^3) [PM_{10}] for all causes mortality and cardiovascular/respiratory mortality, respectively[21]. Even by implementing NAAQS guidelines, analysis of mortality in Santa Clara County (California) 1989-1996 found continuing increases in relative mortality risk with levels of PM, lagged coefficient of haze, nitrate $(NO_3)^-$, sulphate $(SO_4)^{2-}$, NO_2, CO and O_3[22]. Mortality due to respiratory conditions in Madrid 1990-1998 has been associated with increasing levels of O_3 with an increase in respiratory mortality of ~1%/(µg/m^3) [O_3][23]. A study of daily mortality in Inchon 1995 found an increase in mortality by 0.1%/(µg/m^3) of 6-day moving average total suspended particulates and 0.1%/(µg/m^3) 5-day moving average [PM_{10}] after adjustment for weather and time trends; no significant (adjusted) effect was found for SO_2, NO_2, O_3 or CO[24]. In this study the health effect of AQ was well below the Korean Ambient Air Quality Standard. Following the APHEA (Air Pollution and Health: a European Approach) protocol, the effect of AQ on daily mortality in Hong Kong 1995-1997 was carried out by the university of Hong Kong. A.J. Hedley and colleagues found that the effect of AQ was stronger in the cool season, with NO_2, SO_2 and O_3 affecting non-accidental mortality as well as separately cardiovascular and respiratory mortality, while PM_{10} was associated with respiratory mortality only[25].

COPD hospital admissions and asthma

The UK Met Office has particular interest in COPD and specifically related hospital admissions. COPD affects 1% to 2% of the England population. PM has been extensively studied in relation to respiratory disease, although some research has not found significant links[26]. Lippman and Ito[27] report that the study by Van Den Eeeden et al. (1999) found no significant association between chronic respiratory hospital admissions and PM in Los Angeles. The 2008 guidance document published in the Journal of Toxicology and Environmental Health lists 3 studies that fail to find significant links between COPD admissions and PM (Ito 2003; Slaughter et al. 2005; Peel et al. 2005) and 3 studies with positive excess risk estimates (Moolgavkar 2003; Dominici et al. 2006; Chen et al. 2004)[28]. Reviews of COPD admission risk against PM suggest risk increases of 0.1 to 0.3%/(µg/m^3) [PM_{10}][29,30]. J. Sunyer and colleagues in Barcelona have found a weak but significant link between COPD emergency admissions and PM, SO_2 and CO[31]. A study by J.-S. Hwang and C.-C. Chan in Taiwan for 1998 found rates of respiratory clinic visits associated with levels of NO_2, CO, SO_2 and PM_{10}[32]. A study in Pisa measured increases in respiratory admission risk among the elderly of 0.85%/(µg/m^3) [PM_{10}] over the 2 previous days, and 26.5%/(mg/m^3) [CO] over the 4 previous days[33]. For Atlanta 1993-2000, J.L. Peel and colleagues associated respiratory emergency hospital admissions with PM_{10}, O_3, NO_2, CO, as well as upper respiratory infections separately; COPD admissions were linked to NO_2 and CO only, and pneumonia to $PM_{2.5}$ organic carbon[34]. Finally, spirometry studies, closer to potential causal relationships between respiratory syndromes and AQ, have found associations between respiratory health and atmospheric pollution. For example, a reduction of the mean peak expiratory flow rate of 32 L/min/(mg/m^3) [PM_{10}] was estimated by research in Kanpur[35]. In Punjab State, India, differences in the prevalence of chronic respiratory symptoms and obstructive ventilatory defects was linked to AQ (total suspended particulates, NO_x, SO_x, CO, O_3)[36].

Research has also examined the relationship of asthma with AQ. A study of asthma and COPD drug sales revealed increases of 0.07%/(μg/m^3) [NO_2] with a 6 to 7 day lag and of 0.08%/(μg/m^3) black smoke with a 2 to 5 day lag, and in particular for children[37]. An article by Dr. S. Walters and colleagues in the West Midlands concludes that NO_2 is significantly associated with respiratory admissions for children under 5 years of age[38]. Hospital admission for asthma was associated with AQ in Valencia by following the APHEA protocol: admission increases of 0.08%/(μg/m^3) 24-hour mean [NO_2], 0.04%/(μg/m^3) 1-hour mean [NO_2] and 0.06%/(μg/m^3) 1–hour mean [O_3] were measured, though 24 h [NO_2] was significant in the Winter and not the Summer, and 1 h [O_3] was significant in the Summer and not the Winter[39].

Toxicology

The mechanistic study of the health effects of AQ aims to provide causality in a complex field of research. The oxidative stress linked to poor AQ has been identified as a cause of allergy and asthma[40]. A summer study of Peak Expiratory Flow (PEF) in healthy individuals measured drops in PEF by -0.02%/(μg/m^3) [$PM_{2.5}$], -0.02%/(μg/m^3) [PM_{10}], -0.05%/(μg/m^3) coarse particles' mass concentration, and -0.004%/(nmol/m^3) [H^+] in the morning; a drop of -0.03%/(μg/kg) 3-day average [O_3] was measured for evening PEF[41]. More experimental studies have been carried out to determine the mechanisms affecting lung function. Exposure to O_3 causes increased permeability of the pulmonary epithelial barrier, with a measurable increase in serum Clara cell 16 protein; increased epithelium permeability also causes albumin leakage into the lung airways[42]. The effects of exposure to different pollutants have been assessed experimentally, such as for the volatile organic compound methyl tertiary-butyl ether[43]. Work on healthy and asthmatic individuals suggests different mechanistic effects, with exposure to diesel exhaust PM triggering interleukin-8 production for healthy individuals and linked to epithelial interleukin-10 for asthma[44]. A review of experimental and epidemiological studies by the Norwegian Institute of Public Health has highlighted the difficulty of understanding the effects of AQ on health, in particular the effect of the specific composition of PM[45]. Finally, research is being carried out to examine the effect of PM of ever smaller size. Ultrafine PM (diameter < 50 nm) has been linked to fewer adhesion molecules on blood leukocytes and to reduced CO diffusing capacity, contributing to cardiopulmonary health effects[46].

Effect of weather

The health effects of AQ may themselves be dependent on season. Analysis of NMMAPS data found a significant effect of PM on mortality in the United States' summer (up 0.04%/(μg/m^3) [PM_{10}]) but with less seasonal variation in the south suggesting an interaction between AQ and warmer climate[47]. Similarly, an analysis of weather patterns by D.G.C. Rainham and colleagues linked AQ health effects with synoptic weather type, but the resulting effect on mortality was measured to be stronger in the winter. Total mortality was associated in particular with tropical weather type, with cardio-respiratory mortality linked to dry tropical and other causes of mortality to moist weather types (polar and tropical). Examining the effect of AQ on mortality according to season and weather types shows a complex picture where some of the effects of individual pollutants on mortality are different depending on the season and the weather type[48]. Robust analyses are required to ensure that AQ effects are not confounded by weather or other seasonal covariates such as influenza epidemics[49]. This is further

complicated by the type of pollutant which may not always be emitted near the time of AQ measurement: a study in Finland describes the association of weather with the vanadium, lead and iron content of PM[50].

Further methodologies

Linking AQ to the Health Survey for England, B.W. Wheeler and Y. Ben-Shlomo included socioeconomic factors and found that the associations of FEV (Forced Expiratory Volume) with AQ or with social class are of similar magnitude[51]. A. Zeka and J. Schwartz have examined means of controlling for bias/error when analysing NMMAPS data[52]. F. Dominici suggests a unified framework using a hierarchical approach[53]. However, use of spectral decomposition is described as impractical in its practical interpretation[54]. Short-term health effects can be studied using a 'panel study design' yet lack of understanding of the statistical issues related to such designs mean that many published studies could be improved[55]. Cumulative effects of pollutant concentrations are also to be included in analyses, as are confounders and methodological considerations. Modelling of cumulative health effects for Hong Kong data (1994-1997) suggests that even at levels below NAAQS, AQ has an especially important impact on chronic sufferers of respiratory disease[56]. Even with the wealth of data and methods, comprehending the results from analyses is far from straightforward: for example health risks related to NO_2 were estimated to be increasing, while $[NO_2]$ has been decreasing[57]. In addition, while spatial co-linearity has to be accounted for, high spatial resolution is essential to separate health effects close to pollutant sources such as asthma provoked by road traffic[58].

Complexities and recommendations

Policy scenarios have been studied to estimate how much of an effect reduction in pollution has: a reduction of the annual mean $[PM_{10}]$ by 10 $\mu g/m^3$ would entail an expected drop in morbidity of ~8% [59]. Which air pollutants should have their emission reduced? A study in Houston examined 179 different air pollutants, and "definite risks" pollutants are O_3, $PM_{2.5}$, diesel PM, 1,3-butadiene, chromium VI, benzene, ethylene dibromide, acrylonitrile, formaldehyde, acrolein, chlorine, 1,6-hexamethylene and diisocyanate[60]. In the UK, industrial pollutant sources are regulated by the National Air Quality Strategy (NAQS). Health effects from poor AQ in the UK has been researched by the Committee on the Medical Effects of Air Pollutants (COMEAP)[61]. In the United States it is regulated by NAAQS which allows levels of PM higher than the recommendations of the EPA and the Clean Air Scientific Advisory Committee (CASAC), the American Thoracic Society recommending 24-hour $[PM_{2.5}] \leq 25\ \mu g/m^3$ [62]. It has also been difficult for the Clean Air For Europe (CAFE) programme to decide on AQ policy, in particular with respect to PM[63]. Reducing annual average $[PM_{2.5}]$ to the EPA recommendation of 15 $\mu g/m^3$ could save 1781, 491 and 1280 lives per year in Athens, Cracow and Rome, respectively[64]. The APHEA project looked at quantifying the health effects of AQ for 15 European urban areas totalling a population of 25 million[65,66]. The 2006 symposium on *Air Pollution Exposure and Health* organised by the EPA and the United States' Centers for Disease Control (CDC) recognised the "*need to develop new or stronger collaborations, leverage resources, build capacity and facilitate interdisciplinary communications*"[67]. A review of health effects of O_3 for Australia recommended new maximum levels of O_3[68]. An overview of AQ management can be

found in the article by Y. Chen and colleagues[69] and a guidance document for AQ management is available from the Institute for Risk Research (IRR), Canada[70]. The WHO however issues guidelines for AQ, updating of which is focusing on PM, O_3, NO_2 and SO_2[71]. The complex interactions between AQ pollutants, weather, clinical condition and social characteristics makes the study of the effects of AQ on health particularly challenging: there are strong recommendations that toxicological and epidemiological studies need to be carried out much more conjointly to determine both physiological mechanisms and statistical measures.

3. Analysis Methods

3.1 Data and Models Employed

Health Data

The health data considered in this study consist of emergency hospital admissions in England for Chronic Obstructive Pulmonary Disease (COPD). Emergency hospital admissions for COPD were obtained from the HES (Hospital Episodes Statistics) database[72]. COPD admissions were defined as all admission with ICD-10[73] codes J40 to J44 as primary diagnoses. The data extraction consisted in the date of admission, the HES patient identifier, the primary diagnosis and the postcode district of residence of the patient. Data are available for the period from 1st April 1997 to end of March 2007, though the end date 28th February 2007 was used because patients admitted but not discharged before the end of March are not recorded in the database – this flaws the admissions rate especially in the last month of the available series. 975,884 emergency admissions cases were retrieved for England for the 119 months. The geographical information used was the postcode district of residence of the patient, which required recoding to take into account changes in postcodes in the period of interest. This was achieved by using postcode changes information available from Royal Mail. National Grid Reference (NGR) coordinates were computed for the postcode districts existing on 1st September 2005. Postcode information available for each hospital case from HES was recoded using forwards and backwards recoding methods, with the postcode sector as a weighting unit. This allows the splitting of some hospital admissions with estimated weights where a postcode district is split into several areas. There were 2826 postcode changes between April 1997 and February 2007 and 982,411 admitted patients were included in the analysis by recoding their postcodes of residence. It was therefore possible to obtain a count of hospital admission per postcode district j per day i: $N_{i\ j}$

Table 1. Hospital admissions of patients from April 1997 to Feb 2007 whose residence is within 5km from an AURN site.

AURN pollutant	Number of admitted patients residing within 5 km
Carbon monoxide CO	234 687
Nitrogen dioxide NO_2	268 739
Nitric oxide NO	271 172
Ozone O_3	246 596
Particulate matter PM_{10}	204 757

Air Quality Observation Data

The AQ measurements were obtained from the UK Automatic Air Quality Network (AURN)[74]. From this dataset it was possible to obtain AQ measurements for 10 years, giving a substantial period of cross-over of the time between hospital and AQ data. This cross-over is essential when examining annual seasonal effects where several years (ideally many years) of data are necessary.

The AURN AQ data are held on a server external to the UK Met Office. Access to these data was facilitated by the coding of a computational routine that retrieves time series of pollutant concentration measurements from the nearest AQ monitoring site to a specified NGR. In addition, the routine also gets data from the next nearest available site where measurements are missing. This provides complete AQ time series within allowable distance thresholds and includes information about the site so that the measurement can be traced back. The AURN sites are categorised according to type (e.g. rural, urban, roadside, etc.) depending on their location[75] but for the purposes of this study all sites were included. AQ measurements were only included if they were taken within 5 km of the patient's residence. This means that between 20.8% and 27.6% of the admissions were of patients within 5 km of an AQ monitoring site, depending on the pollutant (c.f. table 1). The numbers differ slightly for each pollutant due to (i) the fact that not all sites measure every pollutant and (ii) occasional unavailability of

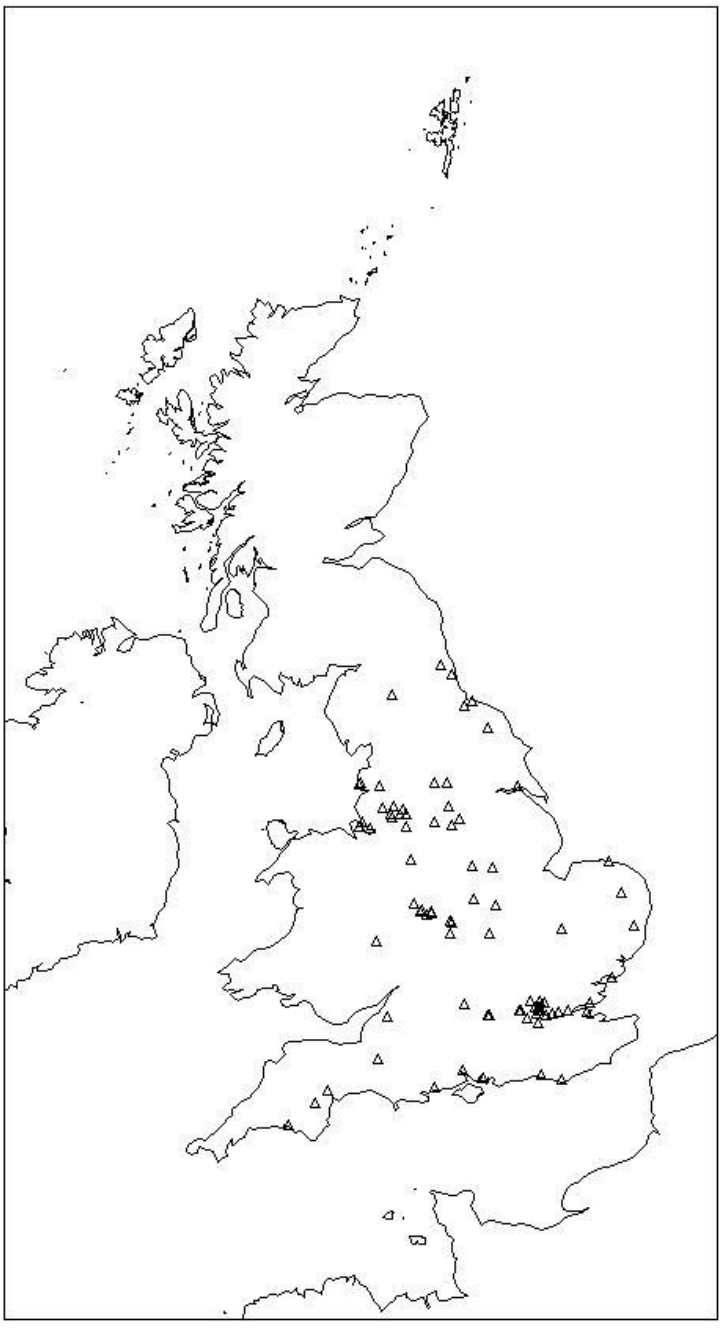

Figure 1. AURN sites monitoring O_3 in England in the period 1997-2007.

measurement data. Furthermore, only monitoring sites in England were included (see Figure 1). The pollutants considered were carbon monoxide (CO), nitrogen dioxide (NO_2), nitric oxide (NO), ozone (O_3), particulate matter (PM_{10}) and sulphur dioxide (SO_2).

Air Quality Model Data

Model hind-cast runs were used for selected years. 2003 was selected by GEMS RAQ for a reanalysis case study[76]. This year contained a severe European ozone episode in August and a number of groups have attempted to model the episode period explicitly. However it is generally acknowledged to present difficulties to models due to the complex nature of the event and unusual factors (such as Portuguese forest fires, a prolonged dry period and hence unusually low soil moisture prior to the episode). Despite these challenges, a number of the GEMS RAQ partners have provided chemical reanalysis data for all of 2003. In our analysis to establish statistical links with health impacts we have used data from the EURAD model - operated by the Rhenish Institute for Environmental Research (RIU) and the SILAM model - operated by the Finnish Meteorological Institute (FMI), as these were available prior to the 2009 final GEMS Assembly. We intend to extend the analysis to the other models in due course. The RIU simulations provide data on concentrations of CO, NO_2, NO, O_3, PM_{10} and SO_2. whilst those of FMI provide concentrations of the same species except. O_3. The UK Met Office NAME model, in the configuration used for the UK national air quality forecast, was also run for the period 1st January 2005 to 31st December 2006. These simulations provided daily mean and maximum concentrations of CO, formaldehyde (HCHO), NO_2, NO, O_3, PM_{10} and SO_2. This configuration of the NAME air quality model differs from the version of NAME used to generate the GEMS forecasts. In particular it employs the National Atmospheric Emissions Inventory (NAEI) at 1km resolution and has a better representation of point sources. In view of these differences the forecasts provide significantly greater skill than the equivalent NAME runs for GEMS.

Taken together, all of these model runs provide matching data to health data for 3 years. It should be borne in mind that with such a small number of years it is not possible to exclude year-on-year differences. All model data are available in gridded format and were subsequently converted to postcode district centroid estimates by interpolation. To achieve this conversion, the postcode district centroids' NGR were converted to latitudes and longitudes using a function developed from Ordnance Survey data and algorithms[77].

3.2 Statistical Model

The key question to be answered in the first part of this study concerns whether the concentrations of pollutant different on days with COPD admissions than on a 'normal' day (i.e. a day considered regardless of COPD admissions). This requires comparing the distributions of pollutant concentrations on the days of COPD admissions with respect to the distributions of pollutant concentrations on a normal day. On a normal day, the distribution is that of pollutant concentrations estimated every day at every postcode district. The distribution of pollutant concentrations on days of COPD admissions is the

distribution of concentrations estimated for each hospital admission on the day of admission and at the postcode district of the patient's residence. This means that the distribution on COPD admissions days is essentially weighted by the number of admissions while on normal days the weight is unity. The mathematical nomenclature used in the following analytical definitions is:

i	index denoting particular days
j	index denoting particular postcode districts
I	total number of days
J	total number of postcode districts
$\Pi_{i\ j}$	uniform kernel function
$[X]$	concentration of pollutant X
$[X]_{i\ j}$	concentration of pollutant X on day i and at postcode district j
$\delta[X]$	half-width of the uniform kernel function $\Pi_{i\ j}$
$N_{i\ j}$	number of COPD hospital admissions on day i and at postcode district j
P	normalised distribution function of pollutant concentration $[X]$
P_{COPD}	normalised distribution function of pollutant concentration $[X]$ for COPD admissions
$T_{i\ j}$	temperature on day i and at postcode district j
ν_0	mean value of temperature distribution or square root of pollutant concentration distribution on normal days
ν_1	mean value of temperature distribution or square root of pollutant concentration distribution on COPD admission days
$\Delta\mu$	relative difference between ν_0 and ν_1 (absolute difference for temperature)
L	number of lag days
C	number of cumulative days (averaging period)
i'	summation index for averaging over the period given by C

Given the kernel $\Pi_{i\ j}$ given by:

$$\Pi_{i\ j}([X]) = \begin{cases} 1 & \text{if } \left|[X]-[X]_{i\ j}\right| \le \delta[X] \\ 0 & \text{if } \left|[X]-[X]_{i\ j}\right| > \delta[X] \end{cases} \quad (1)$$

the distribution for a pollutant X is defined as:

$$P([X]) = \frac{\sum_i \sum_j \Pi_{i\ j}}{2\delta[X]IJ} \quad (2)$$

where J is the total number of postcode districts ($1 \le j \le J$) and I is the total number of days ($1 \le i \le I$). This is compared to the distribution for the pollutant X on days of COPD admissions defined as:

$$P_{COPD}([X]) = \frac{\sum_i \sum_j \Pi_{i\ j} N_{i\ j}}{2\delta[X] \sum_i \sum_j N_{i\ j}} \quad (3)$$

The pollutant concentration distributions are skewed and a square-root transformation was used to render them approximately Gaussian. The mean value of this distribution for the square root of pollutant concentration on a normal day, ν_0, is given by:

$$\nu_0 = \frac{\sum_i \sum_j \sqrt{[X]_{i\ j}}}{IJ} \quad (4)$$

Similarly, the mean value of the distribution for the square root of pollutant concentration on a COPD day, ν_1, is given by:

$$\nu_1 = \frac{\sum_i \sum_j N_{i\ j} \sqrt{[X]_{i\ j}}}{\sum_i \sum_j N_{i\ j}} \quad (5)$$

This transformation to an approximate Gaussian form allows the adaptation of the standard one-sample hypothesis test of the sample mean[78] to help test the hypothesis that there is a difference of pollutant concentrations between days of COPD admissions and the average day. The statistic $\Delta\mu$ analysed, common to all pollutants, is the ratio of the difference of the means with respect to the normal mean:

$$\Delta\mu \equiv \frac{\nu_1 - \nu_0}{\nu_0} \quad (6)$$

To compare the distributions qualitatively and the $\Delta\mu$ statistic quantitatively with distributions of daily mean air temperature $T_{i\ j}$ it is necessary to redefine the $\Delta\mu$ statistic for $T_{i\ j}$ because the distribution of temperature (once adjusted for seasonality) is expected to be already approximately Gaussian. For the analysis of temperature as a precursor of COPD, the following definitions of the statistic $\Delta\mu$ are employed:

$$\Delta\mu \equiv \nu_1 - \nu_0 \text{ where} \begin{cases} \nu_0 = \dfrac{\sum_i \sum_j T_{i\ j}}{IJ} \\ \nu_1 = \dfrac{\sum_i \sum_j N_{i\ j} T_{i\ j}}{\sum_i \sum_j N_{i\ j}} \end{cases} \quad (7)$$

Incorporation of Lag / Cumulative Effects

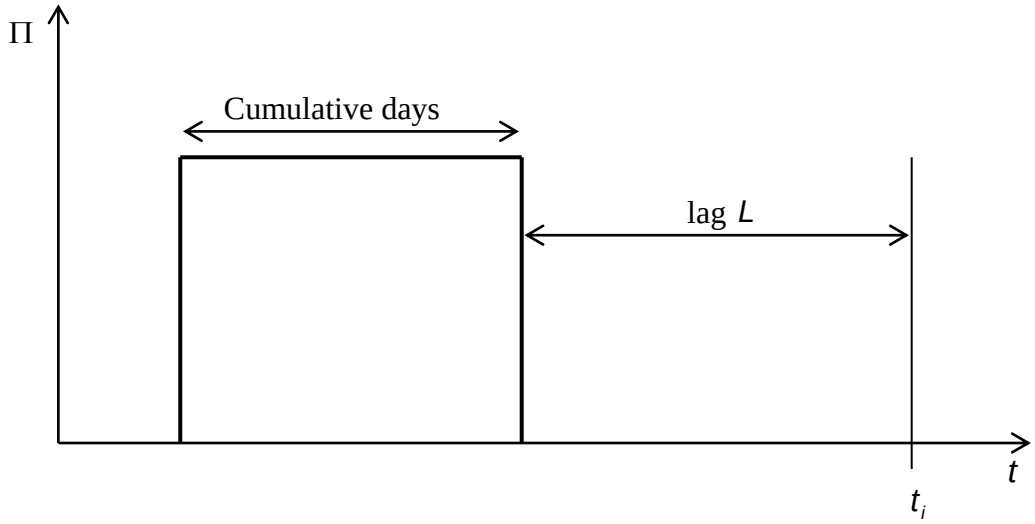

Figure 2. Plot of the kernel function Π against time t showing the averaging period C (number of cumulative days) and lag L (number of lag days) for day t_i.

It has been highlighted that the effect of AQ on COPD admissions is not necessarily immediate. The evaluation of AQ at different days prior to hospital admissions and over a number of days is required to evaluate any lag and cumulative effects. $L \geq 0$ is the number of lag days and $C \geq 1$ is the number of cumulative days (c.f. figure 2). Hence the lagged and cumulative concentration of pollutant X is:

$$[X]_{i\ j}(L;C) = \frac{1}{C}\sum_{i'=i-L-C+1}^{i-L}[X]_{i'\ j} \qquad (8)$$

The lag and cumulative effects can be examined qualitatively by plotting the values $\Delta\mu(L;C)$ against L and C.

4. Results

Analysis with AQ measurements from the AURN monitoring network

Study of the distribution plots of daily mean pollutant concentrations from AURN AQ monitoring sites (c.f. figure A1) shows very little difference between the distributions on the average day compared to that on days of COPD admissions. If anything, [NO_2] and [PM_{10}] are slightly lower on COPD admission days, while [O_3] is somewhat higher. Examining the distributions at different lags up to 5 days shows no difference with the distribution with no lag. Daily maximum concentrations (c.f. figure A2) show no clear link between AQ and COPD hospital admissions and suggest a behaviour for NO_2, O_3, and PM_{10} similar to that of the daily means.

Table 2. Median Pearson correlation coefficients for pollutant concentrations estimated by model data from 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

Analysis with AQ model data from the GEMS partners' models and the UK Met Office NAME model

Examining the AQ data from the models (NAME, RIU and FMI) it was found that the pollutant concentrations estimated are strongly correlated with each other as has been published for air quality observations[79]. The median correlation coefficients are listed in table 2 as each coefficient is of the same order of magnitude for the 3 models. The anti-correlation of ozone with the other pollutants is a consequence of the fact that it is a secondary pollutant, formed downwind from the sources of NO_x via photochemical reactions. Formaldehyde (HCHO) is both a primary and secondary pollutant, being emitted during the combustion of VOCs and also formed during subsequent chemical processes. Depending on whether urban or rural regions are considered on can find either a positive or negative correlation with ozone. The observed anti-correlation of HCHO with ozone confirms that the data are predominantly sampling polluted urban areas.

Finding the pollutant with the strongest link with hospital admissions as a first step allows the estimation of the links with other pollutants: for example, positive correlation of hospital admissions with NO should mean a positive correlation with CO but a negative correlation with O_3.

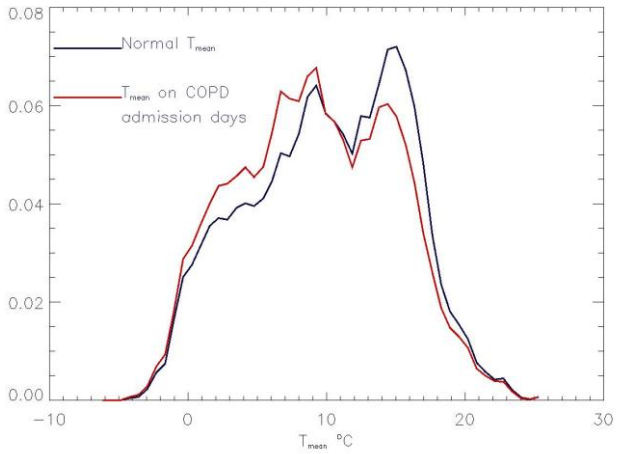

Figure 3. Normalised distributions of daily mean temperature $T_{i\ j}$ estimated by NAME for 2005-2006.

Analysis of Temperature Influence

Temperature data from the NAME model was analysed so as to gain some understanding of the temperature distributions, as the UK Met Office COPD service relies on a model that includes temperature as a principal component. The mean temperature on an average day in the period 2005-2006 was $\nu_0 = 10.7\,°\text{C}$ while on days of COPD admissions it was $\nu_1 = 9.3\,°\text{C}$ hence a difference $\Delta\mu = -1.4\,°\text{C}$ (c.f. figure 3). This difference in daily mean temperatures is significant and confirms the premises for the COPD service of the UK Met Office. It also demonstrates the validity of the analysis technique in identifying factors correlated with COPD hospital admissions.

Analysis of Air Quality Influence

The health effects of HCHO and NO are described by the World Health Organization's air quality guidelines for Europe[80]. NO, NO_2 HCHO and O_3 are linked by photochemistry[81] and their health effects have been described[82]. Weather variables such as temperature are not statistically independent from AQ elements as highlighted by McGregor and colleagues[83] who linked [PM_{10}] to types of weather, and Ordonez and colleagues[84] who linked daily ozone maxima to meteorological parameters. Examination of the AQ distributions from NAME show a different picture to the AURN results. In particular, [CO], [HCHO], [NO_2] (c.f. figure A3) and [NO] (c.f. figure 4) all appear higher on days of COPD admissions. The 'normal day' value of the parameter ν_0^2 derived from the NAME data for [NO] is $6.4\,\mu\text{g/m}^3$. On days of COPD admissions ν_1^2 is $7.33\,\mu\text{g/m}^3$, giving $\Delta\mu = 0.07$.

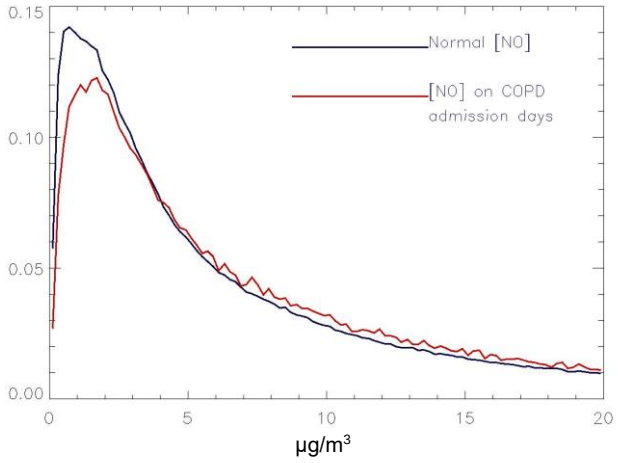

Figure 4. Normalised distributions of [NO] estimated by NAME for 2005-2006.

Influence of Lag

An analysis (see figure A3), focussing on the influence of up to a 5 day lag, failed to show a delayed influence, as with the analysis of air quality measurements. There is some indication in the plot for [O_3] that there are fewer admissions on days with high [O_3], contrary to the observations made on the distributions from the AURN data. However the influence is small if it exists. Plots of the distributions of daily maximum concentrations from NAME show similar patterns to the daily means (compare figures A3 and A4). It is noted that the

distributions from the models have a much better resolution in pollutant concentrations compared to the distributions from AURN monitoring (compare figures A1 and A3).

Analysis of Model Data: GEMS Air Quality Data

Distributions of NO (which showed the highest effect) obtained from the RIU and FMI models for 2003 show a difference similar to that of NAME model data for 2005 and 2006 between normal days and days of COPD hospital admissions (c.f. figure 5): [NO] is generally higher on days of COPD admissions. Distributions of [NO] from the RIU and FMI models have values of $\nu_0^2 = 3.6\ \mu g/m^3$ and 3.7 $\mu g/m^3$, respectively. However these differ significantly to the normal mean concentration from the NAME model for 2005 - 2006 ($\nu_0^2 = 6.4\ \mu g/m^3$).

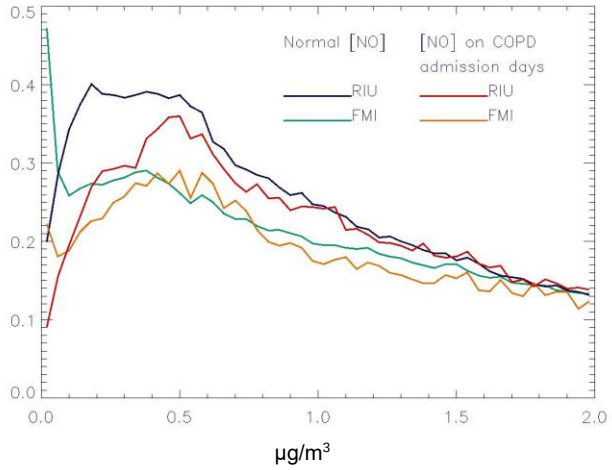

Figure 5. Normalised distributions of [NO] estimated by RIU and FMI for 2003.

Influence of Lag

Results from both models show that the highest $\Delta\mu$ occurs with approximately a 1 week lag and a 4 to 7 day cumulative effect. This is specifically examined for [NO] (the pollutant that shows the highest $\Delta\mu$) by figures 6 and 7. It can be seen that there is a peak in the difference in mean [NO] with a lag of around $L = 8$ and after averaging over about $C = 4$ cumulative days. The magnitude of $\Delta\mu$ is similar to published effects of air pollution on respiratory admissions[85]. The greatest difference in means measured, $\Delta\mu > 13\%$, is apparent on the contour plot of [NO] for the RIU model.

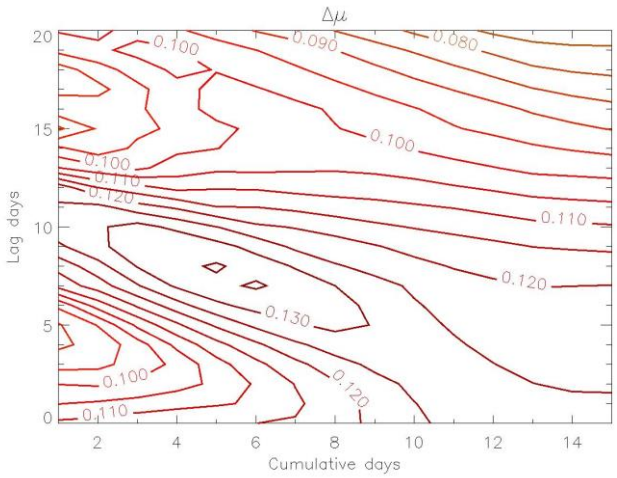

Figure 6. $\Delta\mu$ statistic for COPD hospital admissions for [NO] from the RIU model with lag days $0 \le L \le 20$ and cumulative days $1 \le C \le 15$.

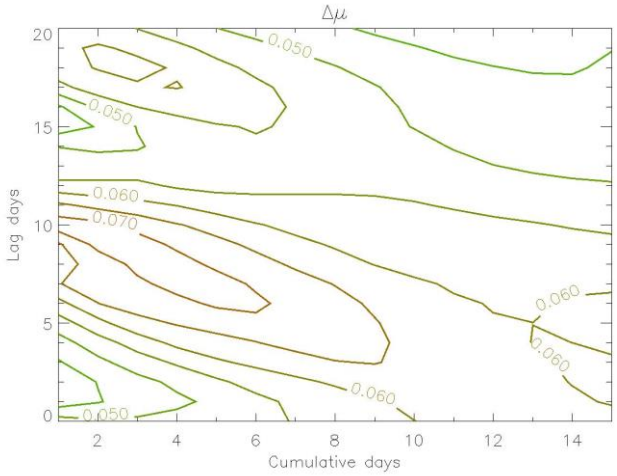

Figure 7. $\Delta\mu$ statistic for COPD hospital admissions for [NO] from the FMI model with lag days $0 \le L \le 20$ and cumulative days $1 \le C \le 15$.

5. Discussion

The results presented above can be summarised as follows:

- In our analysis of surface air quality observations there is no discernible link with COPD hospital admissions, even allowing for time lag and cumulative effects;

- However based on air quality model data, there exists a small but discernible influence of air quality on COPD hospital admissions;
- Nitric oxide (NO) provides the strongest signal (though this does not imply a causal link);
- The influence of air quality on COPD hospital admissions is greatest with a lag of ~1 week and after averaging over 2 - 6 cumulative days.

The first question to address is the apparently different conclusions drawn from analyses of the observation and model data. In the analysis of observation data we enforced a requirement that any given COPD admission should be within 5km of an AURN site measuring the pollutant species in question. This reduced the available data to between 20 to 27% of the total admission dataset and will have resulted in some biased sampling of the data. The model data cover a shorter period than the observation data. However the spatial and temporal coverage is complete over the period considered and thus there is no sampling of the data. Furthermore, the model data do not suffer from the lack of sensitivity of the observation data. These issues are likely to be responsible for the greater ability of the model data to discern a link between air quality and COPD hospital admissions.

The identification of NO as providing the strongest signal correlating poor air quality with COPD hospital admissions does not imply that high NO is a cause of COPD admissions: In fact any attempt to identify a particular pollutant with COPD hospital admissions requires the study of the physiological mechanisms[86,87] as described by Mindell and Joffe[88] (2004). NO is produced via combustion processes when fuels are burned in air. However it is oxidised to nitrogen dioxide relatively quickly and this latter species is associated with respiratory system health impacts. The strongest sources of NO are therefore located in urban areas and plots of atmospheric concentration appear relatively discrete, compared to the more diffuse fields of NO_2 and ozone. This concentration of NO in the areas of the greatest population density probably accounts for its identification as provider of the strongest signal relating to COPD hospital admissions.

The fact that COPD hospital admissions follow poor air quality episodes with a short lag period of some days is important, since this implies that a forecast service can offer maximum impact to patients and health care providers by giving ample warning of an expected exacerbation of symptoms and hospital admissions. Incorporation of an air quality indicator into the COPD index could proceed via the computation of a spatially varying field for a $\Delta\mu$ statistic for NO, calculated as an exceedance over the long-term value of average given by ν_0. The value of gridded numerical model data, such as that provided by the GEMS forecasts, above air quality measurement data in providing input to such a calculation is clearly demonstrated by the present study.

It is worth pointing out explicitly that the present study has focussed on the link between poor air quality and hospital admissions for one particular respiratory illness: COPD. Other conditions, such as asthma, may well exhibit further links and could be investigated using the same methodology.

Acknowledgements

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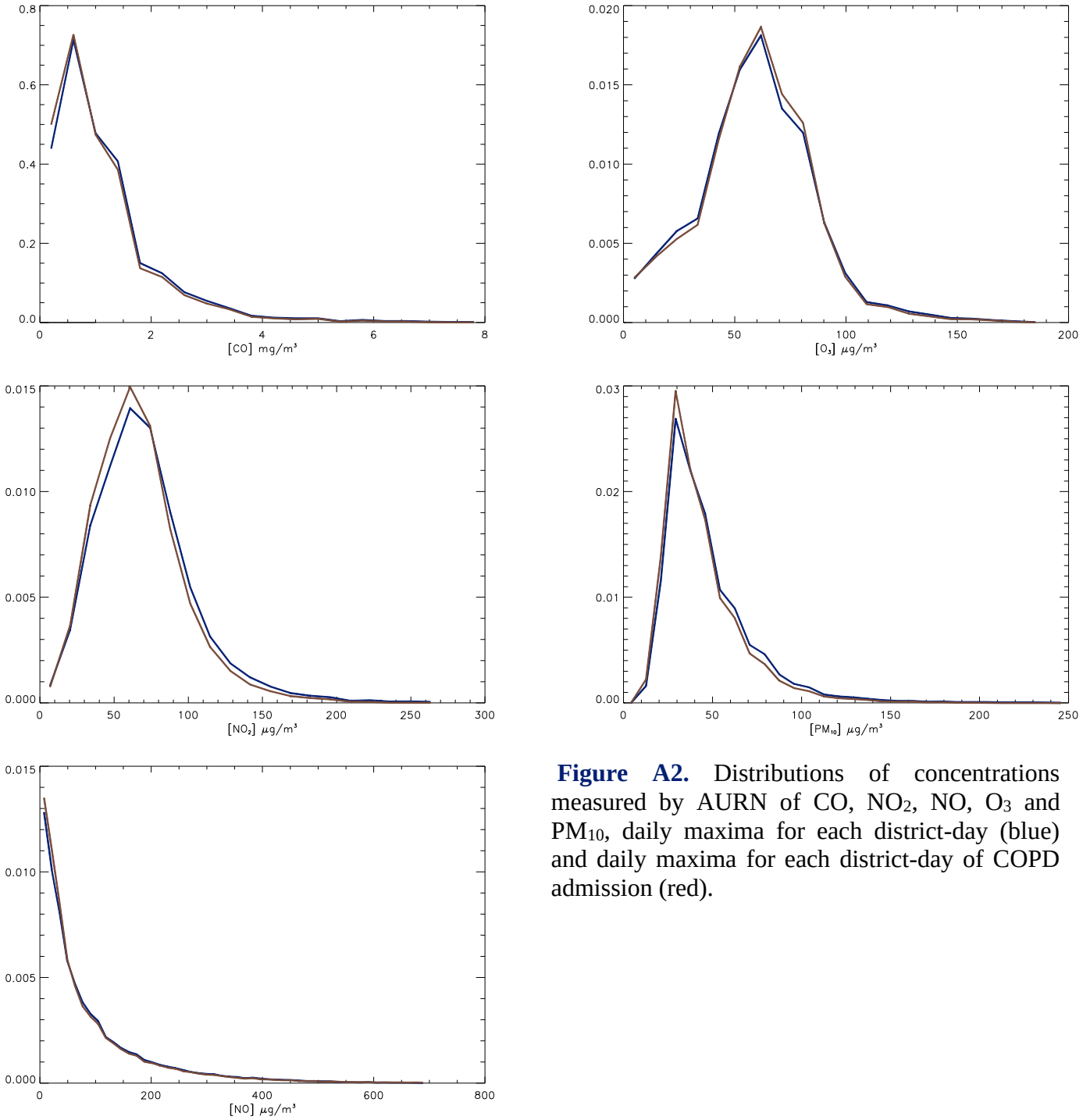

Figure A2. Distributions of concentrations measured by AURN of CO, NO_2, NO, O_3 and PM_{10}, daily maxima for each district-day (blue) and daily maxima for each district-day of COPD admission (red).

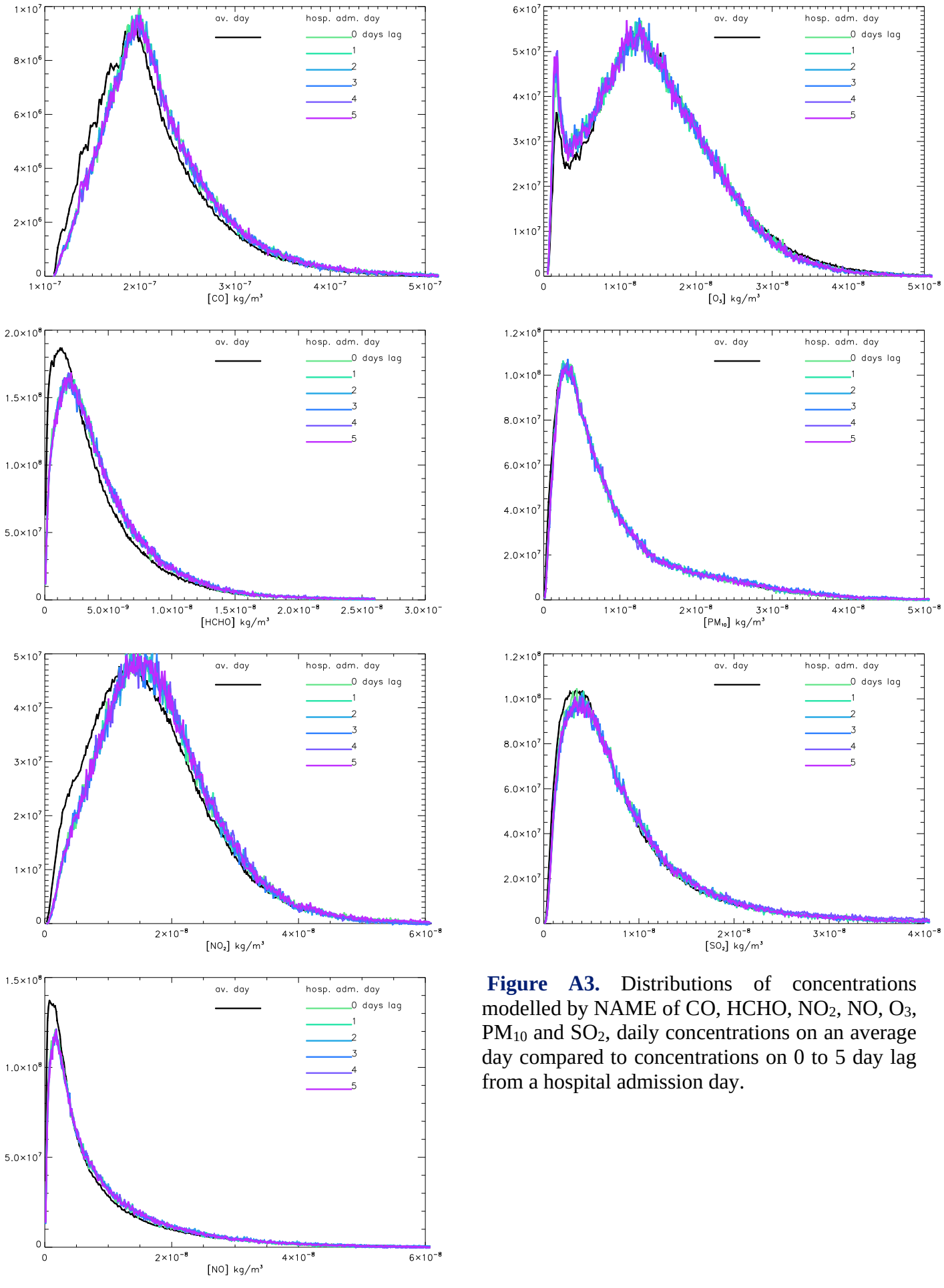

Figure A3. Distributions of concentrations modelled by NAME of CO, HCHO, NO_2, NO, O_3, PM_{10} and SO_2, daily concentrations on an average day compared to concentrations on 0 to 5 day lag from a hospital admission day.

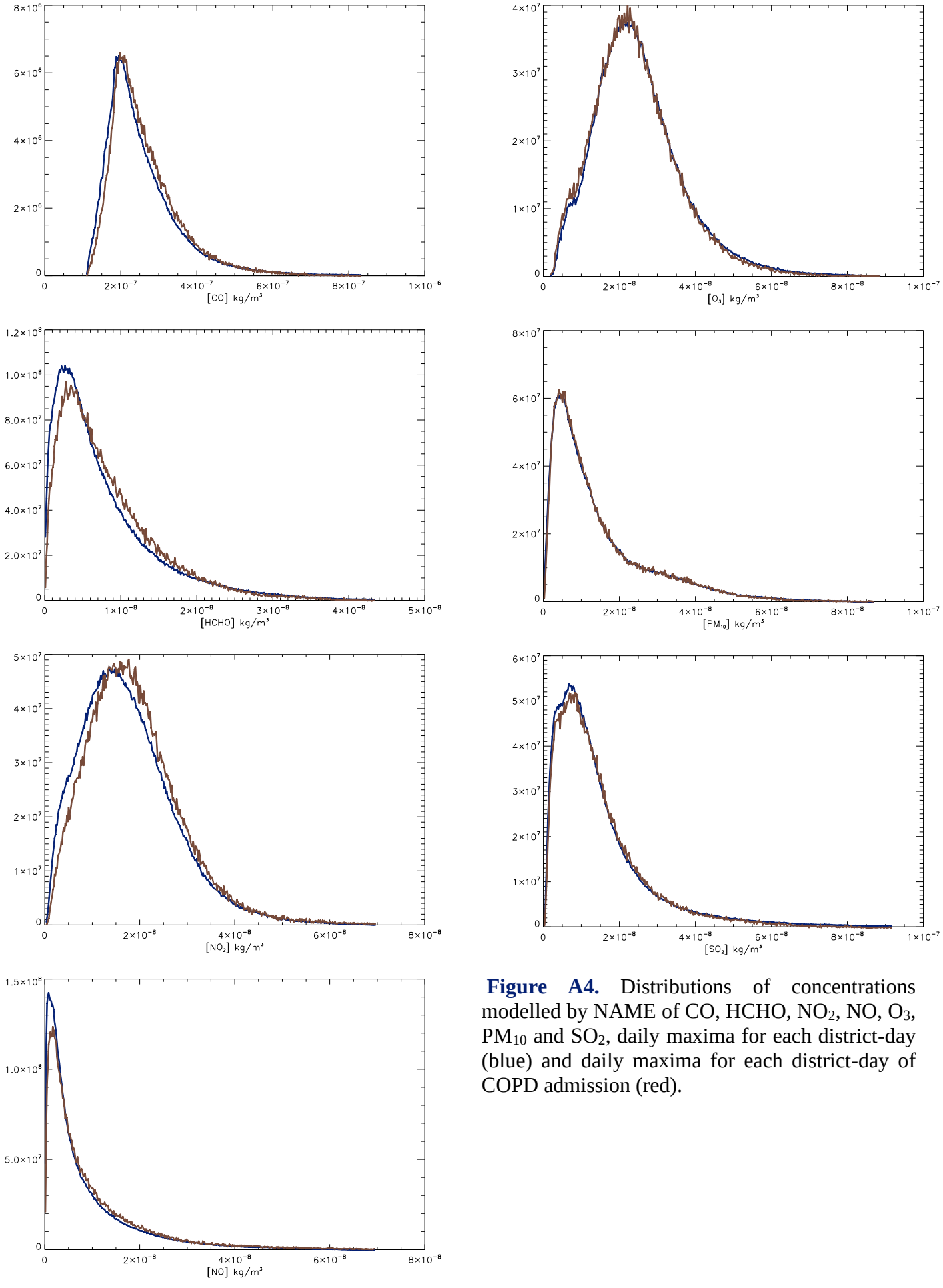

Figure A4. Distributions of concentrations modelled by NAME of CO, HCHO, NO_2, NO, O_3, PM_{10} and SO_2, daily maxima for each district-day (blue) and daily maxima for each district-day of COPD admission (red).

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