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AIR POLLUTION ALERT SERVICES EVIDENCE DEVELOPMENT STRATEGY – PREDICTION OF POSSIBLE EFFECTIVENESS AND ASSESSMENT OF INTERVENTION STUDY FEASIBILITY

King's College London Environmental Research Group,
MRC-PHE Centre for Environment and Health

Prepared for: Department of Health via Sussex Primary Care Trust and the Sussex Air Quality Partnership

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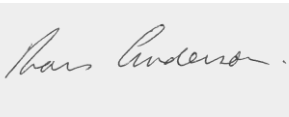
Reviewed by	Ross Anderson		13th December 2013
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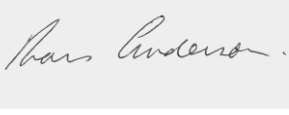
Minor changes reviewed and approved by	Ross Anderson		21st August 2014

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Executive summary

Introduction

1. There has been a national air quality banding system informing the public of daily levels of pollution and implications for their health since the early 1990s. The system classifies air pollution levels into bands according to their effects on health, currently labelled low, moderate, high or very high, according to whether any one of 5 pollutants exceeds specified levels. The national system is available for the public to consult (uk-air.defra.gov.uk/air-pollution/daqi) but there are also now a number of systems that proactively contact members of the public that sign up to receive alerts e.g. by text message or email.

2. airAlert is one such information service that provides messages to registered members of the public, alerting them when the daily air quality index is forecast to be moderate, high or very high (www.airalert.info). It has been in operation since 2006, originally covering the county of Sussex but now also covering Surrey and Southampton.

3. This research was commissioned by the Sussex Air Quality Partnership (Sussex-air) to determine the potential health benefits if the service in Sussex was expanded to a larger population within Sussex and to examine the feasibility of an intervention study to determine directly whether the service leads to actions that are effective in practice. The project concentrates on hospital admissions for respiratory endpoints, including asthma and COPD, as a more severe outcome with available concentration-response relationships and routine statistics. The original rationale for the air quality banding system was based on respiratory effects, given the opportunity for patients to adjust their medication in response to exacerbation of symptoms. For the period studied, the relevant pollutants were ozone (O_3), nitrogen dioxide (NO_2) and PM_{10}.

Methods

4. The first step was to calculate the health impacts on respiratory hospital admissions of moderate, high and very high days in Sussex over the period 2006-2011, i.e. since the start of the airAlert service. The potential benefits cannot be any larger than the current health impacts. A baseline was set for each pollutant at the average concentration of that pollutant on days when all pollutants were low according to the air quality index. For each day, the difference between the concentration of a pollutant on that day and its low day average was derived. Concentration-response relationships, derived from a meta-analysis of studies in the literature in a past report and another project (Table E1), were then used to calculate the expected numbers of additional respiratory, COPD and asthma admissions from the concentration increment above a low day. This process was repeated for other pollutants on that day and the results summed for all moderate, high and very high days.

Table E1 Concentration-response relationships used in calculations of health impacts of moderate, high and very high days

Outcome	Concentration-response relationship % increase per 10 µg/m^3 (95% confidence intervals)		
	O_3 (8 hr ave)	NO_2 (1 hr ave)	PM_{10} (24 hr ave)
Respiratory hospital admissions all ages	0.63 (0.09 – 1.18)	0.15 (-0.08 – 0.38)	1.71 (1.19 – 2.23)
Asthma admissions in children	-0.36 (-1.28 – 0.57)	0.38 (-0.18 – 0.94)	1.69 (0.5 – 2.96)
Asthma admissions in adults aged 15-64	0.14 (-1.18 – 1.47)	0.20 (0.00 – 0.50)	1.00 (0.30 – 1.69)
COPD admissions all ages	1.13 (0.59 – 1.67)	0.26 (0.06 – 0.46)	0.75(0.14 – 1.36)

Results - numbers of hospital admissions for moderate, high and very high days in Sussex 2006-2011

5. The results are shown in Table E2. As nitrogen dioxide and PM_{10} are closely correlated, there is debate over whether there is double counting when including effects of both pollutants. Results are given in this summary summing the effects of ozone and PM_{10} without NO_2 (which has in any case a small effect, about 20 respiratory admissions). Results summing all 3 pollutants are given in the main report. Results for respiratory hospital admissions on moderate, high and very high days in London are also given for comparison. It is emphasised that these are estimated figures based on specific assumptions such as the definition of the low day baseline, with a combination of uncertainties derived from the different inputs – measurement error in daily pollution levels and the baseline low day values; confidence intervals and other uncertainties in the concentration-response relationships; uncertainty in the datasets for population and uncertainty in the baseline rates for hospital admissions. These and other points regarding uncertainties are discussed in Chapter 7 of the report.

Table E2 Summary of total additional emergency hospital admissions for different outcomes in Sussex and for respiratory admissions in London for all pollutants on moderate, high and very high days with at least one raised pollutant compared with low days for period 2006-2011

Outcome	Estimated additional hospital admissions
Respiratory hospital admissions all ages in Sussex	741.7
Asthma admissions in children in Sussex	3.8
Asthma admissions in adults aged 15-64 in Sussex	11.5
COPD admissions all ages in Sussex	118.7
Respiratory hospital admissions all ages in London	4027.5

6. So the patterns of moderate, high and very high days in Sussex over the period 2006-2011 were estimated to have led to 742 respiratory hospital admissions attributable to O_3 and PM_{10} and to around 120 COPD admissions, around 12 asthma admissions in adults and around 5 asthma admissions in children. While the difference between the numbers of respiratory hospital admissions and the sum of the asthma and COPD admissions may be due to the fact that the concentration-relationships come from different groups of studies, there may also be a significant contribution from an effect of air pollution on lower respiratory infections. This effect was not analysed in this report.

7. Numbers of additional respiratory hospital admissions in Sussex were smaller than in London. This was not only due to the larger population in London but also due to the higher number of moderate, high and very high days.

8. The results split by moderate, high and very high days and by pollutant showed that:

   - While high and very high days provided the greatest individual risks, the overall public health impact of moderate days was much greater as there were many more of them.

   - NO_2 contributed only small numbers of respiratory hospital admissions, COPD admissions and asthma admissions to the totals on moderate, high and very high days.

   - Both ozone and PM_{10} contributed to the numbers of respiratory hospital admissions on moderate, high and very high days, with slightly larger numbers for ozone. PM_{10} contributed more to asthma admissions than ozone, and ozone contributed more to COPD admissions than PM_{10}

   - The pattern of daily admissions showed peaks in the spring where accumulations of NO_2 and long-range transported PM_{10} can be combined with springtime elevations of ozone to give moderately raised levels of all pollutants.

   - The greater influence of ozone on COPD admissions related to moderate, high and very high days led to peaks in the summer for air pollution-related COPD admissions in Sussex.

   - PM_{10} contributed the most to air pollution-related respiratory hospital admissions in London. The effect of nitrogen dioxide on respiratory hospital admissions was still lower than that of PM_{10} and ozone but it made more of a contribution than in Sussex.

   - The calculations shown do not represent the overall health effects of air pollution. There will be contributions from variations in pollution within the low band in addition to contributions from other outcomes such as respiratory symptoms, cardiovascular admissions and mortality.

Results – potential size of effect amongst airAlert subscribers

9. Calculations were also done on the estimated size of the effect amongst those signed up to the airAlert service by scaling the results by population and taking into account the fact that a higher proportion of asthmatics and COPD patients sign up. This gave figures of 0.3 COPD admissions, 0.013 asthma admissions in adults and 0.007 asthma admissions in children, which along with a general population group gave a range from 0.39-0.47 admissions over the 6 year period. Put another way, there was a probability of 39-47% of 1 admission amongst airAlert subscribers over the 6 year period.

10. Focus group work suggested that around 67% of those signed up took action in response to the alerts. It is unknown to what degree these actions are effective, but assuming they are, it was estimated that the service would need to be provided to the numbers in the following table in order to avoid 1 admission over 6 years. These are a set of alternative options – they do not add up to one overall figure as they relate to different patient groups.

Table E3 Estimated numbers of people in various categories to which the service would need to be provided to avoid 1 hospital admission

Category	Numbers needed to avoid 1 admission[a] by disease group
COPD	837
Children 1-16 with asthma	14,860
Adults 17-60 with asthma	21,760
Children from schools	102,470
Non COPD/children or young adult asthma i.e. elderly 60+ with asthma, other respiratory, heart disease, other, none, non-asthmatic children from schools	3,190

[a] Numbers to which the service needs to be provided if 67% of participants take action and the action is 100% effective

Results – feasibility of potential future intervention study

11. A simulated dataset was generated using an optimistic scenario of 67% of participants in an intervention study taking action that was 100% effective in averting effects of all pollutants, including NO_2. This represents the test group, the control group being the situation in Sussex as it is now. In essence, this tests expansion of the service beyond the current situation. This showed an estimated reduction in respiratory admissions from about 760 to 520 admissions, representing a change in rate per 100,000 population from 47.6 to 31.9. Statistical power calculations suggested that to detect this change in rate with a power of 0.9 and an alpha (level of significance) equal to 0.05, around 340,600 people would be needed in each group, a total of 681,000. This represents a bit under half of the whole Sussex population.

Conclusions

12. The estimated health impact of raised levels of air pollution on respiratory hospital admissions in Sussex demonstrates that there is still a need for action to improve public health.

13. Spring days with moderately raised levels of several pollutants can be just as important as days with particularly high levels of just one pollutant.

14. Within the category of respiratory hospital admissions, the impact was estimated to be greater on COPD admissions than asthma admissions. Ozone appeared to be the pollutant contributing most to COPD admissions in Sussex.

15. The estimated benefits of the airAlert service are small but the numbers of people to which the service is currently provided is also small. If provided to the whole of the Sussex population, and 67% took action that was 100% effective, around 250 respiratory hospital admissions could potentially be avoided over a 6 year period (Chapter 6). This is over-optimistic. Expanding the service to increased numbers of asthmatics would improve benefits, although tens of thousands would need to receive the service to avoid 1 asthma admission. However, targeting the service at 850 COPD patients could avoid 1 COPD admission over 6 years, with increasing benefits for larger numbers, assuming the actions were effective. Focus group research by others has shown the service is also valued by carers and relatives. Calculations of the numbers of cardiovascular disease patients needed to avoid 1 cardiovascular admission have not been done in this report but the service might also benefit this group by allowing patients to avoid higher levels of exposure on higher air pollution days.

16. An intervention study to examine the benefits of the airAlert service in practice does not appear to be feasible at a county level.

17. This does not mean that the service is not potentially justified in cost-benefit terms, as the incremental costs of air alert messaging are low. The work quantifying potential impacts on health in this project should provide useful inputs should a cost-benefit analysis be considered.

1. Introduction

1.1 Health effects of air pollution

1.1.1 There is substantial evidence for effects of day to day changes in air pollution on health (WHO, 2006; Anderson *et al*, 2007), particularly on respiratory and cardiovascular outcomes. The evidence linking short-term changes in pollutant concentrations and health mainly comes from time-series studies which correlate the changes in pollutant concentrations with changes in routine statistics on health outcomes. There is also some evidence from panel studies which use data on smaller groups of individuals, rather than routine statistics, and from volunteer studies in chambers that expose volunteers to known quantities of specific pollutants rather than real life exposure to mixtures of pollutants.

1.2 Air pollution information service

1.2.1 Clearly, with evidence that suggests that short-term increases in levels of air pollution exacerbate symptoms and increase admissions to hospital, the question arises as to whether people should be prewarned of air pollution episodes and, if so, what advice they should be given. The Department of Health's Medical Advisory Group on Air Pollution Episodes (MAAPE) provided some wording for health advice at different levels of particular air pollutants and for different types of air pollution episode (Department of Health, 1991; 1992; 1993; 1995). Using this information, the Department for the Environment launched an air pollution information service that provided information to the public about present and forecast levels of air pollution and provided health advice linked to the present or forecast level. Air pollution was divided into four bands according to health risk. The bands and health advice were updated in 1998 by the Committee on the Medical Effects of Air Pollutants (COMEAP, 1998) and minor amendments have been made since (COMEAP, 2000; Defra, 2009). Major amendments were made with the launch of the UK Daily Air Quality Index in 2012 bringing the bands into line with the World Health Organisation guidelines and European Union Limit Values and including $PM_{2.5}$ for the first time (COMEAP, 2011; Defra, 2011). This was the most up to date version of the index at the time the analysis was done for this project and is summarised in Table 1.1. The index is on a ten point scale divided into 4 bands – low, moderate, high and very high. There have been minor changes since (Defra, 2013). The current index, bands and health advice can be viewed at http://uk-air.defra.gov.uk/air-pollution/daqi .

Table 1.1 UK Daily air quality index (Defra, 2011) – concentration ranges for low, moderate, high and very high days,

Pollutant	Averaging period	Unit	Low	Moderate	High	Very high
Particulate matter, PM_{10}	24-hour mean	$\mu g/m^3$	0-49	50-74	75-99	100 or more
Particulate matter, $PM_{2.5}$	24-hour mean	$\mu g/m^3$	0-34	35-52	53-69	70 or more
Sulphur dioxide, SO_2	15-minute mean	$\mu g/m^3$	0-265	266-531	532-1063	1064 or more
Ozone, O_3	Running 8-hour mean	$\mu g/m^3$	0-99	100-159	160-239	240 or more
Nitrogen dioxide, NO_2	1-hour mean	$\mu g/m^3$	0-199	200 –399	400 – 599	600 or more

1.2.2 The main objective of the information service is the prevention of adverse effects due to air pollution. There are three aims within this: (i) provision of information before and during air pollution episodes to allow the public to avoid exposure or ameliorate the effects of air pollution (ii) general education and awareness of air quality issues and (iii) some use the system as a means monitoring of progress towards air quality targets. This study was concerned with the first, more direct, aim.

1.3 airAlert (Sussex-air)

1.3.1 airAlert is an air pollution forecasting and warning service http://www.airalert.info/ which informs vulnerable people that air pollution is expected to be moderate, high or very high before an event occurs, so that they may manage their conditions appropriately.

1.3.2 airAlert was developed as part of a forecast service provided by the Sussex Air Quality Partnership (Sussex-air). It is based on the national Defra air pollution information service but proactively contacts registered users directly when air pollution is forecast to be moderate or above rather than leaving it up to the user to find the information. The service was first developed as a pilot-project in 2006. Sussex-air led the project with King's College London (ERG) who provided software and the forecasting system and both groups subsequently involved the University of Brighton in research into the effectiveness of the project service. airAlert is now a fully operational service (since 2008) provided by Sussex-air working in partnership with King's College London and the Sussex local authorities. airAlert also operates in Southampton and east Surrey and new services are being constructed for Sevenoaks, Kent.

1.4 airAlert service principles:

1.4.1 The key principles of the service are to:

- Provide air quality alerts before an air pollution event that has the potential to affect the health and well-being of vulnerable groups in communities.

- Provide a useful, informative and accurate service.
- airAlert is free to the recipient.
- Provide support and information direct to people via message services such as SMS/text, telephone voice message, email, RSS and the web.
- Support the public health system by supplying preventative information to help in patient's health care, help reduce health service burden and costs.

1.4.2 Key groups that airAlert targets:

- People with asthma and other respiratory sensitive groups
- Young (school ages) and the elderly
- People with limited access to services plus the media (radio, newspapers, TV)
- Vulnerable groups in the community

1.5 airTEXT

1.5.1 A similar but separate service called airTEXT operates across the London boroughs and in Liverpool http://www.airtext.info/index.php

1.6 Research questions

1.6.1 The current basis for the airAlert system is that there is evidence that short-term changes in air pollution have effects on health and that alerting people when air pollution levels are increased gives them the chance to reduce their exposure or increase their medication to lessen the chance of symptoms. It is considered that this may be helpful and is unlikely to be seriously harmful. This justification is based on qualitative judgement rather than direct evidence on the effectiveness of the intervention.

1.6.2 However, experience from other public health interventions suggests that the expected benefits may or may not transpire and, if they do, they may not occur for the expected reasons. Unexpected consequences can also occur. As resources are limited, it is important to demonstrate that the intervention is actually effective in practice as well as in theory. Commissioners within the NHS are likely to expect this and to want reassurance that encouraging patients to subscribe to this service would be cost effective. Designing a study to assess the effectiveness of the intervention (particularly if testing not only whether it works but whether it works because air pollution-related exacerbations are being prevented (rather than increasing compliance with medication in general)) is extremely challenging. An evidence development strategy was therefore defined before the project was set up with different stages to collate evidence to optimise the methods, key aims and objectives of future research and to check feasibility.

1.6.3 A previous stage of the evidence development strategy (completed 2008-2010) involved qualitative research into airAlert and similar services (London airTEXT) to address the question of 'how the service and information is perceived' and 'how the patient assesses the benefits to themselves'. This work was performed by Dr Kirsty Smallbone (University of Brighton) (Jenkins, 2008; Smallbone, 2009). 24% of airAlert users were over 55. 73% of (self-selected) users considered the service was helpful in managing their symptoms. Of these users, many took some action in response e.g. 24% used their inhalers and 16% avoided exercise outdoors (Jenkins, 2008). Analogous results have also been produced for a combined group from Sussex, London and Luton (Smallbone, 2009). This work feeds into the current project as described in chapters 5 and 6.

Aims of this project - Assessment of evidence in the literature; prediction of possible quantitative benefits and scoping of feasibility of intervention study

1.6.4 The aims of this study were to answer the following questions:

- Question 1. Using meta-analytical techniques, what is the current quantitative evidence supporting associations between short-term changes in levels of air pollution[4] and effects on health outcomes relevant to the airAlert system[5]?
- Question 2. Bearing in mind wider evidence, how likely are these associations to be causal and can concentration-response relationships be defined for use in quantifying the expected health impact of changes in levels of air pollution?
- Question 3. Applying the concentration-response relationships defined in (2) to information on the increment between the average concentrations of pollutants on days in the low band and the average concentrations of pollutants on days in the high or moderate band and on the frequency of episodes of high or moderate pollution, what is the expected size of the effect of these pollution changes on health impacts within the general population?
- Question 4. Using a variety of reasonable assumptions, what is the expected size of the effect of these pollution changes in the population likely to receive alerts?
- Question 5. Using assumptions guided by qualitative research on whether users respond with action to ameliorate effects, what is the scope of the possible reductions in health outcomes that might be generated by users of the service?
- Question 6. Given the answers to the previous questions, what is the feasibility and likely statistical power of an intervention study to assess the effectiveness of the alert services in reducing adverse health outcomes?

1.6.5 If this project considered it to be feasible, future work would establish a primary real-world intervention study to establish the effectiveness (in terms of reductions in adverse health outcomes) of the airAlert service, in practice as well as in theory. A full cost benefit analysis of the intervention could then be performed (from both a health and a financial perspective). Recommendations could then be made as to the likely benefit to relevant groups of patients of adoption of the service.

1.6.6 The project management arrangements for the project are given in Appendix 2.

[4] PM_{10}, O_3 and NO_2 for the purposes of this report.

[5] Hospital admissions for all respiratory disease, COPD and asthma

2. Quantitative relationship between short-term changes in air pollution and effects on health

2.1 Question 1 Using meta-analytical techniques, what is the current quantitative evidence supporting associations between short-term changes in levels of air pollution and effects on health outcomes relevant to the airAlert system?

2.1.1 The work to address this question has been done in two parts. Part A makes use of a report already prepared that summarises evidence up to 2006 on time-series studies and panel studies. Part B ties in with another project that is preparing reviews of time-series evidence updated to May 2011.

2.2 Question 1 PartA Evidence in systematic review report (Anderson *et al*, 2007)

2.2.1 The Department of Health has previously funded Professor Ross Anderson and Dr Richard Atkinson at St. George's Hospital, University of London to develop a database of epidemiological studies related to air pollution and health. A report was produced for the Department of Health based on studies up to 2006 (henceforward referred to as the Air Pollution Epidemiology Database (APED report))(Anderson *et al*, 2007). The search strings, sifting process for the studies, data extraction method, standardisation to a common metric and selection protocol e.g. which lag between concentration and response to use for inclusion in the meta-analysis are all described in Appendix 1. This project has built on this report to:

- Add detailed commentary in specific subject areas such as respiratory symptoms.
- Group the results by health outcomes such as respiratory hospital admissions and respiratory symptoms to facilitate comparison across pollutants within a particular outcome (the Anderson *et al*, 2007 report is grouped by pollutant rather than outcome to give an overall description of the effects of each pollutant).

2.2.2 So the first step in developing this stage of the airAlert evidence strategy was to group information about different pollutants together by the following health outcomes:

- respiratory hospital admissions
- asthma admissions
- COPD admissions
- emergency room visits
- upper respiratory symptoms
- lower respiratory symptoms
- cough/bronchitic symptoms
- asthma symptoms
- lung function
- medication use

2.2.3 This project has focussed on the averaging times relevant to the banding system i.e. 8 hour average ozone (O_3), 1 hour average nitrogen dioxide (NO_2) and 24 hour average PM_{10}. There were too few studies available on $PM_{2.5}$ and hospital admissions available for meta-analysis prior to the 2006 cut-off for the 2007 report, and $PM_{2.5}$ has only been measured in Sussex since 2009. Levels of sulphur dioxide and carbon monoxide are known to be low so these pollutants were not included and neither of these pollutants were the reasons for days classified as moderate, high or very high pollution in Sussex over the period 2006-2011 (the period for this analysis).

2.2.4 Mortality has not been included in the above list of health outcomes as, fortunately, it is likely to be rarer as an outcome than symptoms or hospital admissions. Cardiovascular endpoints have also not been included as these fit less well into the principles of the airAlert system which is intended to give individuals the

opportunity to respond to an alert. Asthma patients are strongly encouraged to take control of their own treatment, particularly for use of inhalers and this applies to some extent to COPD as well. It is much less likely that patients with heart disease would be expected to adjust their own medication (except possibly for angina).

Respiratory hospital admissions

2.2.5 The number of studies on respiratory hospital admissions is reasonably large, particularly for PM_{10} for which an averaging time of 24 hours is always used. For ozone and nitrogen dioxide, studies use different averaging times, not just the ones selected here. For nitrogen dioxide, it is more common for the 24 hour average to be used. Nonetheless, for single-pollutant models, there were sufficient studies for meta-analysis for all three pollutants (Table 2.1).

Table 2.1 Anderson *et al* (2007) report. Single city meta-analytical estimates for respiratory hospital admissions (% increase per 10 µg/m3) based on studies published up to 2006 (lcl – lower confidence limit; ucl – upper confidence limit) (random effects not adjusted for publication bias for this table)

Pollutant	Averaging time	Studies for meta-analysis	Pooled estimate	95% lcl	95% ucl
Ozone	8 hour	7	0.63	0.09	1.18
NO_2	1 hour	4	0.15	-0.08	0.38
PM_{10}	24 hour	19	1.71	1.19	2.23
(NO_2 update)	(1 hour)	(6)	(0.34)	(-0.02)	(0.7)

Source: Anderson et al (2007) plus an update

2.2.6 On a per 10 µg/m^3 basis, PM_{10} had the largest estimate, followed by ozone and then nitrogen dioxide. It should be noted that comparing the size of the estimates is an observation regarding inputs to the later calculations. It is not a measure of inherent potency of the pollutants. This would require comparison on a molar basis, which is not possible for a mixture of components such as PM_{10}. Nor is it a measure of real-world importance, as this requires combination with real-world concentrations of the pollutants as is done in later chapters. The nitrogen dioxide estimate was only marginally significant statistically, perhaps partly because of the small number of studies. An update including more recent studies suggested a slightly larger marginally significant estimate but it was still lower than the estimates for ozone or PM_{10}. Although not used here, the association between 24 hour average nitrogen dioxide and respiratory hospital admissions was robust, providing some confidence in a real effect for nitrogen dioxide. The report by Anderson *et al* (2007) also analysed heterogeneity and publication bias. The implications of this are discussed in section 7 on uncertainty.

Admissions for specific respiratory diagnoses

2.2.7 The aim was to quantify the effects of all the key pollutants on low, moderate, high and very high days. This required that there were sufficient studies for meta-analysis, or a sufficiently large multi-city study, for all three pollutants. While this was the case for asthma, at the time of Anderson *et al* (2007) report, there were insufficient studies for COPD or lower respiratory infections. It was therefore decided to wait until the updating of the database before defining concentration-response functions for specific respiratory diagnoses. The updated concentration-response functions are described in section 2.3.

Table 2.2 Anderson (2007) report. Number of studies available up to 2006 for meta-analysis of single pollutant single city estimates for hospital admissions for specific respiratory diagnoses

Outcome	Diagnosis	Age group	O_3 8hr	NO_2 1hr	PM_{10} 24hr
			Number of studies for meta-analysis		
HAD	ASTHMA	AA	7	4	7
HAD	ASTHMA	C	5	7	17
HAD	ASTHMA	YA	5	5	9
HAD	ASTHMA	E	4		
HAD	COPDp	AA			
HAD	COPDp	E			14
HAD	COPDm	AA	4		
HAD	COPDm	E			17
HAD	LRI	AA			3
HAD	LRI	C			
HAD	LRI	YA			
HAD	LRI	E			18

HAD = hospital admissions; ASTHMA = asthma, ICD10 codes J45-46; $COPD_p$ = chronic obstructive pulmonary disease including asthma, ICD10 codes J40-47; $COPD_m$ = chronic obstructive pulmonary disease excluding asthma, ICD10 codes J40-47 excluding J45-46; LRI = lower respiratory infections, ICD10 codes J10-J18, J20-J22 or similar; AA = all ages; C=children age 0-14; YA = adults aged 15-64; E = elderly 65+. Source: Anderson et al (2007)

Emergency room visits

2.2.8 At the time of the Anderson *et al* (2007) report, there were insufficient studies of air pollutants and emergency room visits for several pollutant/age group/averaging time combinations. There were no examples where meta-analysis was possible for all 3 pollutants for the same diagnosis and age group. In any case, the application of concentration-response functions for emergency room visits to the UK context is unclear. Emergency room visits in the US are something between GP consultations and accident and emergency attendances and do not map easily to the UK health services context. There are a few UK studies on A&E visits (Atkinson *et al*, 1999; Buchdahl *et al*, 2000) or GP consultations (Hajat *et al* 1999, 2001, 2002) that could be used in future work, but this was not done in this project.

Table 2.3. Anderson (2007) Report Number of studies available up to 2006 for meta-analysis of single-pollutant single city estimates for emergency room visits

Outcome	Diagnosis	Age group	O_3 8hr	NO_2 1hr	PM_{10} 24hr
			Number of studies for meta-analysis		
Emergency Room Visits	RESP	AA			5
Emergency Room Visits	RESP	C			
Emergency Room Visits	RESP	YA			
Emergency Room Visits	RESP	E			4
Emergency Room Visits	ASTHMA	AA			
Emergency Room Visits	ASTHMA	C	5	5	
Emergency Room Visits	ASTHMA	YA			
Emergency Room Visits	ASTHMA	E			

Source: Anderson et al (2007) RESP= all respiratory, ICD10 codes J00-J99. *Had to include main lower respiratory infections (LRI) J10-J18, J20-J22 and chronic obstructive pulmonary diseases (COPD) J40-J47. A few missing ICD codes was acceptable. Other definitions as in Table 2.2.*

Panel studies

2.2.9 Panel studies follow small cohorts of subjects for a short period (weeks) to obtain daily data on symptoms, lung function and medication use and correlate this with ambient pollution concentrations. They are more labour intensive, and few are available relative to studies of routine admissions data. The most frequently reported studies are of PM_{10}, followed by ozone. PM studies tended to be amongst panels of symptomatic children but ozone studies tended to be amongst panels of healthy subjects. There were no studies for the relevant averaging times for ozone and nitrogen dioxide and respiratory symptoms at the time of the 2007 report (there was evidence for other averaging times).

Table 2.4 Anderson (2007) Report Number of studies available up to 2006 for meta-analysis of single-pollutant estimates for panel studies on respiratory outcomes

Outcome[1]	Pop group[2]	Age group	O_3 8hr	NO_2 1hr	PM_{10} 24hr
			Number of studies for meta-analysis		
FEV_1	Healthy	C	12		
FVC	Healthy	C	6		
PEFR	Healthy	C	10		
PEFR	Symptomatic	C			28
PEFR	Unselected	C	4		5
iURS	Symptomatic	C			25
pURS	Symptomatic	C			27
iLRS(O)	Symptomatic	C			25
pLRS(O)	Symptomatic	C			29
iM	Symptomatic	C			18
pM	Symptomatic	C			28

Source: Anderson et al (2007) [1] *PEFR = peak expiratory flow rate, FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, LRS = lower respiratory symptoms, URS = upper respiratory symptoms, (O) other = various, including dyspnoea, decrements or other lung function measurements, e.g. maximum mid expiratory flow, M-medication use. i = incidence; p= prevalence.* [2] *unselected = mixture of healthy/symptomatic children.*

2.3 Question 1 PartB Evidence from updating of air pollution epidemiology database (systematic review project)

2.3.1 The Anderson *et al* (2007) report used studies indexed on online databases until 2006. Studies on hospital admissions have now been updated on the database until May 2011. The intention of the database is that it is a relatively rapid process to produce Forest plots (graphs representing the results visually) and meta-analytical estimates once the database is populated and once the appropriate selection criteria for studies to include in the analysis have been agreed. This section looks at information from a parallel project updating the concentration-response functions, with a particular focus on hospital admissions for specific respiratory diagnoses. Emergency room visit studies for each pollutant have only been updated on the database to 2009 and panel studies have not been updated since 2006. These are therefore not covered here.

2.3.2 This section involved collaboration with St George's, University of London who host the air pollution epidemiology database. This was able to take advantage of a systematic review project to prepare literature review papers on meta-analyses of studies on ozone, particulate matter and nitrogen dioxide. The project is not yet complete but liaison between the project teams allowed concentration-response functions of particular relevance to this project to be defined in advance of the overall systematic review project schedule.

2.3.3 The search strings, sifting process for the studies, data extraction method, standardisation to a common metric and selection protocol e.g. which lag between concentration and response to use for inclusion in the meta-analysis are all as used for the Anderson *et al* (2007) report and described in Appendix 1. In contrast with the Anderson *et al* (2007) report, where multi-city study results were simply quoted rather than meta-

analysed and single city study results were pooled globally, the new project pools single city studies by region and then pools this meta-analysed result with other multi-city studies from the same region in a second stage analysis. Results were also pooled across regions. If there was more than one study in a city, one result was chosen according to a standard protocol based on giving preference to multi-city studies (which have standardised analyses across cities) and more recent studies. For the work reported here, the pooled analyses of single city and multi-city studies for the European region have been used.

2.3.4 Use of concentration-response functions developed in the parallel project has concentrated on hospital admissions for specific respiratory diagnoses as there were not always sufficient studies available at the time of the Anderson *et al* (2007) report. There were sufficient new studies in several cases for a new meta-analysis to be possible. Outcomes were only used where meta-analytical estimates were available for all 3 pollutants with the appropriate averaging times.

Asthma admissions in children

2.3.5 There were sufficient studies of asthma in children age 0-14 in the European region for meta-analysis (Table 2.5). The largest number of studies/cities for meta-analysis was available for PM_{10} (Atkinson *et al*, 2003 (8 cities); Andersen *et al*, 2008; Anderson *et al*, 2001, Thompson *et al*, 2001), and this showed a statistically significant positive association. The relationship for 1 hour average nitrogen dioxide and asthma admissions in children was smaller and was not statistically significant, although this may be the result of the small number of studies available (Sunyer *et al,* 1997 (3 cities); Samoli *et al*, 2011; Anderson *et al*, 2001). The association between 8 hour average ozone and asthma admissions in children (pooled from Sunyer *et al,* 1997 (3 cities); Samoli *et al*, 2011; Fusco *et al*, 2001; Anderson *et al*, 2001) was actually negative, although the negative association was not statistically significant. This negative association may however be the result of negative confounding by PM_{10}, rather than a genuine negative association. Across all regions, not just Europe, the pooled estimate is positive, perhaps because correlations between pollutants vary across the world. It is also worth noting that these differences across pollutants may just be a matter of chance variation, given small effect sizes and small numbers of studies. The implications of these results for views on causality are discussed in section 2.4.

Table 2.5 Meta-analytical estimates asthma hospital admissions in children (European region) (% increase per 10 µg/m^3) (random effects, not adjusted for publication bias for this table)

Pollutant/ Averaging time	Region	Studies / cities for meta-analysis	Pooled estimate	95% lcl	95% ucl
Ozone 8 hour	Europe	4/6	-0.36	-1.28	0.57
NO_2 1 hour	Europe	3/5	0.38	-0.18	0.94
PM_{10} 24 hour	Europe	4/11	1.69	0.50	2.96

Lcl – lower 95% confidence limit, ucl – upper confidence limit

Asthma admissions in 'young' adults (aged 15-64)

2.3.6 The meta-analysis results for asthma admissions in adults aged 15-64 are given in Table 2.6. As with asthma admissions in children, the largest association, on a per 10 μg/m^3 basis, was for PM_{10} and this was statistically significant. The association with 1 hour nitrogen dioxide was again small but lacked statistical precision. Unlike for asthma admissions in children, the association with ozone was not negative but was still not statistically significant. The associations for PM_{10}, nitrogen dioxide and ozone were all based on pooling of results from Sunyer *et al*, (1997) (3 cities) and Anderson *et al* (2001).

Table 2.6 Meta-analytical estimates asthma hospital admissions in adults aged 15-64 (European region) (% increase per 10 μg/m^3) (random effects, not adjusted for publication bias for this table)

Pollutant/ Averaging time	Region	Studies / cities for meta-analysis	Pooled estimate	95% lcl	95% ucl
Ozone **8 hour**	Europe	2/5	0.14	-1.18	1.47
NO_2 **1 hour**	Europe	2/5	0.20	0.00	0.50
PM_{10} **24 hour**	Europe	1/8	1.00	0.30	1.69

Lcl – lower 95% confidence limit, ucl – upper confidence limit

COPD admissions all ages

2.3.7 There were sufficient studies for meta-analysis for COPD admissions all ages for the relevant averaging times but not for COPD admissions in the elderly. It is likely that the results for all ages represent much the same thing, as COPD mostly occurs in the elderly in any case. The analyses are for COPD (ICD9 code 490-496 or a sub-group of these) excluding asthma (ICD 9 code 493). The results are given in Table 2.7. All associations were positive and statistically significant. Ozone had a stronger association with COPD admissions (pooled from Anderson *et al* (1997) (6 cities) and Fusco *et al*, (2001) than PM_{10} on a per 10 μg/m^3 basis (pooled from Dab *et al* 1996; Wordley *et al,* 1997 and Colais *et al* 2009). The association of nitrogen dioxide with COPD admissions was relatively small, based on one European multi-city study, Anderson *et al* (1997).

Table 2.7 Meta-analytical estimates (European region) COPD hospital admissions all ages (% increase per 10 μg/m^3) (random effects, not adjusted for publication bias for this table)

Pollutant	Ave. time	Studies for meta-analysis/no of cities	Pooled estimate	95% lcl	95% ucl
Ozone	8 hour	2/7	1.13	0.59	1.67
NO_2	1 hour	1/6	0.26	0.06	0.46
PM_{10}	24 hour	3/11	0.75	0.14	1.36

Lcl – lower 95% confidence limit, ucl – upper confidence limit

Lower respiratory infections

2.3.8 Meta-analysis results are not yet available from the parallel project for this endpoint. There is some evidence of associations between air pollution and hospital admissions for lower respiratory infections (Anderson *et al*, 2007, Burnett *et al* 1999; Fusco *et al* 2001; Hinwood *et al* 2006; Michelozzi *et al, 2000;* Wong *et al* 1999; Wordley *et al* 1997; Simpson *et al* 2005*;* Medina-Ramon *et al* 2006).

2.4 Question 2 Bearing in mind wider evidence, how likely are these associations to be causal and can concentration-response relationships be defined for use in quantifying the expected health impact of changes in levels of air pollution?

2.4.1 Question 1 relates to the evidence for statistical associations but this does not necessarily mean that the associations are causal. Additional commentary on the material is needed. The coherence (or not) between different related health outcomes needs to be discussed in addition to discussion of key points from the toxicological evidence. A detailed review of this evidence is not within the scope of this project but information from various international evaluations can be highlighted.

2.4.2 For example, the evidence for the association between ozone and respiratory hospital admissions being causal is supported by volunteer studies of direct exposure to ozone alone showing reductions in lung function and increases in lung inflammation. It is also supported by panel studies showing similar effects after real-world exposure to ozone (WHO, 2006; WHO, 2013, US EPA 2013). There is also evidence that ozone is an oxidant that, if antioxidant protection mechanisms are not effective, can damage cell membranes by lipid peroxidation and lead to an inflammatory response to the products of cell damage (Department of Health, 1991; WHO 2006; WHO, 2013,; US EPA 2013). Of the pollutants considered here, the strongest evidence for effects on reduced lung function is for ozone.

2.4.3 A causal effect of PM_{10} on respiratory outcomes is well established (Committee on the Medical Effects of Air Pollutants (COMEAP), 1995; US EPA, 2009; WHO, 2006, 2013). Study of PM_{10} is complicated in that it represents a mixture and its composition can vary across time and place. Thus, toxicological evidence on sources contributing to PM_{10} may also be relevant. Of particular interest in this respect, is the body of literature (reviewed in COMEAP, 2010; Health Effects Institute Panel on the Health Effects of Traffic-related Air Pollution, 2010; US EPA, 2009; WHO 2006; WHO, 2013); indicating that diesel particles, at least at high concentrations, can act as an adjuvant for allergic responses, of clear relevance to the plausibility of an effect of particulate matter on asthma admissions. There are technical challenges in generating/sampling particle mixtures in the laboratory such that volunteer studies are less extensive and more recent than for the other pollutants. Evidence is mixed with there being more focus on cardiovascular than respiratory effects (US EPA, 2009). Taking toxicological and epidemiological evidence together, the cardiovascular effects of PM_{10} are also generally regarded as causal.

2.4.4 The effects of nitrogen dioxide are a matter of considerable debate (COMEAP, 2009). There are large numbers of volunteer studies available for evaluation (Department of Health, 1993; US EPA, 2008). These show evidence for a small effect on airway hyper-responsiveness. There has not always been a clear pattern of effect across doses, although the different doses are often examined in separate studies. Effects are shown at levels above average concentrations of nitrogen dioxide but within the range of peaks shown in some microenvironments close to roadsides (WHO, 2013). Interpretation of the epidemiological studies is complicated by the fact that nitrogen dioxide and particulate matter, particularly its traffic-related constituents, are closely correlated so that each could be acting as an indicator of the other, or some other component of the mixture. As particulate matter has been much more extensively studied in recent years, generating a considerable body of mechanistic evidence, many regard the effects of particulate matter as being more likely to be responsible. However, it is plausible for both pollutants (rather all one or all the other) to have at least some effects, even if there is some element of double-counting. Evidence is increasing for an effect of nitrogen dioxide independent of PM_{10}, although uncertainty still remains regarding overlap with particle metrics more closely related to traffic pollution such as black carbon or ultrafine particles (WHO, 2013).

2.4.5 Overall, PM_{10} and ozone are regarded as having independent effects (WHO, 2013; US EPA, 2013). This has been shown most clearly for mortality (Gryparis *et al* 2004; Bell *et al* 2007).

2.4.6 Within the subset of studies that have studied respiratory hospital admissions, all ages, all year for 8 hour average ozone, as selected for this work, there are relatively few studies that have examined adjusting the ozone association for the effect of particles. Two of those that have examined the issue found the effect of the ozone association to be stable to adjustment for a measure of particulate matter, black smoke in the case of Ponce de Leon *et al* (1996), particulate matter measured by nephelometry in the case of Petroeschevsky *et al* (2001). Another did not (Wong *et al* 1999) but the association increased in size and became statistically significant when controlled for high levels of PM_{10}. This can occur as hospital admissions can appear not to drop with decreasing concentrations of ozone, as PM_{10} levels are often higher at low concentrations of ozone in the winter. This can mask a linear relationship that is revealed after control for PM_{10}.

2.4.7 With regard to asthma admissions, Sunyer *et al* (1997) only used two pollutant models where an association was found, they therefore did not do multi-pollutant models for ozone, despite the possible negative confounding by NO_2 or particles. This is quite a common approach in studies in the literature and can mean that the potential for masking of an effect of ozone by negative confounding is not always tested. Anderson *et al* (1998) found a significant negative association with asthma admissions in children in the cool season which became less negative after control for NO_2 and SO_2 but was unchanged after control for black smoke. The same study found a positive and statistically significant association with asthma admissions in adults age 15-64 which increased after control for NO_2, SO_2 or black smoke.

2.4.8 For COPD admissions (COPD, excluding asthma), 8 hour ozone, all ages, there were no multipollutant models examined amongst the studies in Europe pooled in the meta-analysis. A study outside Europe found that the association with ozone was strongest amongst the pollutants and that the association was stable to adjustment for other pollutants ($PM_{2.5}$ was the particle metric used in this case) (Ko *et al*, 2007). Another study, using 1 hour average ozone in the elderly, did not find that the association was stable to adjustment for other pollutants (Morgan *et al*, 1998) but another study using 24 hour average ozone in the elderly did find the association was stable (Yang *et al*, 2005). A study in Europe for COPD including asthma found the association was stable to adjustment for particle number counts but the association was negative and not significant (Andersen *et al*, 2008).

2.4.9 In order for associations to be considered suitable for use as concentration-response relationships, a number of issues need to be considered in addition to the plausibility of a causal mechanism. The possibility of confounding by other pollutants needs to be considered (as discussed above) and the selection of associations needs to take into account the country or countries where the studies were performed. If there is evidence of effect modification, the concentration response relationship may differ in different circumstances. We have chosen to use studies in Europe as a basis for the concentration-response relationships and have not considered effect modification in this first exercise to calculate effects. There is some evidence of effect modification (Katsouyanni *et al*, 2009; Bell and Dominici, 2008) but it is not well established across studies at this point.

2.4.10 We have chosen to follow the evidence as it is, acknowledging uncertainty. Thus, apparent negative associations have been used, with accompanying commentary, as have associations which are not statistically significant at the 95% level, as this may reflect low statistical power due to the small numbers of studies available. The uncertainties have been transmitted through the calculations as appropriate.

2.4.11 In using these concentration-response functions, we have considered that there is sufficient evidence to regard the associations as causal. The uncertainty regarding nitrogen dioxide has been acknowledged by providing totals with and without inclusion of nitrogen dioxide, to allow for the possibility of some double-counting. It has been assumed that the PM_{10} concentration-response relationships can be applied to reference equivalent measurements, although several of the studies on which it is based used TEOM measurements. We have used single pollutant models but discuss the issue of multi-pollutant models and correlations between pollutants later in the report.

3. Concentration increments between low and moderate, high or very high days

3.1 Methodological approach

3.1.1 Even if there is evidence that an air pollutant causes health effects, this may not be important if the concentrations of the relevant air pollutant are low. In order to consider the size of the health impact that the airAlert service is intended to address, the concentration-response relationship was combined with population size, baseline rates of the relevant outcome, the concentration difference for each pollutant between low and moderate, low and high air pollution days and low and very high days and the frequency of moderate, high or very high air pollution days. This gave the health impact in the general population of Sussex. A similar approach was taken to estimating the health impact in London.

3.1.2 Defining the concentration difference for each pollutant between low and moderate or low and high air pollution days is not entirely straightforward. The method used is attached in Box 1 below. This method takes into account the actual pollutant levels on low, moderate and high days (as these can vary within each band) and also takes into account the contemporaneous levels of pollutants other than those that led to the alert. Each day in the study period was classified using the UK daily air quality index implemented in January 2012 following recommendations by COMEAP[6]. 'Very high' days were defined as days where any urban or rural background site in Sussex (or London) was in the very high band (this is the way days are defined for the national air quality index system and the airAlert service). A day with no urban background, suburban or rural background[7] sites in the very high band but one or more relevant sites in the high band was defined as a 'high day'. A day with no urban or rural background sites in the very high or high band but one or more relevant sites in the moderate band was defined as a 'moderate day'. Any other days were 'low days'. These days were defined retrospectively for the period 1/1/2006-31/12/11. For each high day, the average concentration of, say, ozone across all the background sites in Sussex (or London) was calculated. This average was not necessarily in the high band as not all areas of Sussex (or London) were necessarily in the high band. Even if the high day was for ozone and not other pollutants, it would underestimate the health effects if the average level of other pollutants were not also calculated, taking into account double-counting as appropriate. The level of each pollutant was averaged across all the low days, giving one average for each pollutant to calculate an increment between the 'high day' value and the 'low day average' for each pollutant. The increments between 'moderate day' values and the 'low day average' were similarly calculated.

[6] http://www.comeap.org.uk/documents/reports/39-page/linking/49-review-of-the-uk-air-quality-index

[7] The term 'background sites' will be used in the rest of the report to mean urban background, suburban and rural background sites.

Box 3.1 Method for defining pollutant increments from low to very high days, from low to high days and from low to moderate days

1. The concentration-response relationships come from studies using background concentrations to represent exposure so this calculation used results from urban and rural sites not roadside sites.

2. A very high day was defined as a day where concentrations of any one of NO_2, O_3 or PM_{10} at any urban or rural background site in Sussex was in the very high band, irrespective of the concentrations of the other pollutants. A day with no urban or rural background sites in the very high band but one or more relevant sites in the high band was defined as a 'high day'. The equivalent applied to defining a moderate day. Any other days were defined as 'low days'. These days were defined over several years.

3. For each very high day, the average concentrations of, say, ozone across all the background sites in Sussex were calculated. This average was not necessarily in the very high band as not all areas of Sussex were necessarily in the very high band. (The averaging time used will be that appropriate to the definition of the bands). Even if the very high day was for ozone and not other pollutants, it would underestimate the health effects if the average level of other pollutants were not also calculated. So the average concentrations of nitrogen dioxide and PM_{10} on the same very high day were also calculated.

4. The process was repeated for the high, moderate and low days.

5. The baseline was defined as the average for a particular pollutant across all low days. The difference between the very high, high or moderate day average for a pollutant on a particular day and the 'low day average' for that pollutant was then calculated to define the pollutant increment for that day.

6. This increment was then used in the health impact calculations (see Chapter 4).

3.1.3 Due to the limited monitoring of PM_{10} and ozone away from the coast in Sussex, particularly in the early years of the study, the monitoring data from a long running background location at Sevenoaks, Kent was included in the air pollution data set. This location is geographically close to the border with Sussex and would be expected to experience pollution similar to the large expanse of background locations in Sussex away from the coast.

3.2 Air pollution increments from low to moderate, high and very high days Sussex 2006-2011

3.2.1 To give a general idea of the pollutant climate in Sussex, the number of moderate, high, and very high days for ozone, PM_{10} and nitrogen dioxide is given below, based on urban and rural background sites.

Table 3.1 Numbers of moderate, high and very high days in Sussex for the period 2006-2011

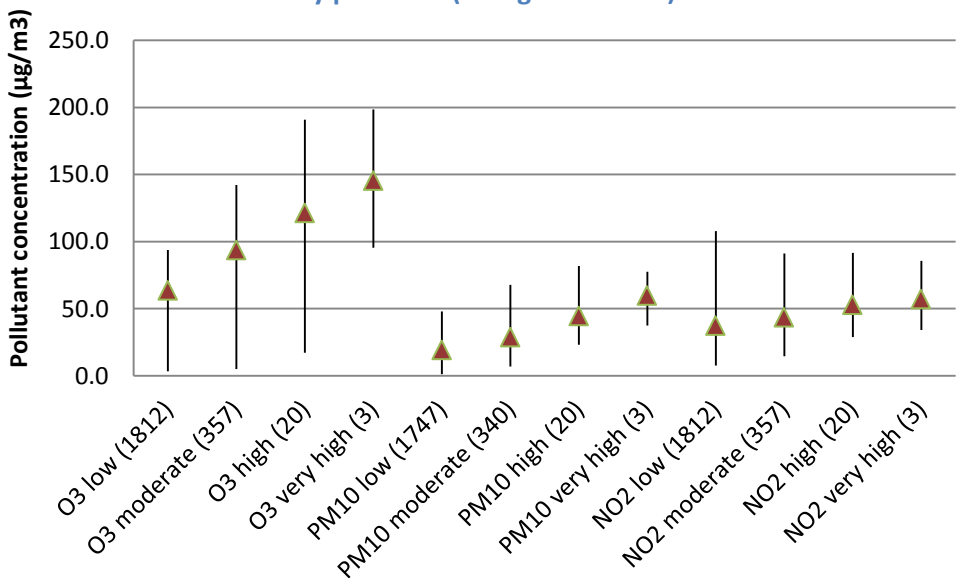
Year	O_3			PM_{10}			NO_2	Episode days for more than 1 pollutant
	Moderate	High	Very high	Moderate	High	Very High	Moderate	
2006	63	12	1	7				1 (O_3/PM_{10}) (moderate)
2007	45			13	3			6 (O_3/PM_{10}) (moderate or moderate/high)
2008	71	1		5	2	1		2 (O_3/PM_{10}) (moderate or moderate/high)
2009	43	1		13				2 (O_3/PM_{10}) (moderate)
2010	34			6				2 (O_3/PM_{10}) (moderate)
2011	59			20	1	1	3	8 (O_3/PM_{10}) (moderate or high/very high), (O_3/PM_{10}/NO_2) (moderate), (O_3/NO_2) (moderate)

3.2.2 The average and range of pollutant concentrations in Sussex on low, moderate, high and very high days are given in Table 3.2, and presented graphically in Figure 3.1.

Table 3.2 Average and range of pollutant concentrations (µg/m^3) for low, moderate, high and very high days in Sussex 2006-2011

Pollutant		Low days	Moderate days	High days	Very high days
O_3	Ave/	63.5	93.6	121.4	145.4
	range	(3.3-93.9)	(4.9-142.2)	(17.3-190.8)	(95.4-198.5)
	No. days	1812	357	20	3
PM_{10}	Ave/	19.2	28.8	44.6	59.7
	range	(1.1-47.9)	(6.8-67.7)	(23.1-81.8)	(37.5-77.5)
	No. days	1747	340	20	3
NO_2	Ave/	37.3	43.5	53.0	57.1
	range	(7.6-107.8)	(14.5-91.2)	(28.8-91.7)	(34.1-85.7)
	No. days	1812	357	20	3

Figure 3.1 Regional average pollutant concentrations (max, ave, min) in Sussex on low, moderate, high and very high days for any pollutant (background sites)



3.2.3 The average pollutant concentrations all increase progressively from low to moderate to high or very high for all pollutants, although the averages do not reach the breakpoints for the index bands. This was for two reasons. Firstly, the average concentration was across all moderate, high or very high days irrespective of the pollutant that led to the relevant banding e.g. the ozone average for high days includes the ozone concentrations on days that are high for PM_{10} rather than ozone. Secondly, any one background site exceeding the breakpoint leads to classification of that day in the new band but the average was calculated across all background sites in Sussex. These points are illustrated in Table 3.3 which gives the daily maximum at any background site and the regional averages for the same day for the three very high days in Sussex

during 2006-2011. On 18/07/2006, ozone was in the very high band but nitrogen dioxide and PM_{10} were in the low band. Nonetheless, these nitrogen dioxide and PM_{10} concentrations contributed to the averages for each pollutant on very high days. The two remaining very high days were for PM_{10}. These days illustrate the point that the daily maximum that leads to the designation of the band can be considerably greater than the regional average across all background, suburban, and rural sites. Figure 3.1 illustrates that the concentrations of ozone in particular can be well below the baseline concentration on some moderate and high days – these are likely to be winter days on which PM_{10} and nitrogen dioxide accumulate, but there is no photochemical generation of ozone, and some ozone destruction by accumulated nitric oxide. This was not the case on very high days as the average was brought up by a very high day due to ozone, and the very high days for PM_{10} were in April rather than the winter (Table 3.3).

Table 3.3 Pollutant concentrations (µg/m^3) on very high days in Sussex 2006-2011

Date	Ozone		PM_{10}		NO_2	
	Daily max	Regional ave	Daily max	Regional ave	Daily max	Regional ave
18/07/2006	241.17*	198.5	38.58	37.51	87.86	51.56
25/04/2008	106.55	95.37	136.41*	77.52	47.78	34.1
21/04/2011	172.61	142.29	101.54*	64.06	154.17	85.75

* Pollutant concentration leading to very high band on each day

3.2.4 The averages across all low days for each pollutant, taken as the baseline, were 63.5, 19.2 and 37.3 µg/m^3 for ozone, PM_{10} and nitrogen dioxide respectively. These were subtracted from the concentrations of each of the relevant pollutants for each moderate, high and very high day. Table 3.4 shows the average and range (minimum to maximum) of the increments across all the moderate, high and very high days representing the low to moderate, low to high and low to very high increments. The negative values represent the fact that the ozone concentrations, for example, include ozone concentrations on high days due to PM_{10} when ozone concentrations are actually lower than on typical low days due to scavenging of ozone by nitric oxide in the cold inversion conditions that can lead to high PM_{10} episodes in winter.

Table 3.4 Increments in pollutant concentrations (µg/m^3) for moderate to low, high to low and very high to low days in Sussex

Pollutant	Ave. (range) difference moderate to low	Ave. (range) difference high to low	Ave. (range) difference very high to low
O_3	30.0	57.8	81.8
	(-58.6 to 78.7)	(-46.3 to 127.3)	(31.8 to 135)
PM_{10}	9.6	25.3	40.5
	(-12.4 to 48.5)	(3.9 to 62.5)	(18.3 to 58.3)
NO_2	6.2	15.6	19.8
	(-22.7 to 53.9)	(-8.5 to 54.4)	(-3.2 to 48.4)

3.3 Air pollution increments from low to moderate, high and very high days London 2006-2011

3.3.1 While the main purpose of this project is aimed at Sussex, it was agreed to do some calculations for London to highlight some the unique features about the Sussex pollution climate. The respiratory hospital admissions calculations are given in Chapter 4. This section describes the pollution concentrations.

3.3.2 To give a general idea of the pollutant climate in London, the number of moderate, high, and very high days for ozone, PM_{10} and nitrogen dioxide is given below, based on urban background sites. In comparison with Table 3.1 for Sussex, there were fewer moderate and high days for ozone and no very high days. There were many more moderate days for PM_{10} and greater numbers of high and very high days as well. There were also many more moderate days for NO_2. This is as expected for a major urban city.

Table 3.5 Numbers of moderate, high and very high days in London for the period 2006-2011

Year	O_3		PM_{10}			NO_2	Episode days for more than 1 pollutant
	Moderate	High	Moderate	High	Very High	Moderate	
2006	43	8	41	4	2	9	15 O_3/PM_{10} (5 high/ moderate; 1 moderate/ high; 9 moderate/ moderate) 9 NO_2/PM_{10} (9 moderate/ moderate)
2007	33		33	6	1	14	7 O_3/PM_{10} (1 moderate/ high; 6 moderate/ moderate) 8 NO_2/PM_{10} (1 moderate/ v high, 1 moderate/ high, 6 moderate/ moderate)
2008	38		27	5	2	14	9 O_3/PM_{10} moderate/ moderate 2 NO_2/PM_{10} (1 moderate/ high; 1 moderate/ moderate 1 NO_2/O_3 moderate/ moderate
2009	23		24	3		8	3 O_3/PM_{10} moderate/ moderate 1 NO_2/PM_{10} moderate/ moderate
2010	24		18	2	2	8	2 O_3/PM_{10} moderate/moderate 3 NO_2/PM_{10} moderate/ moderate
2011	39		29	6	1	4	10 O_3/PM_{10} (1 moderate/ v high; 4 moderate/high; 5 moderate/moderate) 3 NO_2/PM_{10} moderate/ moderate (moderate)

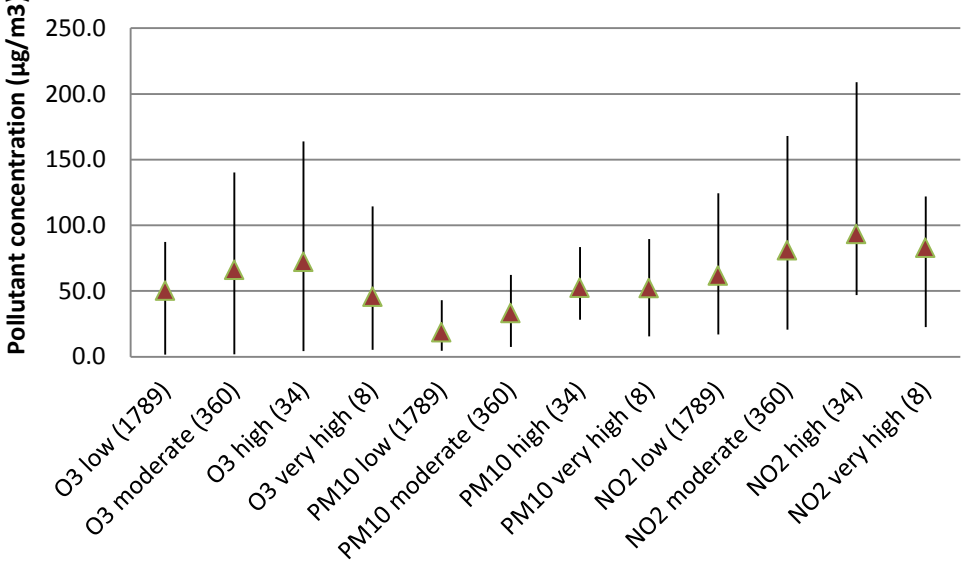
3.3.3 Table 3.6 and Figure 3.2 show the average, maximum and minimum regional average concentrations for all of the pollutants on days defined as low, moderate, high or very high. The average pollutant concentrations

all increased progressively from low to moderate to high for all pollutants, although the averages did not reach the breakpoints for the bands. This was for the same reasons as explained for the Sussex data. Unlike for the Sussex data, the average dropped or did not increase for all pollutants when moving from high to very high days. This was particularly marked for ozone, because there were more very high days for PM_{10} which were often, but not always, on days with cold still conditions when ozone was low. Even for PM_{10}, the average dropped from the high to the very high band. This was presumably because very high days for PM_{10} can be quite localised, such that the regional average was not particularly high, even when a particular site or sites were in the very high band. Figure 3.2 illustrates that the concentrations of ozone in particular can be well below the baseline concentration on some moderate, high and, in contrast to Sussex, very high days – these are likely to be winter days on which PM_{10} and nitrogen dioxide accumulate, but there is no photochemical generation of ozone, and some ozone destruction by accumulated nitric oxide. Nitrogen dioxide concentrations are significantly greater than in Sussex.

Table 3.6 Average and range of pollutant concentrations (µg/m^3) for low, moderate, high and very high days in London 2006-2011

Pollutant		Low days	Moderate days	High days	Very high days
O_3	Ave/	50.3	66.0	72.0	45.7
	range	(1.7 – 87.4)	(1,8 – 140.3)	(4.2 – 163.8)	(5.3 – 114.3)
	No. days	1789	360	34	8
PM_{10}	Ave/	18.5	33.1	52.3	52.1
	range	(4.6 – 43.1)	(7.5 – 62.3)	(28.2 – 83.4)	15.4 – 89.4)
	No. days	1789	360	34	8
NO_2	Ave/	61.8	80.9	93.4	82.9
	range	(16.9 – 124.5)	(20.6 – 168.1)	(47.0 – 209)	(22.7 – 121.9)
	No. days	1789	360	34	8

Figure 3.2 Regional average pollutant concentrations (max, ave, min) in London on low, moderate, high and very high days for any pollutant (background sites)



3.3.4 The averages across all low days for each pollutant, taken as the baseline, were 50.3, 18.5 and 61.8 µg/m^3 for ozone, PM_{10} and nitrogen dioxide respectively. The analogous figures in Sussex were 63.5, 19.2 and 37.3 µg/m^3. The baseline average low day London figures were subtracted from the regional average concentrations of each of the relevant pollutants for each day. Table 3.7 shows the average and range (minimum to maximum) of the increments across all the moderate, high and very high days representing the low to moderate, low to high and low to very high increments. Negative values again appear, representing the fact that pollutants such as ozone can have concentrations lower than the low day average when other pollutants are moderate or high and, in the case of London, very high. These are the increments for use in the health impact calculations in Chapter 4.

Table 3.7 Increments in pollutant concentrations (µg/m^3) for moderate to low, high to low and very high to low days in London

Pollutant	Ave. (range) difference moderate to low	Ave. (range) difference high to low	Ave. (range) difference very high to low
O_3	15.7 (-58.5 to 89.9)	21.7 (-46.1 to 113.5)	-4.7 (-45 to 64)
PM_{10}	14.6 (-11 to 43.7)	33.8 (2 to 64.8)	33.5 (-3.2 to 70.9)
NO_2	19.1 (-41.1 to 106.3)	31.7 (-14.8 to 147.3)	21.1 (-39.1 to 60.2)

4. Quantification of the health impacts on moderate, high and very high days compared with low days

Question 3 Applying the concentration-response relationships defined in question 2 to information on the increment between the average concentrations of pollutants on days in the low band and the average concentrations of pollutants on days in the high or moderate band and on the frequency of episodes of high or moderate pollution, what is the expected size of the effect of these pollution changes on health impacts within the general population?

4.1 General methodological approach using respiratory hospital admissions as an example

4.1.1 Concentration-response relationships for respiratory hospital admissions derived from Anderson *et al* (2007) were applied to the increment between the average concentrations of pollutants on days in the low band and the concentrations of pollutants on days in the high or moderate band in Sussex to give a percentage increase in the response for that concentration increment. This percentage increase was then applied to an estimate of daily baseline emergency respiratory hospital admissions in Sussex (51.2), derived from the total emergency respiratory hospital admissions for England in 2010/11 from HES online[8], the population of England[9] and the population of Sussex (1,563,000). The daily estimates of respiratory hospital admissions were then summed across the total number of high or moderate days for each pollutant.

4.1.2 The time-series studies that generate the concentration-response coefficients were based on Poisson regression of the form:

$E(Ylx) = e^{\beta x}$

where E(Ylx) is the expected value of the event Y (a respiratory hospital admission in this case) conditional on the value of the concentration x and β is the concentration-response coefficient.

4.1.3 This can also be written as RR = exp(βx) where RR is the relative risk. The exponential form of this relationship needs to be taken into account when scaling the coefficient by concentration (for small concentration changes scaling is approximately linear but use of the correct equation allows any calculations to apply in a wide range of circumstances). As an example:

Ozone 0.63% increase per 10 μg/m^3

Relative risk = 1.0063

β = (ln RR)/x = (ln 1.0063)/10 = 0.000628 (per 1 μg/m^3)

New β = 0.000628 x new concentration change

The process is then reversed to get a new % increase.

4.1.4 Putting the previous three paragraphs together, the calculation can be expressed as follows in Box 4.1 (CR = concentration-response function in % increase per 10 μg/m^3):

[8] http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=202

[9] http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2010-population-estimates/index.html

Box 4.1 Calculation method

$RHA_{day\ t} = ((EXP(((LN((CR/100)+1)/10) \times \Delta(P_t - P_{low}))) - 1) \times (((RHA_{base,yeart}/pop\ Eng_{yeart})/365) \times pop\ Ssx_{yeart})$

$((CR/100)+1)$ is the relative risk per 10 $\mu g/m^3$

$\Delta(P_t - P_{low})$ is the concentration increment between the concentration of the relevant pollutant on that day and the average of the relevant pollutant across all low days

$(((LN((CR/100)+1)/10) \times \Delta(P_t - P_{low}))$ converts the RR to the slope β and scales it to the new increment

$((EXP(((LN((CR/100)+1)/10) \times \Delta(P_t - P_{low}))) - 1)$ converts back to a % increase to multiply by $(((RHA_{base,yeart}/pop\ Eng_{yeart})/365) \times pop\ Ssx_{yeart})$, the baseline rate of emergency respiratory hospital admissions per year scaled per day and for Sussex rather than England to give:

$RHA_{day\ t}$, the number of extra emergency respiratory hospital admissions that day due to the increment over the low day average

4.1.5 It could be argued that the effects of pollution are already incorporated within the baseline rates. This is true, but, given the low proportion of air pollution-related admissions relative to total admissions, leaving this point aside still allows a reasonable approximation of the size of the effect to be made. It could also be argued that the benefits of the airAlert service are already included in the baseline, but again this is a small proportion of the total (see Chapter 5).

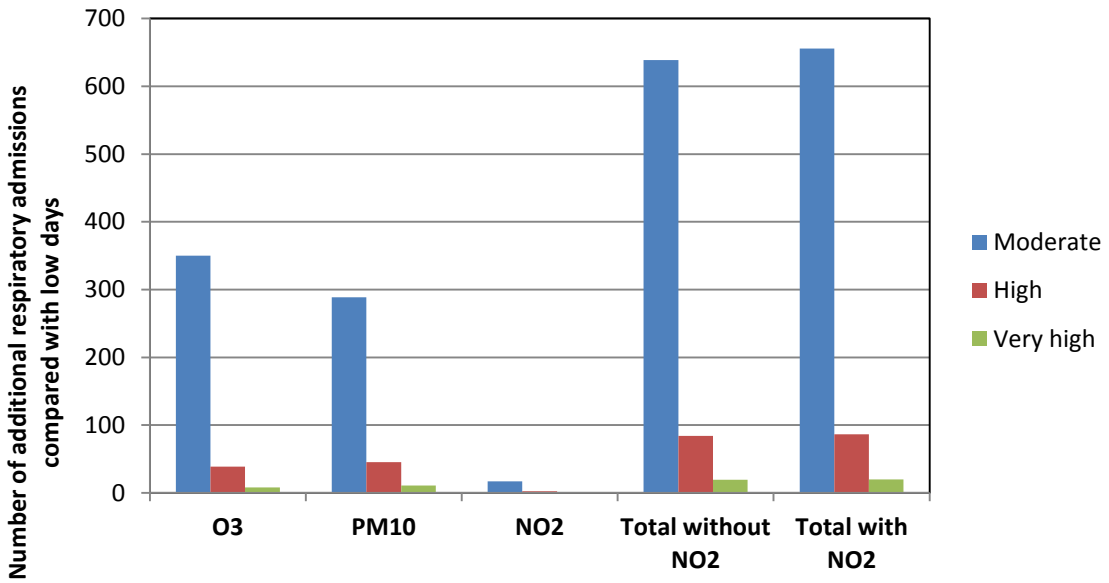
4.2 Predicted additional respiratory hospital admissions on moderate, high and very high days in Sussex 2006-2011.

4.2.1 Using the information from Table 2.1 and the daily increments in pollutant concentrations above or below the baseline average across all low days (increments summarised in Table 3.4), the number of additional emergency respiratory hospital admissions on very high, high and moderate days can be calculated to give the results shown in Table 4.1 and Figure 4.1. This analysis was calculated using respiratory admissions for the whole of Sussex (2010) and the Sussex population (2010). This was then applied to the pollution data (2006-2011) assuming the same admissions and population each year. It has been assumed that the PM_{10} concentration-response relationship can be applied to reference equivalent measurements, although several of the studies on which it was based used TEOM measurements. If a TEOM basis were assumed for the concentration-response relationship, the figures for respiratory hospital admissions due to PM_{10} would be about three quarters of the figures given. The confidence intervals include uncertainty in the pollution measurements and in the concentration-response relationships, as explained in detail in Chapter 7.

Table 4.1 Total additional emergency respiratory hospital admissions all ages in Sussex for each and all pollutants on moderate, high and very high days vs. low days for period 2006-2011

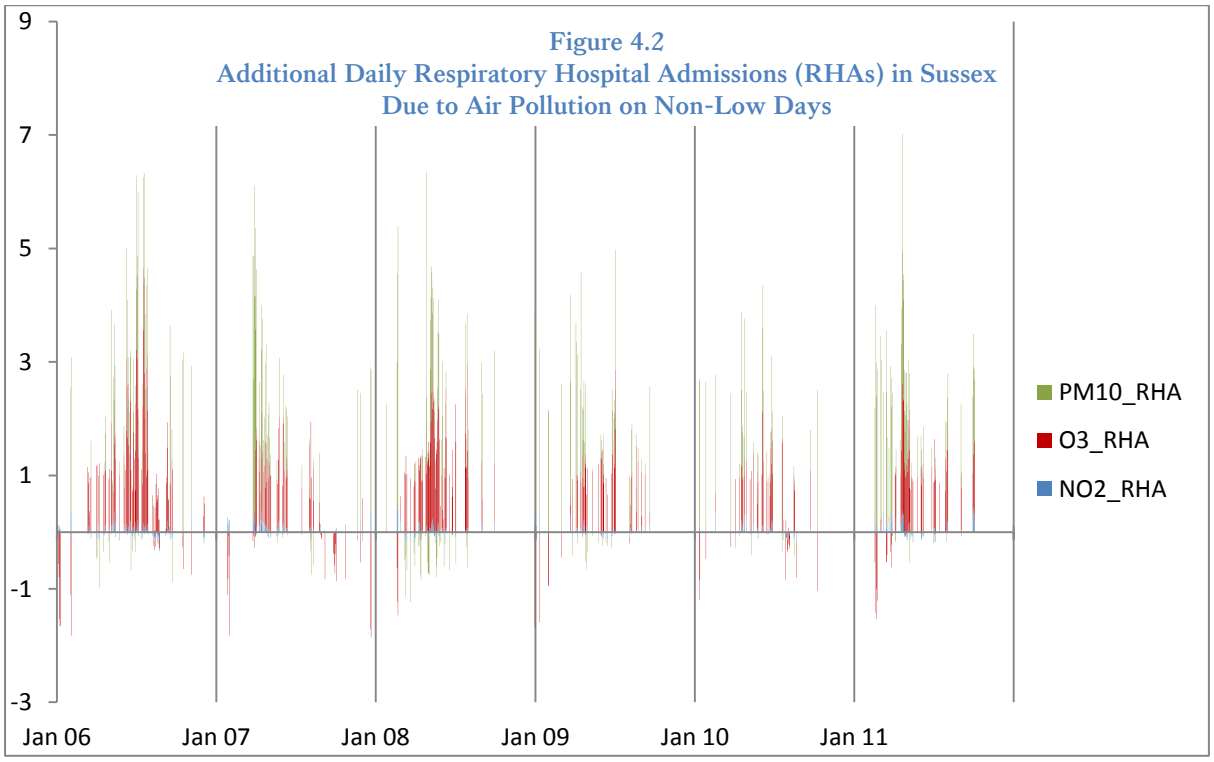
Pollutant	Moderate days (for any pollutant)		High days (for any pollutant)		Very high days (for any pollutant)	
	Total	Range daily values	Total	Range daily values	Total	Range daily values
Ozone	350.1	-1.9 – 2.6	38.5	-1.5 – 4.3	8.2	1.0 – 4.5
Nitrogen Dioxide (NO_2)	17.0	-0.2 – 0.4	2.4	-0.1 – 0.4	0.5	-0.0 – 0.4
PM_{10}	288.5	-1.1 – 4.4	45.4	0.3 – 5.7	11.0	1.6 – 5.3
Total without NO_2	638.6	-0.1 – 5.9	83.9	2.4 – 6.2	19.2	6.2 – 6.6
Total with NO_2	655.7	-0.3 – 6.0	86.3	2.4 – 6.3	19.6	6.3 – 7.0
Overall total 761.6 (around **762**) with NO_2 or 741.7 (around **742**) without NO_2						

Figure 4.1 Total additional respiratory hospital admissions all ages in Sussex 2006-2011 for moderate, high and very high days compared with low days



4.2.2 The number of additional emergency respiratory hospital admissions over and above the baseline on low days in Sussex was relatively small on a daily basis with a maximum of 7 for a very high day and 6 for moderate and high days. The overall public health impact over the time period 2006 to 2011 was most important for the moderate days (around 650 estimated additional admissions in Sussex), particularly days in the spring (Figure 4.2) when accumulations of NO_2 and long-range transported PM_{10} can be combined with springtime elevations in background ozone to give moderately raised levels of all three pollutants. Overall, PM_{10} was somewhat more important than ozone for high and very high days. Ozone was more important for moderate days in Sussex. Nitrogen dioxide was predicted to have only a minor effect, but the small concentration-response function in Table 2.1 was based on only 4 studies. If updated with new studies, the concentration-response function approximately doubled (Table 2.1) but was still within the confidence intervals of the original relationship, and was still smaller than the concentration-response relationships for ozone and PM_{10}. The implications of changes in the input factors are discussed in Chapter 7.

Figure 4.2
Additional Daily Respiratory Hospital Admissions (RHAs) in Sussex Due to Air Pollution on Non-Low Days



4.2.3 The total additional respiratory hospital admissions across all pollutants and all moderate, high and very high days for the six year period 2006-2011 was around 740-760, depending on whether the effects of NO_2 and PM_{10} are regarded as independent or whether both are acting as indicators of the same effect.

4.3 Methodological approach – asthma hospital admissions in children

4.3.1 Concentration-response relationships for asthma hospital admissions in children derived from the APED update (Table 2.5) were applied to the increment between the average concentrations of pollutants on days in the low band and the concentrations of pollutants on days in the high or moderate band in Sussex to give a percentage increase in the baseline rate for that increment, in an equivalent calculation to that for respiratory hospital admissions. This percentage increase was then applied to an estimate of the numbers of daily baseline emergency asthma hospital admissions in children in Sussex obtained from the West Sussex County Council and NHS Sussex West Sussex Research Unit. These were derived from the Sussex Database of hospital admissions data September 2012. The annual baseline figures were as follows:

Table 4.2 Asthma admissions in children per year in West Sussex

Year	Asthma in Children (0-15)
2006	407
2007	350
2008	337
2009	312
2010	287
2011	Assumed as 2010
2006-2011	1980

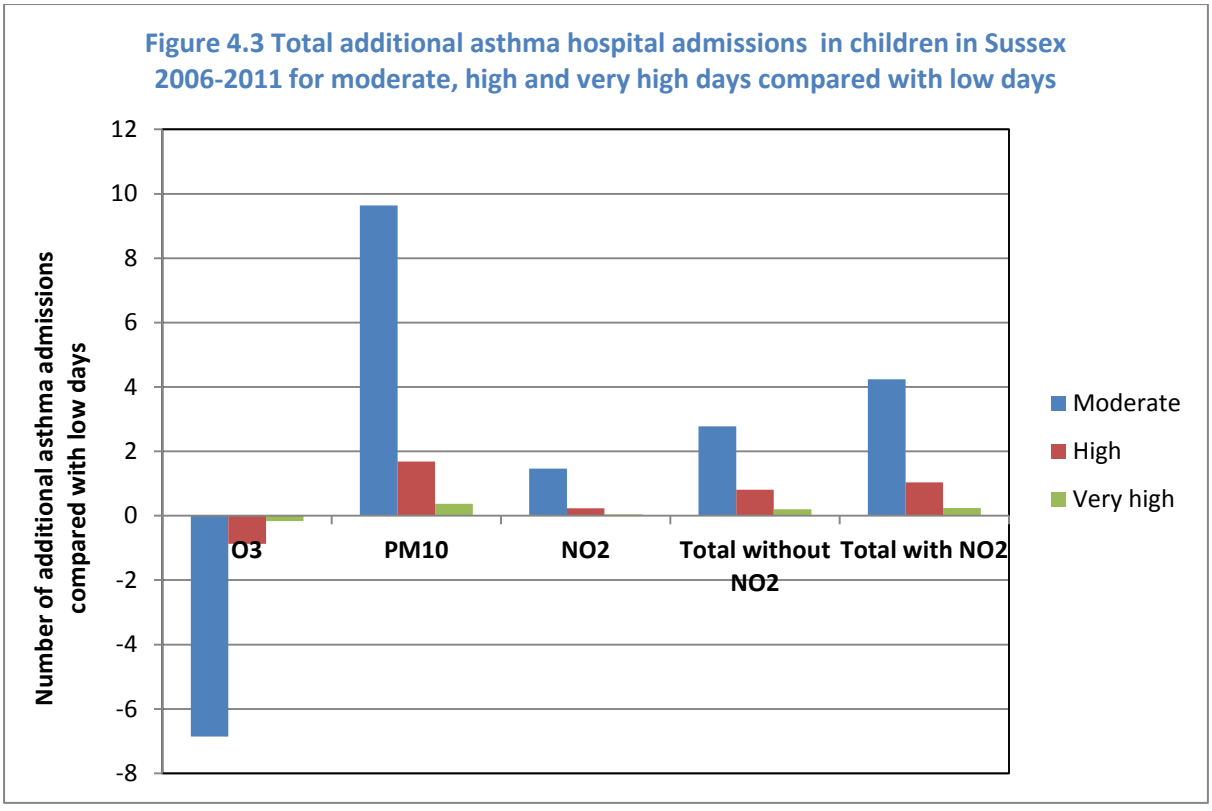
4.3.2 This analysis was calculated using yearly West Sussex children asthma admissions (year on year 2006-2010) scaled for the whole Sussex population (2010) relative to the West Sussex population (2010). Admissions in 2011 were assumed to be the same as 2010 since 2011 data was not initially available. The daily estimates of additional asthma hospital admissions were then summed across the total number of very high, high or moderate days for each pollutant.

4.4 Predicted additional asthma hospital admissions in children on moderate, high and very high days in Sussex 2006-2011.

4.4.1 The predicted additional asthma hospital admissions in children for Sussex 2006-2011 on moderate, high or very high days compared with low days are given in Table 4.3 and Figure 4.3.

Table 4.3 Total additional emergency asthma hospital admissions in children in Sussex for each and all pollutants on moderate, high and very high days vs. low days for period 2006-2011

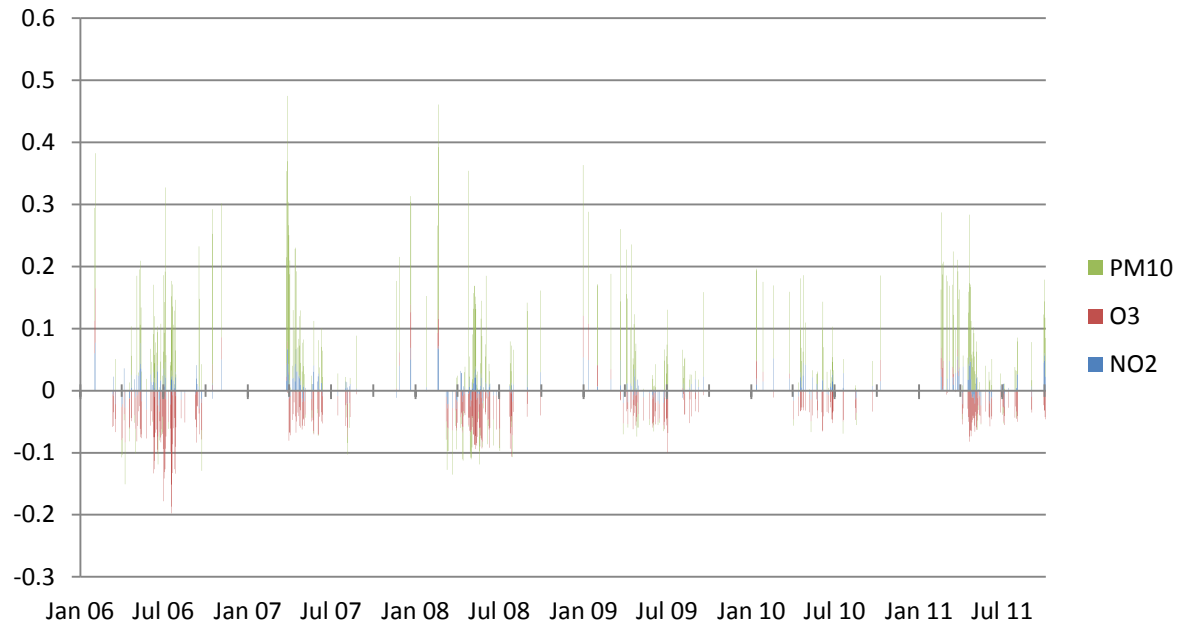
Pollutant	Moderate days (for any pollutant)		High days (for any pollutant)		Very high days (for any pollutant)	
	Total	Range daily values	Total	Range daily values	Total	Range daily values
Ozone	-6.7	-0.06 – 0.05	-0.9	-0.1 – 0.03	-0.2	-0.01 - -0.02
Nitrogen Dioxide (NO_2)	1.5	-0.02 – 0.04	0.2	-0.01 – 0.03	0.0	-0.00 – 0.03
PM_{10}	9.6	-0.04 – 0.16	1.7	0.01 – 0.21	0.4	0.07 – 0.18
Total without NO_2	2.8	-0.06 – 0.16	1.0	-0.03 – 0.25	0.2	-0.04 – 0.16
Total with NO_2	4.2	-0.08 – 0.2	0.8	-0.04 – 0.21	0.2	-0.02 – 0.16
	Overall total 5.5 with NO_2 or 3.8 without NO_2					



4.4.2 For asthma admissions in children, there are complex issues of interpretation. The concentration-response relationship between ozone and asthma admissions in children was actually negative. Although the concentration-response relationship for PM_{10} was positive and considerably larger, it was only just sufficiently large to compensate for the predicted reductions in asthma hospital admissions due to increased ozone. In Figure 4.4, a springtime pattern can still be seen but mainly due to PM_{10} with an opposite effect of ozone. Net additional asthma admissions in children were therefore predicted to be very low. The prediction was also

lower than that for respiratory hospital admissions because there are of course fewer children than there are people in the whole population, and the baseline rates are lower than for respiratory hospital admissions.

Figure 4.4 Additional Daily Asthma Hospital Admissions in Sussex for Children (0-15) due to Air Pollution on Non-Low Days (Based on West Sussex admissions)



4.4.3 The total calculated additional asthma hospital admissions in children across all pollutants and all moderate, high and very high days for the six year period 2006-2011 was around 4- 6, depending on whether the effects of NO_2 and PM_{10} are regarded as independent or whether both are acting as indicators of the same effect.

4.5 Methodological approach – asthma hospital admissions in adults aged 15-64

4.5.1 Concentration-response relationships for asthma hospital admissions in adults derived from the APED update (Table 2.6) were applied to the increment between the average concentrations of pollutants on days in the low band and the concentrations of pollutants on days in the high or moderate band in Sussex to give a percentage increase in the baseline rate for that increment,t in an equivalent calculation to that for respiratory hospital admissions. This percentage increase was then applied to an estimate of the numbers of daily baseline emergency asthma hospital admissions in adults aged 15-64 in Sussex obtained by adding data from the West Sussex County Council and NHS Sussex West Sussex Research Unit, East Sussex County Council and Brighton and Hove City Council. These were derived from the Sussex Database of hospital admissions data September 2012. The annual baseline figures were as in Table 4.4. The daily estimates of additional asthma hospital admissions were then summed across the total number of very high, high or moderate days for each pollutant.

Table 4.4 Baseline asthma hospital admissions aged 15-64 in West Sussex, East Sussex and Brighton and Hove

Year	West Sussex	East Sussex	Brighton and Hove	Total for Sussex
2006	320	244	135	699
2007	348	269	182	799
2008	370	290	207	867
2009	350	249	154	753
2010	349	241	202	792
2011	343	162	144	649
2006-2011	2080	1455	1024	4559

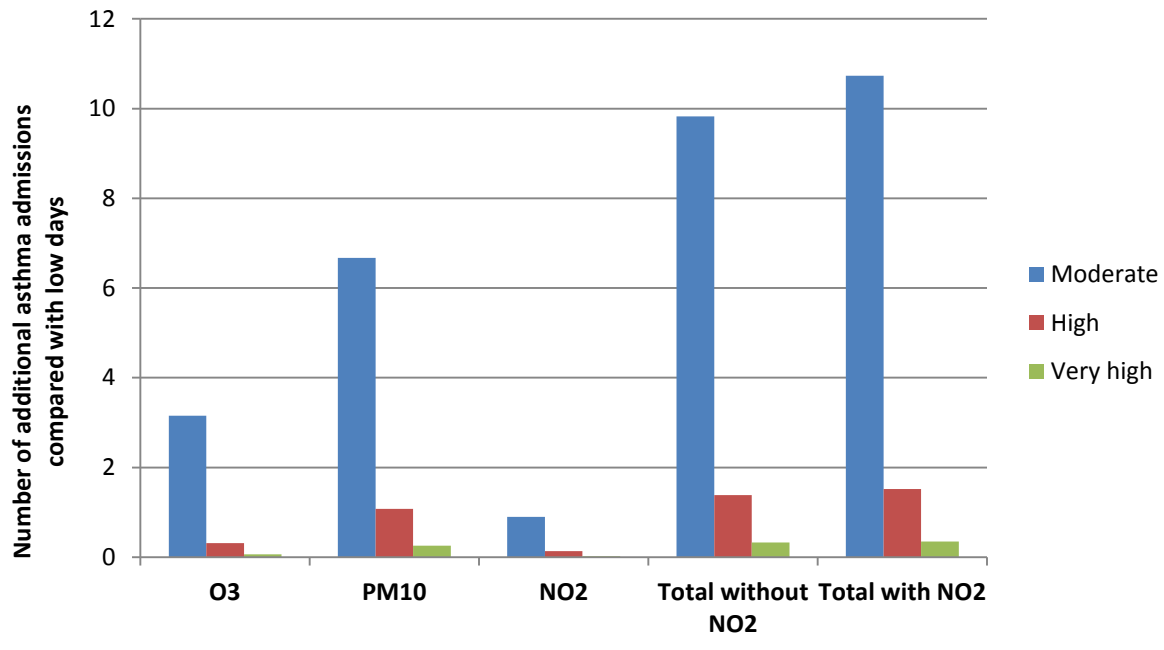
4.6 Predicted additional asthma hospital admissions in adults aged 15-64 on moderate, high and very high days in Sussex 2006-2011.

4.6.1 The predicted additional asthma hospital admissions in adults aged 15-64 for Sussex 2006-2011 on moderate, high or very high days compared with low days are given in Table 4.5 and Figure 4.5.

Table 4.5 Total additional emergency asthma hospital admissions in adults aged 15-64 in Sussex for each and all pollutants on moderate, high and very high days vs. low days for period 2006-2011

Pollutant	Moderate days (for any pollutant)		High days (for any pollutant)		Very high days (for any pollutant)	
	Total	Range daily values	Total	Range daily values	Total	Range daily values
Ozone	3.2	-0.02 to 0.03	0.3	-0.02 to 0.03	0.1	0.01 to 0.04
Nitrogen Dioxide (NO_2)	0.9	-0.01 to 0.03	0.1	-0.00 to 0.03	0	-0 to 0.02
PM_{10}	6.7	-0.03 to 0.11	1.1	0.01 to 0.14	0.3	0.04 to 0.14
Total without NO_2	9.8	-0.02 to0.11	1.4	0.02 to 0.14	0.3	0.07 to 0.15
Total with NO_2	10.7	-0.03 to 0.13	1.5	0.03 to 0.16	0.4	0.08 to 0.15
	Overall total 12.6 with NO_2 or 11.5 without NO_2					

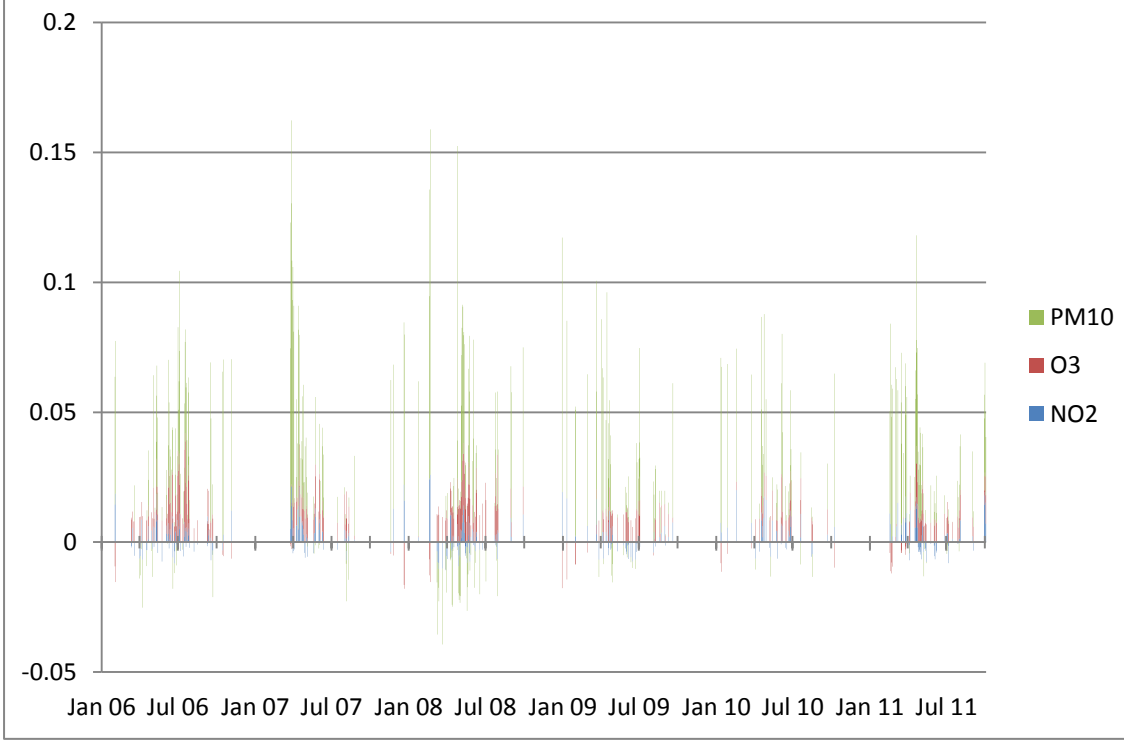
Figure 4.5 Total additional asthma hospital admissions in adults aged 15-64 at background sites in Sussex 2006-2011 for moderate, high and very high days compared with low days



4.6.2 The results for asthma in adults do not have the same issues in terms of negative relationships as the results for asthma admissions in children, but the numbers are still small. The effects of PM_{10} were slightly greater than those of ozone, and less uncertain, but of a similar order. In Figure 4.6, a springtime pattern can still be seen mainly due to PM_{10} with the effect of ozone now positive, compared with Figure 4.4, but small.

4.6.3 The total calculated additional asthma hospital admissions in adults aged 15-64 across all pollutants and all moderate, high and very high days for the six year period 2006-2011 was around 12-13 admissions, depending on whether the effects of NO_2 and PM_{10} are regarded as independent or whether both are acting as indicators of the same effect.

Figure 4.6 Additional Daily Asthma Hospital Admissions in Sussex for Adults (15-64) due to Air Pollution on Non-Low Days



4.7 Methodological approach – COPD hospital admissions all ages

4.7.1 Concentration-response relationships for COPD hospital admissions all ages derived from the APED update (Table 2.7) were applied to the increment between the average concentrations of pollutants on days in the low band and the concentrations of pollutants on days in the high or moderate band in Sussex to give a percentage increase in the baseline rate for that increment, in an equivalent calculation to that for respiratory hospital admissions. This percentage increase was then applied to an estimate of daily baseline emergency COPD hospital admissions in Sussex obtained from the West Sussex County Council and NHS Sussex West Sussex Research Unit. These were derived from the Sussex Database of hospital admissions data Sep 2012 and ONS mid-year population estimates for 2006-2010. The annual baseline numbers were as follows:

Table 4.6 COPD all ages admissions in West Sussex before scaling to the Sussex population

Year	Annual number of COPD admissions in all age groups
2006	1,118
2007	1,137
2008	1,395
2009	1,279
2010	1,302
2011	Assumed to be as 2010
2006-2011	7533

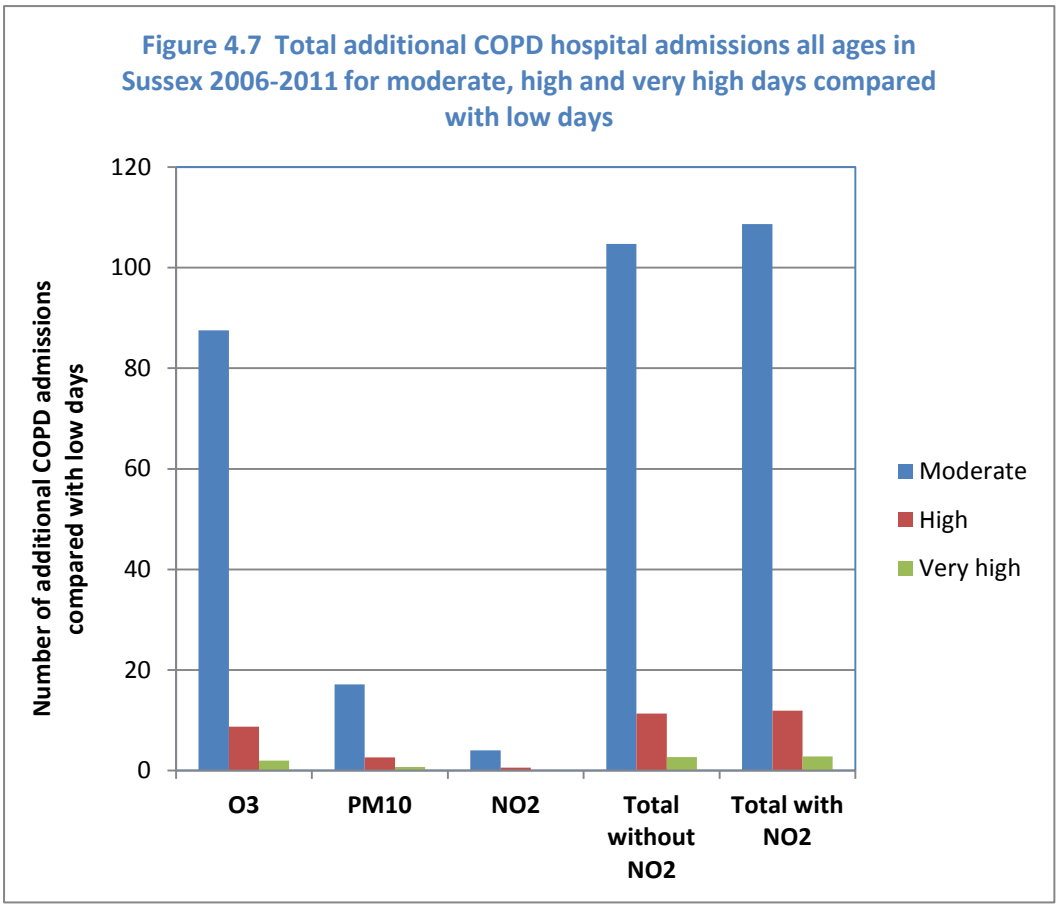
This analysis was calculated using yearly West Sussex COPD admissions (year on year 2006-2010) scaled for the whole Sussex population (2010) relative to the West Sussex population (2010). Admissions in 2011 were assumed to be the same as 2010 since 2011 data was not initially available.

4.8 Predicted additional COPD hospital admissions for all ages on moderate, high and very high days in Sussex 2006-2011.

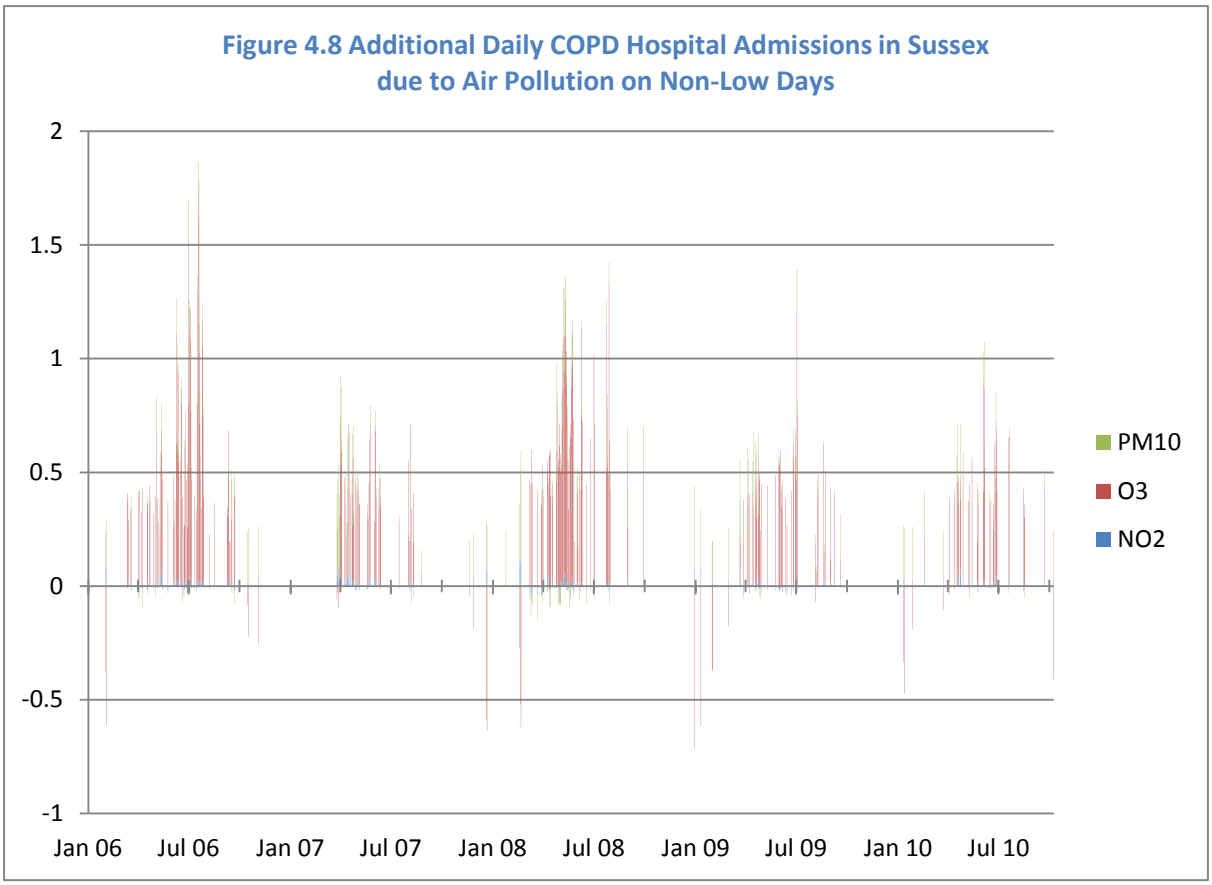
4.8.1 The predicted additional COPD hospital admissions for all ages for Sussex 2006-2011 on moderate, high or very high days compared with low days are given in Table 4.7 and Figure 4.7.

Table 4.7 Total additional emergency COPD hospital admissions all ages in Sussex for each and all pollutants on moderate, high and very high days vs. low days for period 2006-2011

Pollutant	Moderate days (for any pollutant)		High days (for any pollutant)		Very high days (for any pollutant)	
	Total	Range daily values	Total	Range daily values	Total	Range daily values
Ozone	87.6	-0.5 to 0.7	8.7	-0.4 to 1.0	2.0	0.3 to 1.0
Nitrogen Dioxide (NO_2)	4.0	-0.1 to 0.1	0.6	-0.0 to 0.1	0.1	-0 to 0.1
PM_{10}	17.1	-0.1 to 0.2	2.6	0.0 to 0.3	0.7	0.1 to 0.4
Total without NO_2	104.7	-0.3 to 0.8	11.3	-0.1 to 1.1	2.7	0.6 to 1.1
Total with NO_2	108.7	-0.2 to 0.9	11.9	0.0 to 1.1	2.8	0.6 to 1.1
	Overall total 123.4 with NO_2 or 118.7 without NO_2					



4.8.2 The totals are lower than for all respiratory hospital admissions as this was for only one outcome. It was noticeable that, for this endpoint, ozone-related COPD admissions dominated. In contrast to the situation with respiratory hospital admissions, the concentration-response coefficient for ozone and COPD admissions all ages was larger than that for PM_{10} on a per 10 $\mu g/m^3$ basis. The domination of ozone-related COPD admissions was also seen in the fact that the seasonal patterns showed summer peaks such as in summer 2006 (figure 4.8). The confidence intervals were tighter than for asthma admissions, reflecting the tighter confidence intervals in the original concentration-response relationships for ozone, in particular.



4.8.3 The total calculated additional hospital admissions for COPD, all ages, across all pollutants and all moderate, high and very high days for the six year period 2006-2011 was around 119-123 admissions, depending on whether the effects of NO_2 and PM_{10} are regarded as independent or whether both are acting as indicators of the same effect.

4.9 Methodological approach – respiratory hospital admissions in London

4.9.1 As explained in Chapter 3, while the main purpose of this project is aimed at Sussex, it was agreed to do some calculations for London to highlight some the unique features about the Sussex pollution climate and its implications for hospital admissions as a result of the moderate, high and very high air pollution days. The method was the same as for respiratory hospital admissions in Sussex except that the national baseline rate for respiratory hospital admissions was scaled to the London population rather than that for Sussex. The London population used was that for mid-year 2010 i.e. 7,830,000[10]. The calculations were applied to the pollution increments for London described in Table 3.7. The calculations were just done for respiratory hospital admissions as London was not the main focus of this study.

4.10 Predicted additional respiratory hospital admissions on moderate, high and very high days in London 2006-2011

4.10.1 The predicted additional respiratory hospital admissions for all ages for London 2006-2011 on moderate, high or very high days compared with low days are given in Table 4.8 and Figure 4.9. The

[10] http://www.london.gov.uk/sites/default/files/Update%2011-2011%20Mid-2010%20population%20estimates.pdf

numbers were greater in London, given the higher pollution levels and population (maximum 41 for very high days and 29 and 34 for moderate and high days). The overall public health impact over the time period 2006 to 2011 was most important for the moderate days (around 650 estimated additional admissions in Sussex and 3,500 in London), particularly days in the spring (Figure 4.10) when accumulations of nitrogen dioxide and long-range transported PM_{10} can be combined with springtime elevations in background ozone to give moderately raised levels of all three pollutants. Overall, PM_{10} had a greater impact on hospital admissions than ozone for high and very high days, particularly in London. Ozone was more important for moderate days in Sussex but not in London. Nitrogen dioxide was predicted to have only a minor effect, even in London where concentrations were higher. This was partly the result of the small concentration-response function in Table 2.1 (which would be increased when updated see section 2.2.6) but also because of where the breakpoints are set in the UK Daily Air Quality Index, relative to typical concentrations.

Table 4.8 Total additional emergency respiratory hospital admissions all ages in London for each and all pollutants on moderate, high and very high days vs. low days for period 2006-2011

Pollutant	Moderate days (for any pollutant)		High days (for any pollutant)		Very high days (for any pollutant)	
	Total	Range daily values	Total	Range daily values	Total	Range daily values
Ozone	938.8	-7.7 - 14.9	124.3	-7.3 - 19	-5.5	-7.2 – 10.5
NO_2	266.1	-1.6 – 4.1	41.6	-0.6 – 5.7	6.5	-1.5 – 2.3
PM_{10}	2,328.7	-4.7 – 19.7	518.2	0.9 – 29.8	123.1	-1.4 – 32.8
Total without NO_2	3,267.5	-4.4 – 29.6	642.5	-1.6 – 31.4	117.5	-4.6 – 38.9
Total with NO_2	3,533.7	-3.5 – 29.2	684	-1.1 – 33.5	124.1	-6.1 – 41.2
Overall total 4,341.8 with NO_2 or 4,027.5 without NO_2						

Figure 4.9 Total additional respiratory hospital admissions all ages in London 2006-2011 for moderate, high and very high days compared with low days

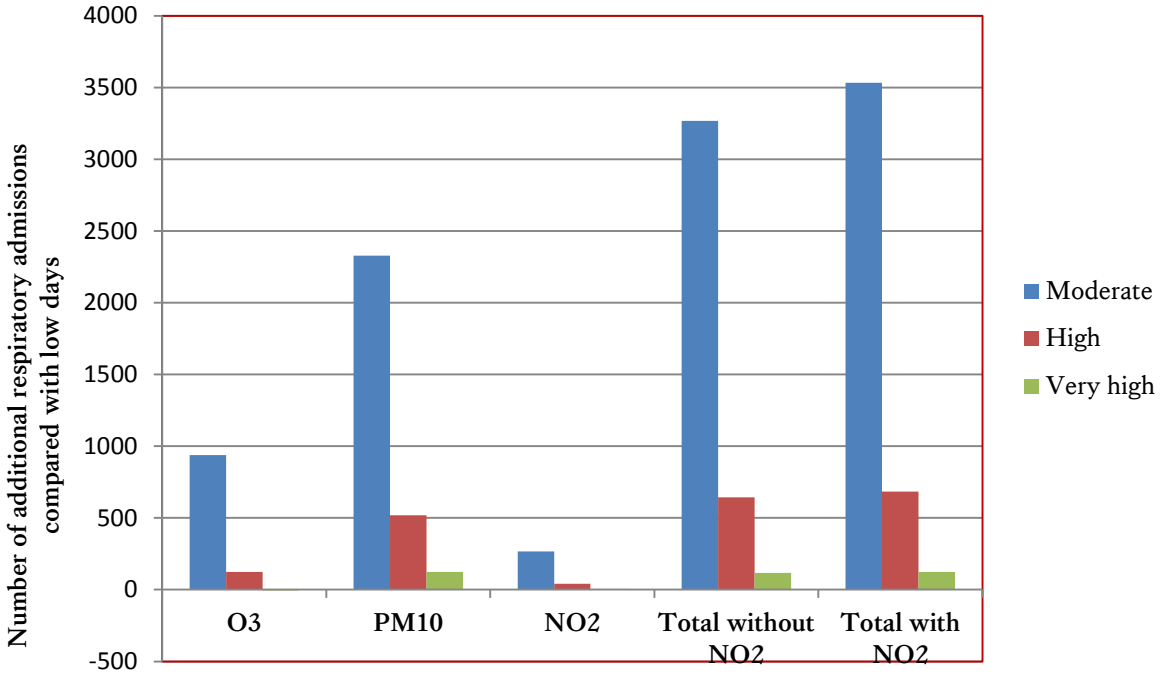
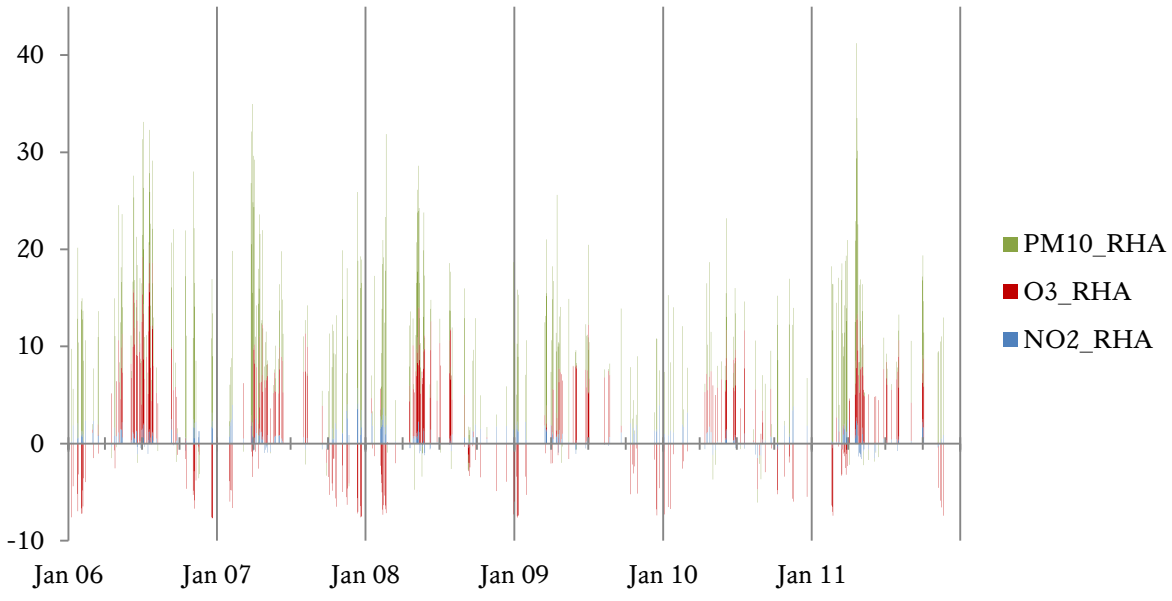


Figure 4.10 Additional Daily Respiratory Hospital Admissions in London Due to Air Pollution on Non-Low Days



4.10.2 The total calculated additional respiratory hospital admissions in London across all pollutants and all moderate, high and very high days for the six year period 2006-2011 was around 4,030 – 4,340, depending on whether the effects of NO_2 and PM_{10} are regarded as independent or whether both are acting as indicators of the same effect. This compares with 740-760 in Sussex for the same time period.

5. Expected size of effects in the population receiving the airAlert service

Question 4 Using a variety of reasonable assumptions, what is the expected size of the effect of these pollution changes in the population likely to receive alerts?

5.1 Expected size of effect – general population basis

5.1.1 The calculations in section 4 relate to the whole population. In order to estimate the possible reductions in health effects as a result of the airAlert service, it was first necessary to estimate the expected number of hospital admissions in the population receiving the service. No more hospital admissions could have been avoided than those estimated to have occurred.

5.1.2 To recap from section 4, the total number of predicted respiratory hospital admissions as a result of moderate, high or very high days for the population of Sussex over 2006-2011 was 742 assuming overlap between the effects of PM_{10} and NO_2 or 762 assuming the effects of PM_{10} and NO_2 are independent. The total number of predicted COPD admissions was 119 without or 123 with the inclusion of admissions due to NO_2. The equivalent figures were 6 or 4 for asthma in children and 13 or 12 for asthma admissions in adults aged 15-64, with or without admissions due to NO_2. For the purposes of this chapter we have used the figures without NO_2 but analogous calculations can be done with the figures including NO_2.

5.1.3 The population receiving the air Alert service is around 760[11]. If the same rate of respiratory hospital admissions were assumed, this would reduce the predicted number of respiratory hospital admissions in proportion to the size of the population receiving the airAlert service, relative to the size of the Sussex population. This would estimate the number of respiratory hospital admissions in the population receiving the airAlert service as (742/1,563,000) x 760 = 0.36 admissions with a similar number if the starting point is 762 admissions in the population of Sussex. Put another way there would be a 36% chance of 1 additional respiratory hospital admission in the population signed up to airAlert over a 6 year period with a pattern of pollution like that from 2006-2011. Another way to present this would be to note that the service would need to be provided to around 2,100 people to prevent one respiratory hospital admission over a 6 year period with similar pollution levels, if every participant took action and the action was 100% effective.

5.1.4 These calculations assume an age distribution in the airAlert participants equivalent to that in the general population, which is not the case (Table 5.1). However, it is difficult to predict the implications of this. The population of airAlert participants has a lower proportion of adults but both a higher proportion of children and a higher proportion of the elderly, factors that would act in opposite directions in relation to rates of respiratory hospital admissions.

[11] In 2013, there were around 560 individual subscribers plus another 200 or so via 18 schools, estimated in 2012. There may in fact be more people benefitting, if one member of a family subscribes on behalf of others in the family. Others may obtain information from the web, rather than subscribing to the alert service, but this was not counted in this evaluation. The calculations assume these numbers throughout 2006-2011.

Table 5.1 Age distribution of those signed up to the airAlert service

Number signed up to airAlert direct in 2013 (airAlert age group category)	% of airAlert recipients	Number of airAlert recipients (with approx. 200 children signed up via schools in 2012)	% of airAlert recipients (with school-children)	General population age category (2010)*	% of age group in Sussex population
48 (age 1-16)	9%	248 approx (age 1 -?16)	33%	260,900 (age 0-14)	16%
280 (age 17-59)	50%	280 (age 17-59)	37%	910,000 (age 15-59)	57%
232 (age 60+)	41%	232 (age 60+)	31%	319,106 (60+)	20%
512 (age 17-59 plus 60+)	91%	512 (age 17-59 plus 60+)	67%	1,335,200 (15+)	84%
560 (total)		760 approx (total)		1,596,400 (total)	

***** ONS (2010) corrected for 2011 census.

5.1.5 The equivalent number for predicted COPD admissions in the airAlert participant population is (119/1,563,000) X 760 = 0.06 (a 6% chance of 1 admission over a 6 year period with similar levels of pollution). Assuming the same baseline rate for COPD admissions as in the general population, the service would need to be provided to around 13,000 of the general population to prevent 1 COPD admission over a 6 year period with similar levels of pollution, if all participants took action and the action was 100% effective. This does not, however, take into account the fact that the airAlert service is targeted at particular susceptible groups, including those with COPD, or the higher proportion of elderly participants amongst airAlert participants (even though the calculation in Chapter 4 was for COPD all ages, COPD admissions are higher in the elderly).

5.1.6 Similar calculations for asthma admissions are more complicated in that the calculations in Chapter 4 of this report were split up by age. Using the size of the population of children aged 0-14 (260,900) and adults aged 15-64 (1,016,000) in Sussex, and the numbers of children aged 1-16 (approx. 248) and adults aged (17-59) (280) signed up to the airAlert service, the estimated figures for asthma admissions in children and adults are 0.004 and 0.003 respectively. Assuming the same baseline rate for asthma admissions as in the general population, the service would need to be provided to around 68,660 of the general population of children to prevent 1 asthma admission over a 6 year period with similar levels of pollution, if all participants took action and the action was 100% effective. The equivalent figures for the general population of adults aged 15-64 are 88,350. Again, though, this does not take into account the targeting of airAlert at asthmatics.

5.2 Expected size of effect given the disease groups of airAlert participants

5.2.1 *Characteristics of airAlert participants:* In July 2013, there were 560 participants that signed up directly to airAlert, rather than through schools. The disease categories of the participants are summarised in Table 5.2. This is also shown as a percentage of the 560 participants and of the relevant population in that disease category in Sussex. The numbers in Sussex with that disease were estimated as described in the paragraphs below the table.

5.2.2 There are also around 200 schoolchildren signed up via schools. Information on their health condition is not collected. It has been assumed that these children have the same distribution of asthma as the general population of children, although there may in fact be a higher proportion of asthmatics.

Table 5.2 Disease categories of subjects signed up directly for airAlert in 2013 (overlapping categories)

Category (not exclusive)	Number	% of participants with that diseae amongst airAlert participants that sign up directly	% of the population with that disease in Sussex (selected outcomes)	Comments
COPD	166	30%	0.28%	
asthma	314	56%		
Children 1-16 with asthma	41	7%	0.1%	More sign up via schools (200 children would predict around 30 asthmatics if no selective sign up amongst asthmatics)
Adults 17-60 with asthma	187	33%	0.02%	
Elderly 60+ with asthma	86	15%		
Allergies	7	1.25%		
Respiratory	485	86%		
Heart disease	6	1%		
Other conditions	3	0.5%		
Null/None	69	12%		

Note: Categories were compiled from free text answers from participants.

5.2.3 The above information overlaps e.g. the respiratory category includes those with asthma and COPD. At a later timepoint, the characteristics of the participants were analysed into unique categories giving the percentages on the left hand side of table 5.3. For this purpose, participants with any mention of COPD were assigned to the COPD category, any mention of asthma or allergies without COPD to the allergies and asthma category, any mention of respiratory conditions without COPD or asthma to respiratory, any mention of heart disease without respiratory disease to the heart disease category and any mention of other conditions without respiratory or heart disease to 'other'. The resulting percentages were applied to the numbers of airAlert participants as at July 2013 to give a typical dataset of airAlert participants (the actual numbers are constantly varying as people sign up or discontinue receiving alerts).

Table 5.3 Typical dataset of airAlert participants assigned to unique disease categories

Category (exclusive)	% in each unique category	Equivalent number for 560 airAlert participants that sign up directly	% of asthmatics in different age groups	Equivalent numbers in different age groups for 316 asthmatics
COPD	*29.7*	166		
Allergies and/or asthma	56.4	316		
Children 1-16 with asthma			*13.1*	*41*
Adults 17-60 with asthma			*59.6*	*188*
Elderly 60+ with asthma			*27.4*	*87*
Other respiratory	1.1	6		
Heart disease	0.7	4		
Other conditions	0.4	*2*		
Null/None	11.8	66		

Note: Categories were compiled from free text answers from participants.

5.2.4 *Numbers of specific disease groups in Sussex and rates of air pollution-related admissions in these groups* - to calculate the rates of air pollution-related specific disease hospital admissions in a specific disease group e.g. asthmatics, we need to divide the air pollution-related asthma admissions calculated for Sussex in Chapter 4 by the numbers in that specific disease group in Sussex.

5.2.5 *COPD* - the Health Survey for England (2010) gives the lifetime prevalence of doctor-diagnosed chronic bronchitis, emphysema or COPD as 4% in men and 5% in women, predicting about 60,084 people in Sussex with these conditions out of 1,335,200 adults aged 15+ in 2010 (ONS, 2013). Both of these figures are likely to underestimate the lifetime prevalence of the disease but, for the purpose of this exercise, it is more likely that it is mostly those who know they have the disease who would have an incentive to sign up.

5.2.6 It should be noted that the time-series studies do not distinguish whether additional COPD admissions are each in new patients or re-occur in the same patients. The National COPD Resources and Outcomes Project audit of COPD admissions in 2008 (NCROP, 2008) showed that 10% of admissions for acute exacerbations of COPD in England were in people whose COPD was previously undiagnosed and about 33% of COPD admissions were readmissions within 90 days of an index admission.

5.2.7 It is unknown whether air pollution has a disproportionate effect on either people with undiagnosed COPD (who may have less controlled disease than some of those with treated COPD) or people with diagnosed COPD (who will include those most seriously ill). Assuming no disproportionate effect on either group suggests that only 90% of the 119 predicted air pollution-related admissions from Chapter 4 (107 admissions) should be allocated to the group who already have COPD.

5.2.8 The population impact can then be expressed as a proportion of COPD patients affected. Thus, the 107 (101-113) predicted air pollution-related COPD admissions can be expressed as a proportion of the total number of COPD patients in Sussex (60,084) giving a rate of 178.3 air pollution-related COPD admissions per 100,000 COPD patients over the 6 year period 2006-2011.

5.2.9 The remaining 12 COPD admissions expected to arise in those without a COPD diagnosis, would need to be allocated to the elderly general population without previously diagnosed COPD. For the purposes of the calculations here, these have been subsumed into a calculation for all respiratory hospital admissions in those without asthma or COPD (see paragraph 5.2.20).

5.2.10 *Asthma* - the Health Survey for England (2010) gives the lifetime prevalence of doctor-diagnosed asthma as about 16% in men and 17% in women aged 16+, predicting about 220,300 adults in Sussex with doctor-diagnosed asthma out of 1,335,200 adults aged 15+ in 2010 (ONS, 2013)[12]. If this lifetime prevalence also applies in adults aged 15-64, the equivalent figure would be 167,673 adults aged 15-64 in Sussex with doctor-diagnosed asthma out of 1,016,200 adults aged 15-64 in 2010 (ONS, 2013). Allocating the 12 estimated asthma admissions in adults aged 15-64 would estimate a rate for air pollution-related hospital admissions over a 6 year period of (12/167,673)*100,000 = 6.9 per 100,000 asthmatic adults aged 15-64, for the period 2006-2011.

5.2.11 The lifetime prevalence of doctor-diagnosed asthma in children was 17% in boys and 12% in girls (14.5% in children under 15 assuming equal numbers of boys and girls) (Health Survey for England, 2010), predicting about 37,800 children with asthma in Sussex out of 260,900 children in total. Allocating the 4 predicted asthma admissions in children from Chapter 4 would predict a rate for air pollution-related hospital admissions over a 6 year period of (4/37,831)*100,000 = 10.0 per 100,000 asthmatic children, for the period 2006-2011.

5.2.12 Adults or children with asthma serious enough to lead to a hospital admission are likely to already know that they have asthma, so an adjustment to take into account undiagnosed asthmatic subjects in the general population is not required. (There is underdiagnosis of asthma but not so much at the serious end).

5.2.13 *Predicted hospital admissions given the characteristics of the airAlert participants.* The air pollution-related admission rates over 6 years in the specific disease groups from paragraphs 5.2.7-5.2.12 can then be applied to the numbers of airAlert participants in the relevant disease groups from Table 5.3.

5.2.14 *COPD* - The rate of air-pollution-related COPD admissions amongst COPD patients (178.3 per 100,000) applied to the number of subjects with COPD signed up to airAlert (166) predicts 0.30 admissions or a 30% chance of 1 admission in the airAlert subjects with COPD over the 6 year period 2006-2011. This compares with 0.06 (6% probability) for the calculation assuming airAlert participants were the same as the general population. The service would need to be provided to around 561 COPD patients, to prevent 1 COPD admission over the 6 year period, if all participants took action and the action was 100% effective. This compares with the calculation of 13,000 for the general population, showing the advantages of targeting the service at susceptible groups.

5.2.15 *Asthma* - Similar calculations can be done for asthma in adults. The rate of air pollution-related asthma admissions in asthmatics aged 15-64 (6.9 per 100,000) applied to the number of adults aged 17-60 with asthma signed up to airAlert (188) predicts 0.013 admissions or an 1.3% chance of 1 admission in the airAlert adults age 17-60 with asthma over the 6 year period 2006-2011. The service would need to be provided to around 14,580 asthmatics aged 17-60, to prevent 1 asthma admission over the 6 year period, if all participants took action and the action was 100% effective. This compares with the calculation of 88,350 for the general population, again showing the advantages of targeting the service at susceptible groups, although the numbers are still large.

[12] Corrected for the 2011 Census.

5.2.16 The calculations for asthma in children are as follows. The rate of air pollution-related asthma admissions in children (10 per 100,000) applied to the number of children aged 1-16 with asthma signed up to airAlert (41) predicts 0.004 admissions or a 0.4% chance of 1 admission in the children with asthma signed up directly to airAlert over a 6 year period 2006-2011. The service would need to be provided to around 9,960 asthmatic children to prevent 1 asthma admission over the 6 year period, if all participants took action and the action was 100% effective. This compares with the calculation of 68,660 for children in general and 14,480 for asthmatic adults, the latter comparison showing that the smaller numbers of admissions in children compared with adults is primarily due to the relative size of the populations of asthmatic adults and children, rather than lesser effects. Again, though, the number needed is large compared with that for COPD patients.

5.2.17 For the 200 or so children signed up through schools where we do not know the number of asthmatic children, the rate of air pollution-related asthma admissions in the general population can be used. This is the 4 admissions from Chapter 4 divided by the number of children in Sussex (260,900) or 1.5 per 100,000. This would predict 0.003 admissions in this group, with the numbers needed to prevent 1 asthma admission the same as in paragraph 5.1.6.

5.2.18 *Other groups* - for the remaining groups of airAlert participants defining the appropriate calculation is more difficult. They form a mixture of groups at extra but difficult to define risks (elderly asthmatics (see below), people with respiratory conditions other than asthma and COPD, and those with heart disease but not respiratory disease) and groups with less risk than the general population as they do not have a specified condition, or an unrelated condition. Before setting out the approach that was taken for these groups, some further observations about asthma in the elderly are given in the paragraph below.

5.2.19 Calculations for asthma in the elderly were not done in Chapter 4. While studies of ozone, NO_2 and PM_{10} and asthma in the elderly do exist, with mixed results, there are rather few studies (only two for PM_{10}). One of the reasons for this is that, as COPD is more common in the elderly, there can be misclassification between COPD and asthma admissions. Studies therefore choose either the potentially more serious outcome (COPD admissions), or the more general 'all respiratory admissions' outcome when doing studies in the elderly.

5.2.20 While not ideal, it was decided to put the groups described in paragraph 5.2.18 together as if they were a general population sample and calculate the expected number of respiratory hospital admissions, excluding those COPD and asthma admissions already allocated to the COPD and asthma in children and non elderly adult asthmatic groups. In other words, the 107 additional COPD admissions, the 12 additional asthma admissions in adults and the 4 asthma admissions in children were subtracted from the 742 all respiratory hospital admissions calculated in Chapter 4, to leave 607 respiratory hospital admissions. This was then allocated to the population of Sussex excluding COPD patients, asthmatic children and asthmatic adults aged 15-64 (1,563,000 – 265,588 = 1,297,413) giving a rate of air pollution-related respiratory hospital admissions of 46.8 per 100,000. This would predict 0.08 respiratory hospital admissions in this group with the service needing to be provided to 2,140 people to avoid one respiratory hospital admission. Note that this number is smaller than for the specific group – this might be considered unexpected as it is untargeted but the latter effect is counteracted by the fact that it also includes other types of respiratory hospital admissions.

5.2.21 The calculation in paragraph 5.2.20 did not include the children from schools. It could be argued that only some of these children are asthmatic and accounted for in estimating the numbers of asthma admissions likely to occur in a group of schoolchildren. The remaining children may potentially experience other types of respiratory admissions (for respiratory infections, for example). This was taken into account by an alternative calculation in which the expected proportion of non-asthmatic children amongst the schoolchildren (100%-14.5% = 85.5%, giving 171 children from the 200) were added into the mixed group described above, giving a group of 336. This gave an alternative estimate of air pollution-related respiratory hospital admissions excluding COPD and asthma of 0.16. The rate of air pollution-related respiratory hospital admissions and the numbers needed to avoid 1 respiratory hospital admission are the same as in the previous paragraph as they do not depend on the number currently signed up to airAlert.

5.2.22 The calculations from all the preceding paragraphs in section 5.2 are summarised in Table 5.4.

Table 5.4 Predicted air pollution-related hospital admissions and rates over the 6 year period 2006-2011 arising in airAlert participants given a typical distribution of disease categories.

Category (exclusive)	Number in each unique category	Estimated rate of relevant disease admission in relevant disease group per 100,000 for 2006-2011	Estimated number of relevant disease admissions in airAlert recipients for 2006-2011[a]	Numbers of relevant group needed to avoid 1 relevant disease admission[b]
COPD	166	178.3	0.30	561
Children 1-16 with asthma	41	10.0	0.004	9,960
Adults 17-60 with asthma	188	6.9	0.013	14,580
Children from schools	Approx 200	1.5 (asthma admissions)	0.003	68,660
Non COPD/children or young adult asthma i.e. elderly 60+ with asthma, other respiratory, heart disease, other, none	165	46.8 (respiratory hospital admissions)	0.077	2,140
Alternative non COPD/children or young adult asthma i.e. elderly 60+ with asthma, other respiratory, heart disease, other, none with non-asthmatic children from schools added	165 + 171 = 336	As above	0.157	As above
Total	560		0.39 or 0.47 (39% or 47% probability)	

Table based on Health Survey for England (2010) prevalence of COPD and asthma, giving estimated populations in Sussex with COPD (60,084), asthma (167,673 in adults 15-64; 37,800 in children 0-14)

[a] Obviously fractions of hospital admissions do not occur – these results multiplied by 100 can also be considered as the probability of 1 additional hospital admission occurring over the period 2006-2011. The numbers assume the current numbers of airAlert recipients applied across all 6 years.

[b] Numbers to which the service needs to be provided if all participants take action and the action is 100% effective.

5.2.23 The total calculated taking into account disease categories was 0.39 or 0.47 admissions rather than the 0.36 calculated assuming a general population sample (section 5.1). It might have been expected that the estimate would have been larger than this, given the fact that the service is targeted at susceptible groups. One

minor reason is the negative relationship for ozone and asthma admissions in children, although this figure is small. The main reason is that the estimated number of respiratory admissions (742) is much greater than that for asthma and COPD combined (119 + 12 +4 = 135). This may be because the concentration-response relationships come from different groups of studies from different locations and time periods, or it may be a real difference due to other respiratory outcomes for which specific calculations were not done. It is known, for example, that air pollution is related to pneumonia admissions (see Chapter 2). This point deserves further investigation.

5.2.24 The overall numbers of people to which the service needs to be provided to avoid 1 respiratory hospital admission is not a total but a series of alternative options. With the assumptions made that all participants take action, which are all 100% effective, the most efficient approach is targeting at COPD patients. Targeting asthmatics is theoretically more effective in terms of avoiding asthma admissions specifically but if an asthma admission is regarded as just an example of a respiratory admission, it is less effective than for the general population, probably due to, for example, respiratory infections in the elderly occurring in the general population. Of course, it could be argued that the opportunity to modify treatment to alleviate symptoms is greatest in asthmatics so that the above numerical comparison misses the point that actions in response to air alerts vary in effectiveness and are greater for some groups than others.

5.3 Question 5 Using assumptions guided by qualitative research on whether users respond with action to ameliorate effects, what is the scope of the possible reductions in health outcomes that might be generated by users of the service?

5.3.1 The qualitative research done in Stage 1 of the evidence development strategy (Jenkins, 2008; Smallbone, 2009) suggests that some but not all users take action in response to receiving an airAlert message. Using assumptions based on this evidence, the likely reduction in health impacts, assuming these actions are effective, can be calculated.

5.3.2 If people were able to respond to alert messages in such a way as to remove their risk, then the effect on public health could be important. However, not everyone signs up to receive airAlert messages, although those that sign up are probably more likely to be in the relevant susceptible groups. In addition, of those that do sign up, not everyone takes action in response.

5.3.3 Focus group work by Smallbone (2009) suggested that 67% took specific action in response to alerts including ensuring they carried their reliever medication, taking additional medication, avoiding strenuous exercise and avoiding areas mentioned in the alerts. It is unknown whether these actions taken in response are actually effective in reducing risks, in practice. However, quantification of the potential size of the risk should help to see whether a study to address this directly would be feasible.

5.3.4 If it is assumed that these actions are effective, but only undertaken by 67% of those receiving the alerts, then the potential admissions avoided would be lower and the numbers to which the service would need to be provided would be higher to avoid 1 hospital admission. The resulting figures are given in Table 5.5. These are still likely to be over- and under-estimates, respectively, as they assume that the actions are 100% effective. This is unlikely.

Table 5.5 Predicted hospital admissions avoided amongst airAlert participants over a 6 year period with pollution as in Sussex 2006-2011, assuming only 67% take action in response.

Category	Maximum number of avoidable admissions for relevant disease admissions over 6 year period assuming pollution patterns as for 2006-2011	Avoidable admissions if only 67% take action but this action is effective	Numbers of relevant group needed to avoid 1 relevant disease admission[a] if only 67% take action
COPD	0.30	0.20	837
Children 1-16 with asthma	0.004	0.003	14,860
Adults 17-60 with asthma	0.013	0.009	21,760
Children from schools	0.003	0.002	102,470
Non COPD/children or young adult asthma i.e. elderly 60+ with asthma, other respiratory, heart disease, other, none	0.077	0.052	3,190
Alternative non COPD/children or young adult asthma i.e. elderly 60+ with asthma, other respiratory, heart disease, other, none with non-asthmatic children from schools added	0.157	0.105	As above
Total	0.39 or 0.47	0.26 or 0.32	

[a] Numbers to which the service needs to be provided if 67% of participants take action and the action is 100% effective

6. Feasibility of a possible future intervention study

6.1 Question 6 What is the feasibility and likely statistical power of an intervention study to assess the effectiveness of the alert services in reducing adverse health outcomes?

6.1.1 One of the aims of the project is to use the theoretical calculations of numbers of additional hospital admissions on moderate, high and very high days to examine the feasibility of a possible future intervention study, in particular, whether such a study would have sufficient statistical power.

6.1.2 In order to do this, it is necessary to postulate the potential size of the effect. There are several possible assumptions that could be made. An optimistic scenario for effectiveness was taken. This was to assume that the effects of nitrogen dioxide are additional to those of particles, that the whole of the intervention study population signs up for the alert service, that 67% take action in response to the alerts and that this action is sufficient to prevent a hospital admission. If the population size required for a future intervention study is very large for an optimistic scenario, it will be even larger for less optimistic scenarios.

6.1.3 To compare the expected rates of respiratory hospital admissions in a control group and an intervention group, a dataset was used where the pattern of low, moderate, high and very high days were as in Sussex 2006-2011. The predicted additional respiratory hospital admissions above (or below) the average on low days calculated for the Sussex population over the time period 2006-2011 (as calculated in the previous chapters, except for including variations on low days) were taken as the baseline dataset. (The take up of airAlert is currently small and is already in the baseline – the study would effectively be a study of a major expansion of the air Alert service.) A new simulated dataset was calculated in which the number of respiratory hospital admissions was reduced by 67% on all moderate, high or very high days. The calculated respiratory hospital admissions remain the same as the baseline on low days. Only days with measurements of all 3 pollutants were used for this analysis.

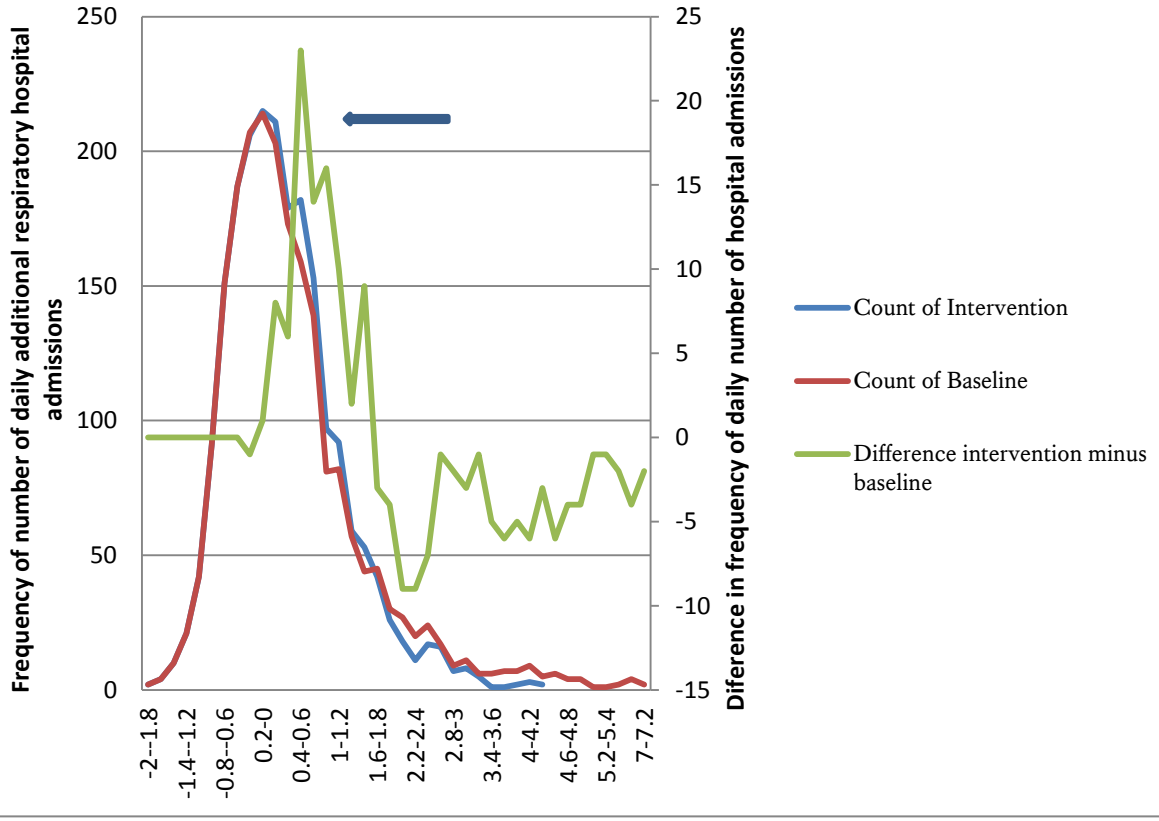
6.1.4 The characteristics of the dataset are given in Table 6.1. It can be seen that the total calculated number of hospital admissions is expected to come down as expected – from 763 to 518. It is also clear, again as expected, that the reductions occur at the higher end of the distribution of numbers of daily respiratory hospital admissions. The data are also skewed (Figure 6.1), more in the case of the baseline than for the intervention, where the upper tail has been reduced.

Table 6.1 Calculated air pollution-related hospital admissions in the population of Sussex from 2006-2011 with and without an assumed 67% reduction on moderate, high or very high days (all days with measurements of all 3 pollutants)

	Baseline, all days	67% reduction on moderate, high or very high days
Total	762.97	517.46
Mean	0.36	0.25
Standard deviation	1.13	0.89
Median	0.13	0.13
Interquartile range	1.15	1.08
Minimum	-1.96	-1.96
Maximum	7.02	4.70

6.1.5 The frequency distribution is shown in Figure 6.1.

Figure 6.1 Frequency distribution of calculated air pollution-related hospital admissions in the population of Sussex from 2006-2011 with and without an assumed 67% reduction on episode days (all days with measurements of all 3 pollutants)



6.1.6 Figure 6.1 shows that the distribution has a tail up to the higher values of calculated daily respiratory hospital admissions. Unsurprisingly, the two distributions are identical at the far left of the distribution (representing low days). The 'intervention' dataset shows differences above calculated daily respiratory hospital admissions of about –0.2 to –0.4. The 'intervention' dataset has more days with lower calculated daily hospital admissions in the range 0-1.2 and fewer above 1.2 i.e. the distribution has been shifted to the left. The green line shows the increase in frequency at the lower numbers of hospital admissions in the 'intervention' dataset. (Daily respiratory hospital admissions expressed as fractions e.g. 0.5 are equivalent to there being a 50% probability of a respiratory hospital admission or of there being a respiratory hospital admission in an area twice the size of Sussex.)

6.1.7 Figure 6.1 indicates as expected that there are no predicted differences between the two groups on low days as no action is expected to be taken if no alert is issued. (This is not to say that there are no effects due to changes within the low band, but the net effect is the same between the two groups). Therefore, a hypothetical study would only need to examine numbers of hospital admissions on moderate, high or very high days. Table 6.2 is the equivalent of Table 6.1 but only for moderate, high and very high days. This table also gives the total expressed as a rate per 100,000 population over a 6 year period rather than annual. This is used in the statistical power calculations.

Table 6.2 Calculated air pollution-related hospital admissions in the population of Sussex from 2006-2011 with and without an assumed 67% reduction on episode days (episode days only)

	Current impact on moderate, high and very high days	67% reduction on moderate, high and very high days
Total for Sussex population (1,563,000)	743.98	498.46
Rate per 100,000 for 6 year period	47.60	31.89
Mean	2.04	1.37
Standard deviation	1.31	0.88
Median	1.74	1.16
Interquartile range	1.62	1.08
Minimum	-0.29	-0.19
Maximum	7.02	4.70

6.1.8 To determine the size of the required study population, the difference in the rates between the two groups (the effect size) is needed, along with the variation in the data, the desired power (the probability of rejecting a hypothesis of no effect), the level of significance (alpha) to be used for any test of a statistically significant difference between the groups and the appropriate statistical test for the statistical distribution of the data. The calculation was done using the 'estimated sample size for two-sample comparison of proportions' option in STATA.

6.1.9 If you wished to detect a change in rates of admissions from 48/100,000 to 32/100,000 with power=0.9 and alpha=0.05, you would need a population of 340,609, in each group. This calculation assumes independent groups. So the study population would need to be at least 681,000 with half receiving the air alert service and half not.

6.1.10 This total study size would be just under 45% of the general population of Sussex. The incentive to sign up would be unlikely to apply in the general population. The current number of people signed up is about 0.05% of the population. The Health Survey for England (2010) gives the lifetime prevalence of doctor-diagnosed asthma as about 16% in men and 17% in women, predicting about 250,000 people in Sussex with doctor-diagnosed asthma. The lifetime prevalence of doctor-diagnosed chronic bronchitis, emphysema or COPD was given as 4% in men and 5% in women, predicting about 98,000 people in Sussex with these conditions. Both of these figures are likely to underestimate the lifetime prevalence of the disease but, for the purpose of this exercise, it is more likely that those who know they have the disease would have an incentive to sign up. This total of about 350,000 people is smaller than the total population size predicted to be needed for an intervention study so even if all COPD patients and asthmatics signed up, more participants would still be needed. In addition, the calculations are based on a six year study period over which time recruitment would need to be maintained. It thus appears unlikely that this size of study is practical at a local county level.

6.1.11 These calculations use the rates of hospital admissions in the general population as this is the basis of the routine statistics that are studied in the time-series studies of the effects of air pollution. The numbers of hospital admissions could be greater within a selected population with asthma or COPD but this has rarely been studied directly. (See Chapter 5 for information that can be inferred). The calculations in Chapter 5 do not suggest, however, that the predicted numbers of admissions in the susceptible groups is so much greater that it would make an intervention study feasible at a local county level.

6.1.12 It is important to realise that there are other potential benefits that have not been examined in this report. Air pollution probably shifts some individuals through a clinical threshold, be it onset of symptoms, use of medication, attendance at a GP practice or a hospital admission. Hospital admissions are a small tip of a pyramid of symptoms, so the effect on symptom reduction could be considerable (see further work in Chapter 8). The panel study literature has not been updated on the Air Pollution Epidemiology Database at St. George's, the numbers of studies are smaller and some studies have not shown effects but further investigation of quantitative predictions on the basis of the panel study literature, or time-series studies of GP consultations, would be worthwhile as a separate project.

6.2 Other factors influencing the design and feasibility of an intervention study

6.2.1 The discussion in section 6.1 was based on a simple comparison between two theoretical groups, one receiving the air pollution alert service and one that did not. However, the issues to be considered with regard to performing such a study are more complicated. Ideally, two groups would be compared with and without use of the airAlert service but with blinding as to whether or not the individuals were receiving the intervention. Blinding would be difficult to achieve, although two groups in different areas with matched characteristics could be compared, one with and one without the service.

6.2.2 Even if such an ideal study could be performed, it would also need to be shown that the intervention was preventing air pollution-induced exacerbations of symptoms, rather than just improving compliance with medication as a result of reminders to carry an inhaler. (Improving medication compliance could probably be addressed with a simpler system). This could potentially be tested by comparing the group receiving airAlert messages with a group that received random reminders to make sure that they used their medication as needed, with no mention of air pollution. Interpretation might be complicated if these random messages occurred on days that happened to be high air pollution days, for example, so another option would be to issue random messages only on low days, although this might introduce bias. These options would require larger study populations as the difference between the groups is likely to be smaller – there would probably be some beneficial effect in the 'general medication compliance' control group.

6.2.3 The design described in paragraph 6.2.2 does not test for behavioural factors as a result of the alert messages that could affect admissions separately from avoiding air pollution-related respiratory hospital admissions. For example, the alert messages could increase anxiety and perhaps even worsen asthma symptoms. This could be tested, in theory, by issuing airAlert messages to the control group on low days. However, this is probably unethical and, if participants were warned that this was one of the possibilities, it might lessen the effectiveness of the messages in the group that were receiving genuine messages. In addition, there are other routes available to find out the true air pollution levels such as news reports during bad episodes (a point that applies to control groups for other possible designs). The designs that try to account for a general behavioural effect of alert messages could need larger or smaller study populations depending on the expected direction of the behavioural effect in the control group. On the other hand, it might be considered that any effects of issues such as anxiety in some people are an inevitable part of the intervention so should not be separated out.

6.2.4 A final possibility is to do a case-crossover study in which one study group is studied for a period without the airAlert service, followed by a period with the airAlert service. One element of this has advantages in that each individual acts as their own control. The before and after intervention groups would not be independent, as the same subjects would be included. Ideally, such a study would apply the intervention in a random order, first or second. If the period without the airAlert service came second, it might be difficult to ensure that the participants did not check the other sources of information about low, moderate, high or very high days, given they would already have had contact with the system. One option would be to have a run in period to establish a baseline before the airAlert service period, followed by a further period without the service. The first and third periods could then be compared to see whether the third control period was a true 'absence of service' test or was influenced by knowing about the existence of the service. Having a baseline 'run-in' applies also to group designs. In both group and case-crossover designs the provision of service and control periods/groups would need to occur at a similar time of year and adjust for weather conditions.

6.2.5 These possible study designs are summarised in Table 6.3.

Table 6.3 Possible designs for an intervention study

	Intervention group	Control group
Simplest	Air pollution alert messages	No alert messages
Controlling for medication compliance effect	Air pollution alert messages	Random medication alert messages or medication alert messages on low days
Controlling for medication compliance and behaviour	Air pollution alert messages	'Mock air pollution alert messages' (not ethical)
Case crossover?	Air pollution alert messages	Options as above

6.2.6 The quantitative discussions so far have assumed a general population basis and the qualitative discussions have assumed a population with respiratory disease in general. However, it may be that effectiveness could be increased by identifying those that would benefit most. It may be that those committed to signing up to the service already have good compliance with their medication and that those that have less good compliance are more vulnerable to the effects of air pollution.

6.2.7 There may also be more general indirect benefits of the service. For example, if COPD patients take action to reduce their exposure to air pollution, this may not only reduce their respiratory exacerbations (the aim of the *airAlert* system) but may also reduce the cardiovascular outcomes in these patients, as a result of reduced air pollution exposure. About a third of COPD patients die from cardiovascular causes (McGarvey *et al* 2007).

6.3 Cost-effectiveness analysis and cost-benefit analysis

6.3.1 While doing a study investigating the benefits of the airAlert service in practice could be challenging, predicting a range of possible benefits and disbenefits for comparison against the costs could still be performed. Given that the costs of monitoring and predicting air pollution levels are already covered by local or central Government and have other aims in addition to the air pollution information service, the incremental costs of the alert messaging itself are low. Therefore, the service may well still be reasonable in theoretical public health/cost-benefit analysis terms. Although cost-benefit analysis or cost-effectiveness analysis is not part of the scope of this project, the work quantifying potential health impacts in this report provide a basis for quantifying the potential benefits.

7. Uncertainties

7.1 Introduction

7.1.1 This section describes the method for incorporating uncertainty into confidence intervals and for transmitting these through the various calculations. A wider discussion of other possible contributors to uncertainty is also discussed.

7.2 Confidence intervals for the concentration-response relationships and air pollution measurements

7.2.1 We looked into estimating confidence intervals based on two sources of uncertainty; the uncertainty in the effects estimate and the uncertainty in the air pollution measurements. Some information on this is given below but it should be emphasised that there are many more contributions to uncertainty than reflected in these aspects. We concluded overall that giving confidence intervals throughout would give a false sense of having fully characterised the uncertainty when substantial further work would be needed to do this.

7.2.2 Upper and lower confidence intervals for the concentration-response relationships have been given in Chapter 2 derived from the meta analysis. This represents statistical uncertainty. Other aspects of uncertainty in the concentration-response relationships are discussed later in this chapter.

7.2.3 Uncertainty in the air pollution measurements has been estimated from minimum performance criteria for air pollution measurements as required in the EU Air Quality Directive 2008/50/EC. For gaseous measurements at an individual measurement site these are 15 % (coverage factor[13] k= 2, ~ 2σ) at the short-term limit value concentration and averaging period. The short-term limit value concentration and averaging periods are close to the definition of a moderate day. In the case of this study uncertainty is likely to be less than this 15 % limit for two reasons.

- First, the air pollution assessment is based on a mean of measurements across a number of monitoring sites and the random aspects of the measurement uncertainty would be reduced.
- Second, the analysis has been based on the difference between mean concentrations on low days compared with that on moderate, high or very high days. The same instruments and standards were used in the assessment of low and non-low days and thus some of the systematic uncertainty that would be expected due to instrument calibration standards in individual measurements at individual sites would not be experienced in this case. The uncertainty in commercially available gas calibration standards is typically around 5%.

For these reasons an uncertainty estimate of 15% would be excessive. We therefore assumed an uncertainty estimate of 10% (coverage factor k= 2, ~ 2σ) for the mean gaseous concentrations.

7.2.4 For PM measurements the uncertainty is harder to estimate. The EU Air Quality Directive requires a maximum uncertainty of 25% for type approval for instrumentation when comparing with the reference method. This includes differences that relate not just to the calibration but also to differences in sensitivity to volatile PM components and particle bound water between measurement methods. However all measurements in Sussex are made with one of two measurement techniques, the TEOM corrected using the Volatile Correction model (Green *et al* 2009) and the Filter Dynamics Measurement System; two closely related methods with similar approaches to volatile PM and particle bound water assessment. For this reason and those discussed for gaseous measurements an uncertainty estimate based on the instrument performance requirements in the Directive would be too high. We therefore also assumed an uncertainty estimate of 10% (coverage factor k= 2, ~ 2σ) for PM measurements.

[13] The coverage factor k is a factor set to determine the desired span of uncertainty across a normal distribution. A coverage factor of 2 represents approximately 2 standard deviations from the mean, roughly equivalent to a 95% confidence interval.

7.2.5 The increments in the pollutant concentrations were derived by subtracting a baseline we defined as the average of the relevant pollutants on all low days. There are substantial potential errors/possible different assumption underlying this low day average value. These are not covered by the illustration of combining a subset of the known uncertainties below.

7.3 Other uncertainties in the inputs to the calculations

7.3.1 The above paragraphs explain how the statistical uncertainties in the air pollution measurements and concentration-response relationships were incorporated. The other uncertainties are discussed in qualitative terms below.

Population data and baseline rates

7.3.2 Collection of population data is well established and uncertainties are small relative to the totals. Some idea of the uncertainty in the population data can be found by comparing the original 2010 estimates for Sussex with those corrected for the 2011 Census and with the original, locally obtained, estimates. This resulted in a variation of about 1-2%, well within the variation encompassed by the confidence intervals for total respiratory admissions of about 7%.

7.3.3 Hospital episode statistics are also a well established system. There can, of course, be errors in coding the diagnosis at discharge, but this is not expected to be extensive. Our approach to defining baseline rates evolved as the project progressed. The baseline rate for respiratory admissions, all ages, was obtained by scaling the national rate by the ratio of the Sussex population to the population of England. For specific respiratory diagnoses we obtained local data, first from West Sussex scaled up to the Sussex population and then by adding numbers of admissions from West Sussex, East Sussex and Brighton and Hove.

7.3.4 For asthma admissions in children in Sussex, there was around a 20% difference between the baseline rate scaled from the rate for England and the baseline rate scaled from West Sussex. The latter was used. For asthma admissions in adults aged 15-64, a comparison could be made between the baseline rate for Sussex derived by scaling from West Sussex data and that derived by adding data from West Sussex, East Sussex and Brighton and Hove. The latter was about 11% higher and this was what was used. For COPD admissions, the admissions for Sussex derived from West Sussex data were about 30% lower than they would have been had they been derived from national data. These variations are likely to have a substantial component that represents real regional variation. We recommend use of local rates in future work.

Exposure measurement error

7.3.5 The time-series studies on which the concentration-response relationships are based use background monitoring site concentrations on each day to represent the exposure of the population. Health impact assessment relies on the assumption that the way in which the background monitoring site concentrations act as surrogates for the distribution of personal exposure in the population is approximately equivalent in the area in which the health impact assessment applies compared with the areas used in the time-series studies used to define the concentration-response relationship. Many of these studies are based on large urban cities so there is some uncertainty in the way in which this applies to the rural parts of Sussex. This uncertainty can only be noted rather than quantified, but it is an uncertainty that also applies in other contexts such as national health impact assessments that include rural areas of the country.

Variations in choice of concentration-response relationships

7.3.6 In the calculations of the confidence intervals described above, the statistical uncertainty in the concentration-response relationship was greater than in the air pollution measurements. This is not surprising as the epidemiological studies are studying endpoints influenced by a variety of real-life factors including human behavioural factors influencing air pollution exposure. Nonetheless, this uncertainty only represents the statistical variation aspects of the chosen concentration-response relationship.

7.3.7 The concentration-response relationships are based on systematic review according to specified criteria and pooling of estimates from the European region in meta-analysis. Other choices could have been made, such as pooling estimates from studies worldwide. This would have increased the numbers of studies available but might also bring in additional heterogeneity. In addition, the results change over time as more studies are published, for example the increase in the size of the updated concentration-response relationship for nitrogen dioxide and respiratory hospital admissions (Table 2.1). For some endpoints and pollutants such as for all cause mortality or for PM_{10} and respiratory hospital admissions, there are sufficient numbers of

studies for the concentration-response relationships to be less likely to change substantially on publication of new studies. For others, there is more potential for changes in concentration-response relationships according to the choices made. In general, time-series estimates as percentage increases in baseline rates per 10 $\mu g/m^3$ of pollutant vary from a few % to tenths of a % to negative tenths of a %. This could clearly make several fold differences to the answers. This is why it is important to pool the estimates according to pre-defined criteria, as has been done here.

Heterogeneity

7.3.8 There was evidence of heterogeneity across the studies contributing to the pooled estimates for PM_{10} and 8 hour average ozone and respiratory hospital admissions but not for nitrogen dioxide (Anderson *et al* 2007). Investigation of heterogeneity in the more recent analyses similarly has found evidence of heterogeneity between studies in some but not most cases of the relationships considered here, although this still needs to be confirmed. Heterogeneity has implications for health impact assessment in that it suggests that it might be appropriate to apply different concentration-response relationships according to the presence or not of the relevant effect modifiers. However, the causes of heterogeneity are not sufficiently understood for this to be possible at this stage.

Publication bias

7.3.9 We have not adjusted for publication bias for this work but it should be noted that publication bias exists in the time-series literature (Anderson *et al*, 2005). For the respiratory hospital admissions concentration-response relationships, there was some indication of publication bias for the estimate for 1 hour average nitrogen dioxide (suggesting positive associations were more likely to have been published) but not for PM_{10} or ozone, pollutants that are more commonly studied (Anderson *et al* 2007). For the specific respiratory diagnoses, the indications are that publication bias was not marked in most cases but the parallel systematic review project is not yet complete.

Potential for confounding between pollutants

7.3.10 One of the significant points of discussion in health impact assessment at the moment is how to deal with multi-pollutant model results. This project has followed the approach of many health impact assessments in that single pollutant models have been used, with commentary on the results of multi-pollutant models in which the effects of one pollutant are adjusted for those of other pollutants. It still remains the case that there are many more results for single pollutant models such that using multi-pollutant model results instead would reduce the number of studies available for consideration. In addition, appropriate methods to choose to select multi-pollutant model estimates for pooling are unclear since the studies often vary in which pollutants are included in the multi-pollutant models. It should also be noted that interpretation of multi-pollutant model results is complicated, and potentially misleading, when pollutants are closely correlated and when there is differential exposure measurement error between pollutants.

7.3.11 It is nonetheless important to consider the potential implications of confounding between pollutants. This was discussed in Chapter 2 and also comes up in other parts of the report, particularly in regard to negative confounding of ozone relationships by other pollutants that accumulate in the winter when ozone is low. There is a tendency in the literature to test positive associations that are statistically significant for confounding by other pollutants but not associations that are not statistically significant or even negative. This may produce bias in terms of (lack of) publication of results for associations with ozone that are subject to negative confounding, particularly in the winter, and therefore, potentially, leading to an underestimate of the size of ozone associations. Overall, the discussion in Chapter 2 concluded that, where studied, the effects of ozone in all year studies were generally independent of PM_{10} and that the evidence for an effect of nitrogen dioxide independent of PM_{10} was increasing.

Seasonal effects

7.3.12 The concentration-response relationships used here are based on all year studies. However, it is known that the time-series estimates can vary by season. This is probably for a variety of reasons including different correlation patterns between pollutants in different seasons and different behaviour patterns in different seasons leading to differences in population exposure. This project has applied all year estimates to all year baseline rates. Future work could include sensitivity analyses on whether different answers would be produced if analysing by season. For example, COPD admissions are lower in the summer when ozone levels are higher, an effect that might give a smaller answer than for the all year calculation. Conversely, applying the lower concentrations of ozone in the winter to higher COPD admission rates in the winter might give a larger answer. The overall effect is thus difficult to predict without doing the relevant sensitivity analyses.

Summary

7.3.13 It is important to be aware of these various facets of uncertainty and the possible implications for any conclusions based on subtle differences in results. On the other hand, every effort has been made to use reasonable choices of assumptions, so it is considered unlikely that these uncertainties will affect the major conclusions.

8. Conclusions

8.1 Aims of the project

8.1.1 The primary aims of the project were to assess the potential size of the effect of moderate, high and very high days of air pollution on respiratory, COPD and asthma admissions in the population of Sussex over the period 2006-2011 and to use this to assess the potential for avoiding hospital admissions as a result of the airAlert service. This, in turn, would contribute to investigating the feasibility of an intervention study to examine the potential benefits of the airAlert service directly.

8.1.2 A series of questions were set out in the specification. These are revisited below, along with the conclusions arising from the project.

8.1.3 Other work in the field and suggestions for further work are also described below.

8.2 Evidence on effects of air pollution on health – respiratory, COPD and asthma admissions

8.2.1 The responses to the questions relating the background evidence on air pollution and health developed as a result of this project and a parallel systematic review project are given below.

1. Using meta-analytical techniques, what is the current quantitative evidence supporting associations between short-term changes in levels of air pollution and effects on health outcomes relevant to the airAlert system?

8.2.2 PM_{10} had positive and statistically significant associations with all respiratory, COPD and asthma admissions in adults and children.

8.2.3 The size of these PM_{10} associations was largest on a per 10 $\mu g/m^3$ basis for all respiratory admissions and asthma in children, followed by asthma admissions in adults aged 15-64 and then COPD admissions, but the confidence intervals overlapped.

8.2.4 Ozone had positive and statistically significant associations with all respiratory and COPD admissions but associations with asthma admissions were not statistically significant and were even negative, but not significant, in the case of asthma in children.

8.2.5 The associations for ozone were largest for COPD, followed by all respiratory admissions, asthma in adults and then asthma in children. The confidence intervals overlapped, except for the size of the effect on COPD admissions being clearly greater than that on asthma in children.

8.2.6 Nitrogen dioxide associations were all positive, statistically significant in the case of COPD admissions, marginally significant for asthma in adults and not significant for asthma in children and all respiratory admissions. It should be noted though that there were generally the fewest studies for nitrogen dioxide, partly because the 1 hour averaging time examined here is not the most common averaging time studied.

8.2.7 The effects of 1 hour average nitrogen dioxide were generally small on a per 10 $\mu g/m^3$ basis, with confidence intervals overlapping. The central estimates were a little greater for asthma in children than for asthma in adults and COPD, with all respiratory admissions the smallest, but the latter would change if taking into account more recent studies.

8.2.8 Comparing pollutants within the same outcomes, PM_{10} had greater effects than ozone and then nitrogen dioxide on all respiratory admissions, although confidence intervals overlapped, taking into account newer studies on nitrogen dioxide. These comparisons are on a per 10 $\mu g/m^3$ basis. Ideally, they would be made on a molar basis, but this is not possible for PM_{10}, which is formed from a mixture of components.

8.2.9 For asthma admissions in children, PM_{10} had greater effects than nitrogen dioxide and then ozone (where the associations were not significant) but, again the confidence intervals overlapped. The order was the same for asthma in adults, although in this case the effect of nitrogen dioxide was significant. While the evidence remains only suggestive, this consistency across age groups adds some support to the view that PM_{10} may have the greatest effect on asthma admissions.

8.2.10 In contrast, for COPD admissions it was ozone that had the greatest effect per 10 $\mu g/m^3$, followed by PM_{10} and then nitrogen dioxide. All associations were statistically significant but the confidence intervals overlapped. As with the other endpoints, this comparison is across different groups of studies, rather than within the same study, although there is also suggestive evidence within some studies e.g. Ko *et al* (2007).

8.2.11 Another way to compare the relative importance of the different pollutants across the different respiratory outcomes is to compare them on the basis of the actual relative levels of the different pollutants, rather than per 10 $\mu g/m^3$. The context of this report allows this comparison to be made, as discussed later.

8.2.12 In general, it should be noted that there is a wider literature than the group of studies defined for this work to match the averaging times with those used for the air quality index and to provide objective selection criteria. These conclusions are specific to this group of studies but not obviously out of line with data on other averaging times. The parallel project mentioned in Chapter 2 covers other averaging times and will be submitting systematic review and meta-analysis papers on ozone, nitrogen dioxide and components of particulate matter in the near future.

2. Bearing in mind wider evidence, how likely are these associations to be causal and can concentration-response relationships be defined for use in quantifying the expected health impact of changes in levels of air pollution?

8.2.13 The discussion in Chapter 2 concluded that these associations could be regarded as causal, at least to the extent of using the concentration-response relationships in calculations, while acknowledging the uncertainties. There is particular uncertainty with regard to ozone and asthma, but the fact that ozone is negatively correlated with other pollutants in the winter, means that there is a possibility of some masking of the association. This suggests some caution is needed before ruling out an effect.

8.2.14 The discussion of uncertainties in Chapter 7 highlighted the need to bear in mind the points that there is some evidence of heterogeneity and publication bias in some cases, and that it is not always easy to disentangle the effects of different pollutants from each other.

8.3 Estimated size of the effect of air pollution on moderate, high and very high days compared with low days in Sussex over the 6 year period 2006-2011

3. Applying the concentration-response relationships defined in (2) to information on the increment between the average concentrations of pollutants on days in the low band and the average concentrations of pollutants on days in the high or moderate band and on the frequency of episodes of high or moderate pollution, what is the expected size of the effect of these pollution changes on health impacts within the general population?

Pollution concentrations

8.3.1 Chapter 3 sets out how the appropriate concentration increments were defined for the purpose of evaluating the effects of moderate, high and very high days. The approach taken was to calculate the increment between the regional average level of a particular pollutant on a moderate, high or very high day and the average of regional levels of that pollutant on days when all pollutants were low. The approach calculates the effect of all air pollutants on a moderate, high or very high day – not just the air pollutant that led to defining the day as one above the low band. This is because we are evaluating the overall effect of air pollution on moderate, high and very high days.

8.3.2 This approach showed that it was possible for one pollutant e.g. ozone to even be below its average on low days when other pollutants were moderate, high or very high. This was consistent with scavenging of ozone by accumulated nitric oxide in cold still conditions, which also leads to accumulation of other pollutants. There were also examples where the regional average for the pollutant that defined the moderate, high or very high day was not above the breakpoint in the band. This was because a moderate, high or very high day was defined if 1 site was above the breakpoint and sometimes local conditions led to higher levels at a particular site, that were not reflected regionally.

8.3.3 London was also included to provide a comparison for the pollution climate in Sussex. In Sussex, raised ozone concentrations were the most common reason for moderate and high days, although there were some moderate and high days for PM_{10} as well. There were 2 very high days for PM_{10} and 1 for ozone. Nitrogen dioxide only resulted in three moderate days, all in 2011. In comparison with Sussex, there were fewer moderate and high days for ozone and no very high days for ozone in London. There were many more moderate days for PM_{10} and greater numbers of high and very high days as well. There were also many more moderate days for NO_2. This is as expected for a major urban city.

8.3.4 The baseline average concentrations on low days were higher in London for PM_{10} and NO_2 but lower for ozone. The average increment between low days and moderate, high or very high days for ozone was greater in Sussex, and was even negative in London on very high days, although the range for different days included positive increments. These increments for each day were then used for the calculations of the estimated size of the effects on admissions on moderate, high and very high days.

8.3.5 The headline figures were that the pattern of moderate, high and very high days in Sussex over the period 2006-2011 were estimated to have led to around 740 or 760 additional respiratory hospital admissions, depending on whether or not nitrogen dioxide was included. These figures are calculated, not counted, as air pollution-related hospital admissions are not clinically identifiable and may, in any case, result from a combination of causes. The design of the studies used to detect associations indicate whether the hospital admissions are additional on days with higher air pollution but not whether the hospital admissions would have occurred in any case at a later point. It is, however, likely that air pollution does exacerbate disease and leads to hospital admissions as a result.

8.3.6 While the risks for an individual from a particular pollutant increase from moderate to high to very high days, the greatest effect in public health terms is from moderate days, as there are many more of these overall.

8.3.7 Although the results for respiratory admissions and admissions for other diagnoses have been presented in various tables already, it is helpful to summarise the results for the various outcomes in one table (Table 8.1 below). It can clearly be seen from this table that the impact on asthma admissions is small. This is to some extent expected as the population of children and even of adults aged 15-64 is smaller than the size of the whole population and the baseline rates for asthma emergency admissions are only around 10-20% of the rate for emergency respiratory hospital admissions. In addition, the concentration-response relationship per 10 $\mu g/m^3$ for ozone and asthma admissions is smaller (-0.36%/0.14% in children and adults vs 0.63% for respiratory admissions), while that for PM_{10} is similar for asthma in children (1.69%) and a bit smaller for asthma in adults (1%) compared with that for respiratory hospital admissions (1.71%). As the increment between NO_2 concentrations on moderate, high and very high days and NO_2 concentrations on low days is small (the moderate, high or very high days being more often defined by raised concentrations of ozone or PM_{10}), differences in concentration-response relationships for NO_2 between outcomes are less relevant. PM_{10} is the most important pollutant for asthma admissions. The fact that diesel exhaust is an adjuvant, increasing the allergic response (see section 2,4), may contribute to this, although this has only been shown at high doses and is only one amongst many sources of PM_{10}.

8.3.8 The estimated totals for COPD admissions are much greater than for asthma and less than that for respiratory admissions. The calculation applies to the whole population rather than sub age groups as for asthma (although in practice COPD admissions are concentrated in the elderly, the calculation can still be done on a whole population basis). The baseline rates for COPD admissions are much greater than those for asthma admissions. For the comparison with respiratory hospital admissions, the reasons for lower numbers of COPD admissions are a combination of the difference in baseline rate (about 20% of those for respiratory admissions) and the differences in concentration response relationships – higher for ozone (1.13 vs 0.63%) and lower for PM_{10} (0.75 vs 1.71%). The suggestive evidence of a greater effect of ozone on COPD admissions is interesting in terms of a risk factor for COPD admissions that is greater in rural rather than urban areas and greater in the summer than the winter. COPD admissions are larger in the winter, so there are obviously other risk factors involved, such as cold weather. This increased effect of ozone needs to be confirmed, but there is some plausibility to it as ozone is known to suppress phagocytosis (Karavitis and Kovacs, 2011), a process important for the clearance of infection. Many COPD exacerbations are due to infections.

8.3.9 It can also be seen that the results for all respiratory hospital admissions are greater than for asthma and COPD combined. While asthma in the elderly is not covered and variations are to be expected due to the fact that the concentration-response relationships are derived from different studies, the extent of the difference is sufficiently large for other factors to be considered. One of these is that air pollution has also been shown to have effects on lower respiratory infections such as pneumonia (Burnett *et al* 1999; Fusco *et al* 2001; Hinwood *et al* 2006; Michelozzi *et al,* 2000*;* Wong *et al* 1999; Wordley *et al* 1997; Simpson *et al* 2005*;* Medina-Ramon *et al* 2006) although this has been less studied than for other outcomes. It would be worth considering this in future work.

8.3.10 Table 8.1 also shows that the effect of moderate, high and very high days was greater in London, compared with Sussex. This was mainly due to its larger population, but also due to higher levels of pollution. The additional air pollution-related hospital admissions per 100,000 were about 47.5 – 48.7 per 100,000 in Sussex and 51.4 – 55.5 per 100,000 in London, over a 6 year period. PM_{10} was estimated to be the dominant contributor to respiratory hospital admissions in London, compared with other pollutants, whereas in Sussex the effect of ozone was slightly greater than for PM_{10}.

Table 8.1 Summary of total additional emergency hospital admissions for different outcomes in Sussex and for respiratory admissions in London for all pollutants on moderate, high and very high days vs. low days for period 2006-2011

Outcome	Total without NO_2	Total with NO_2
Respiratory hospital admissions all ages in Sussex	741.7	761.6
Asthma admissions in children in Sussex	3.8	5.5
Asthma admissions in adults aged 15-64 in Sussex	11.5	12.6
COPD admissions all ages in Sussex	118.7	123.4
Respiratory hospital admissions all ages in London	4027.5	4341.8

8.3.11 The estimates above do not measure the entirety of effects on health as variations within the low band will also contribute. In addition, there is evidence for the effects of air pollution on mortality and on admissions for cardiovascular disease, as well as for effects on symptoms and GP consultations. These outcomes are not covered here. The aim was to consider the total numbers of admissions that might be avoidable by modifying treatment e.g. by the use of inhalers or avoiding exposure. This is, of course, an unrealistic maximum number of admissions that could be avoided but it does give some indication of the scope of the problem.

8.4 Estimated size of the effects on health amongst those that use the airAlert service

4. Using a variety of reasonable assumptions, what is the expected size of the effect of these pollution changes in the population likely to receive alerts?

8.4.1 The effects described in section 8.3 relate to the whole population of Sussex or sub-groups by age of that population. The estimated size of the effects, assuming no avoiding action, was also calculated for those receiving the air Alert service.

8.4.2 The size of the population receiving the airAlert service is much much smaller than the population of Sussex (760 vs 1,563,000). Hence the estimated numbers of admissions are also much smaller, in fact they are often fractions of an admission. Obviously, fractional admissions do not occur, so these numbers are best regarded as the probability of 1 admission occurring or as the numbers needed to use the service in order to avoid one hospital admissions, as described in paragraph 8.4.4.

8.4.3 Calculations done on a general population basis suggested a figure of 0.36 respiratory admissions, or a 36% probability of 1 admission, might be expected amongst airAlert recipients. The equivalent figures for COPD, asthma in adults and asthma in children were 0.06, 0.003 and 0.004. However, it was recognised that the service was targeted at particular susceptible groups that might be more at risk of respiratory admissions than the general population. Calculations, taking this into account, suggested figures of 0.3 COPD admissions, 0.013 asthma admissions in adults and 0.007 asthma admissions in children, which along with a general population group gave a total of 0.39-0.47 admissions over the 6 year period, depending on assumptions about the composition of the general population group.

8.4.4 The small size of these numbers is to a large extent determined by the size of the population receiving the airAlert service, as well as the small effect size. As noted above, the effects can also be expressed as the number of people to whom the service would need to be provided to potentially avoid one respiratory, COPD or asthma admission. Assuming all participants took action and the action was 100% effective, the rounded numbers (with the confidence intervals given in Table 5.4) were estimated to be:

- 560 COPD patients to avoid 1 COPD admission
- 9,960 asthmatic children to avoid 1 asthma admission
- 68,660 children in general to avoid 1 asthma admission
- 14,580 adult asthmatics to avoid 1 asthma admission
- 2,140 of the general population to avoid 1 respiratory admission

8.4.5 These figures show the advantage of targeting the service at susceptible groups. Although the numbers needed to potentially avoid 1 asthma admissions if avoiding action was completely effective are greater than for the general population, this does not take into account the fact that asthmatics are more likely to be able to help their situation by using their inhaler. For the general population, the only option is to reduce exposure. Effectiveness of action for COPD patients is somewhere between these two.

8.5 Potential effectiveness of the service in avoiding admissions

5. Using assumptions guided by qualitative research on whether users respond with action to ameliorate effects, what is the scope of the possible reductions in health outcomes that might be generated by users of the service?

8.5.1 Focus group work by Smallbone (2009) suggested that 67% took specific action in response to alerts including ensuring they carried their reliever medication, taking additional medication, avoiding strenuous exercise and avoiding areas mentioned in the alerts. Later work (Smallbone, 2011) noted that over half of those with respiratory conditions would change their behaviour. It is unknown to what degree the actions taken actually work, but assuming that they do, assuming 67% rather than 100% took action would reduce the potential numbers of admissions avoided and increase the numbers needed to whom the service would need to be provided to avoid 1 hospital admission.

8.5.2 The predicted avoidable admissions, assuming 67% took action, were 0.2 COPD admissions, 0.005 asthma admissions in children, 0.009 asthma admissions in adults and 0.05 – 0.11 respiratory admissions in the general population. The rounded numbers needing to receive the service to avoid 1 admission were estimated to be:

- 840 COPD patients to avoid 1 COPD admission
- 14,860 asthmatic children to avoid 1 asthma admission
- 102,470 children in general to avoid 1 asthma admission
- 3,190 of the general population to avoid 1 respiratory admission.

8.6 Feasibility of a possible future intervention study

6. Given the answers to the previous questions, what is the feasibility and likely statistical power of an intervention study to assess the effectiveness of the alert services in reducing adverse health outcomes?

8.6.1 A simulated dataset was generated using an optimistic scenario of 67% of participants in an intervention study taking action that was 100% effective. This represents the test group, the control group being the situation in Sussex as it is now. In essence, this tests expansion of the service beyond the current situation.

8.6.2 The simulated dataset showed an estimated reduction in respiratory admissions – the total being about 520 admissions compared with 760 admissions now, a saving of around 240 admissions. This represented a change in rate per 100,000 population from 47.6 to 31.9. Statistical power calculations suggested that to detect this change in rate with a power of 0.9 and an alpha (level of significance) equal to 0.05, around 340,600 would be needed in each group, a total of 681,000. This represents a bit under half of the whole Sussex population (who do not all have an incentive to sign up) and more than the total population of asthma and COPD patients in Sussex. It thus appears unlikely that this size of study is practical at a local county level.

8.6.3 Other factors would need to be considered in the feasibility of performing an intervention study. The simple comparison represented by the paragraph above, would only show whether or not the service was effective but not why. It is possible that the service would lead to improved compliance with medication leading to an improvement in health that was nothing to do with reducing effects of air pollution-related admissions. It is also possible that alerts would increase anxiety and actually increase admissions as a result.

To test these points would require the use of mock alerts when air pollution was not actually high, which is probably unethical. Overall, design of such a study would be very challenging.

8.6.4 It should be noted that although the size of the potential benefits makes performing an intervention study very, probably too challenging, this does not mean that the service itself is not justified in cost-benefit terms, as the incremental costs of air alert messaging are low. The work quantifying potential impacts on health in this project should provide useful inputs should a cost-benefit analysis be considered.

8.6.5 In summary, if the service were provided to the whole of the Sussex population, and 67% took action that was 100% effective, around 250 respiratory hospital admissions could potentially be avoided over a 6 year period (Chapter 6). This is over-optimistic. Expanding the service to increased numbers of asthmatics would improve benefits, although tens of thousands would need to receive the service to avoid 1 asthma admission. However, targeting the service at 850 COPD patients could avoid 1 COPD admission over 6 years, with increasing benefits for larger numbers, assuming the actions were effective. It should be noted that focus group research by Dr Kirsty Smallbone shows that the service is also valued by carers and relatives in addition to the individuals directly affected. Health professionals may also find it useful.

8.7 Other work in the field

8.7.1 While the health effects of air pollution in general are often discussed in the context of air quality information services, it is rare for studies to quantify health impacts in relation to the different days defined by the index.

8.7.2 There has been work in Canada developing a new index on the basis of the health impacts of a combination of pollutants (Stieb *et al* 2005; Stieb *et al* 2008). This used the distribution of the percentage increase in mortality due to the relevant concentrations of each pollutant on each day. This was then summed across pollutants and the distribution across days examined to define the index. The maximum percent excess mortality was around 11%, this was scaled back to 10% for convenience. The majority of days were within the range 3-6% (Stieb *et al* 2005). Subsequent work involved performing a dedicated time-series study of 3 hour averages of the pollutants, examining the interactions between them, to provide input into calculation of the index. The largest numbers of days were within the range 3-5% percent excess mortality (Stieb *et al* 2008).

8.7.3 Chen *et al* (2013) evaluated the application of the above approach in Shanghai. They developed the index on the basis of percent excess mortality from PM_{10}, $PM_{2.5}$ and NO_2. Most days fell between the 2 and 5% range. They also examined the associations between the air quality and health index based on mortality and numbers of hospital admissions, outpatient visits and emergency room visits. It was concluded that the new index could predict same day hospital admissions, outpatient visits and emergency visits. The results were expressed as % increase in the health outcome for an interquartile range increase in the air quality and health index rather than as absolute numbers as done in this project.

8.7.4 Soyiri *et al* (2013) investigated forecasting of asthma admissions in London. This study did not analyse admissions by index days as such. They developed a predictive model and noted that short-term weather factors and air quality made little difference to the predictive power of the model once season was included as a predictive factor. Given the small effects on asthma admissions shown in this work, this may not be surprising.

8.7.5 Other than that, the use of air quality warning systems, in general, has been reviewed (Kelly *et al* 2013). Other studies include discussion of a new index in terms of concentrations (Lu *et al* 2011) and studies on public awareness and views on air quality information services (some noting that awareness of the information services can be low) (Beaumont *et al,* 1999; Dorevitch *et al,* 2008; Williams and Bird, 2003; Semenza *et al* 2008; McDermott *et al* 2006). Dorevitch *et al* (2008) found that awareness could be increased by education workshops but that awareness of how to find air quality information had dropped again 1 year after the workshop.

8.7.6 Some studies have examined whether members of the public take action in response to alerts. Semenza *et al* 2008 found a proportion as low as 10-15% of a general population sample taking action apparently in response to alerts, although interviewing elicited the information that this was as much to do with their own perception of the pollution level as to the alert itself. McDermott *et al* (2006) found that 64% of parents of asthmatic children sometimes restricted children's play when air pollution was high, higher than the 45% amongst parents of non-asthmatic children. Even amongst those that did take action,

this did not necessarily apply every time there was an alert. Wen *et al* (2009) found that the prevalence of change in outdoor activity in response to air quality index media alerts in the US was 31% amongst adults with lifetime asthma and 16% amongst those without asthma. Rather than using surveys, Neidell *et al* (2010) examined attendance figures at Los Angeles Zoo which dropped at 200 ppb ozone, the point at which an alert was issued. Attendance increased again above 200 ppb ozone but at a lower level than below 200 ppb. Attendance also dropped at the Griffith Park Observatory. The latter authors argue that this reduction in exposure outdoors in response to alerts means that time-series studies underestimate the true effect of ozone as the way in which the monitoring site is a surrogate for exposure in the population changes once alerts are issued and people reduce their exposure.

8.7.7 The studies vary in the proportion of people reported as taking action in response to alerts – as intended, the assumption in this project that as many as 67% take action and these actions are effective does indeed represent an optimistic scenario.

8.8 Further work

8.8.1 Further work to investigate how best to propagate the uncertainties in the various inputs through to the final results would be useful, in addition to sensitivity analyses around the various assumptions made.

8.8.2 This work did not consider less severe respiratory endpoints than respiratory hospital admissions. There is evidence for an effect of air pollution on respiratory symptoms. At the time of the Anderson *et al* (2007) report there were insufficient studies of respiratory symptoms or emergency room visits across all 3 pollutants for the relevant averaging times. This may have changed. There are also studies on GP consultations. The Air Pollution Epidemiology Database has not been updated for these endpoints, so any further work on these aspects would require defining concentration-response relationships from scratch. Nevertheless, it would then be possible to model the potential benefits of the airAlert service in terms of effects on symptoms, medication use and impact on primary care services.

8.8.3 Calculations were not done for cardiovascular admissions. This was because cardiovascular disease patients do not usually modulate their own medication day to day, in the way that asthmatics or COPD patients do. Nonetheless, there could be benefits to this group through reduction of exposure in response to air alerts. This should be examined in further work.

8.8.4 This work highlighted greater effects on respiratory admissions than on asthma and COPD admissions combined. It was noted that this might be accounted for by an effect on respiratory infections. Provided sufficient studies were available for meta-analysis, calculations could be done specifically for admissions for lower respiratory infections.

8.8.5 This work suggests that different pollutants are most important for different outcomes, but this was not entirely clear cut as the confidence intervals often overlapped. Further studies/updated reviews would be needed to confirm this. Review work could examine the effects of pollutants on COPD compared with asthma within the same studies, lessening the uncertainties to making comparisons across different groups of studies.

8.8.6 Analyses of numbers of respiratory hospital admissions have been done in London for comparison with Sussex. This has not been done for asthma and COPD admissions. This would be interesting as the balance between effects on asthma and COPD might be different in London, given the different balance in concentrations of PM_{10} and ozone.

8.8.7 This project was set up to see whether an intervention study was feasible. This does not appear to be the case. Nonetheless, cost-benefit analysis work would be feasible as the methods developed in this report can be used to quantify the potential benefits.

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Appendix 1 Air Pollution Epidemiology Database APED - search strings, sifting criteria, estimate selection protocol (based on Anderson *et al* (2007)

DATA COLLECTION FOR APED

APED comprises two Reference Manager databases (one for time series studies and one for panel studies) and two Access databases (also one for each study design). The process of adding data to these databases involves three steps: 1) systematic searching of the medical peer reviewed literature to identify potential studies for inclusion in the databases and an assessment of their suitability for inclusion in APED; 2) data extraction and 3) data entry (into Access) and subsequent standardization of effect estimates.

Step 1 - Systematic ascertainment of relevant papers

Medline, Embase and Web of Science databases were used to identify, without constraint on language or publication date, all peer-reviewed time series and panel papers published up to January 2006. The search strings used are shown in Table A.1. Where appropriate, these results are supplemented with papers identified by colleagues (especially useful with foreign language journals), citations and published reviews.

Table A.1. Search strings
Separate search strings for time series and panel studies were developed and tested against known literature until they were sensitive enough to pick up all relevant studies. They define the pollutants, study types and health outcomes that are of interest and are used to search three bibliographic databases: Web of Science (via Web of Knowledge), Medline and Embase. There is a slight variation between the notation used in Web of Science and the other two databases; Web of Science uses *'s as wildcard characters and Medline and Embase use ?'s. The type of symbol that defines an exact phrase is also different and details on which ones to use are given below. The search strings are as follows:

Web of Science	
Time Series	(air pollution or pollution or smog or particle* or particulate* or ozone or black smoke or sulphate* or sulphur dioxide* or nitric oxide* or nitrogen dioxide* or carbon monoxide*) and (timeseries or time-series or time series or daily) and (mortality or death* or dying or hospital admission* or admission* or emergency room or visit* or attendance* or 'a&e' or 'a and e' or accident and emergency or general pract* or physician* or consultation* or emergency department*)
Panel studies	(air pollution or pollut* or smog or black smoke or smoke or partic* or particle* or ozone or sulfur dioxide or sulphur dioxide or nitrogen dioxide or nitric oxide or sulfate or sulphate or carbon monoxide) and (lung function or pulmonary function or pefr or pef or peak expiratory flow or peak flow or peak expiratory flow rate or peak expiratory flow rates or forced expiratory flow or forced expiratory flow rate or fvc or ventilatory lung function or fev or fev1 or acute effects or short-term effects or respiratory health or respiratory symptoms or chronic obstructive lung disease or copd) and (panel or panel study or panel studies or longitudinal study or longitudinal or diary or diaries)
Medline and Embase	
Time series	(air pollution or pollution or smog or particle? or particulate? or ozone or black smoke or sulphate? or sulphur dioxide? or nitric oxide? or nitrogen dioxide? or carbon monoxide?) and (timeseries or time-series or time series or daily) and (mortality or death? or dying or hospital admission? Or admission? or emergency room or visit? or attendance? or "a&e" or "a and e" or accident and emergency or general pract? or physician? Or consultation? or emergency department?)
Panel studies	(air pollution or pollut? or smog or black smoke or smoke or partic? Or particle? or ozone or sulfur dioxide or sulphur dioxide or nitrogen dioxide or nitric oxide or sulfate or sulphate or carbon monoxide) and (lung function or pulmonary function or pefr or pef or peak expiratory flow or peak flow or peak expiratory flow rate or peak expiratory flow rates or forced expiratory flow or forced expiratory flow rate or fvc or ventilatory lung function or fev or fev1 or acute effects or short-term effects or respiratory health or respiratory symptoms or chronic obstructive lung disease or copd) and (panel or panel study or panel studies or longitudinal study or longitudinal or diary or diaries)

The full reference and abstract for each paper identified were downloaded into the appropriate Reference Manager database (Reference Manager, ISI Researchsoft, Carlsbad, CA). A multilevel sifting process was then applied to identify those studies suitable for inclusion in APED. This began with a review of the abstracts to identify those that might contain time series or panel results and to obtain the entire paper. These papers were then assessed to identify studies with sufficient quantitative information to enable the calculation of standardized effect estimates (for example, the change in pollutant to which the estimate

relates is not always given, some results are quoted as correlation coefficients and, in other cases, only the statistical significance of the result is given). Studies that did not provide sufficient information or contained key weaknesses were retained in the Reference Manager databases but coded appropriately. The minimum quality criteria for time series studies were: 1) minimum time period of 1 year; 2) some method of seasonal adjustment; 3) some adjustment for temperature and 4) analyses of specific cohorts were excluded. No panel studies were excluded from the database.

The time series and panel studies were sifted to remove duplicates and to categorise the studies. For each study design the resulting Reference Manager databases contain only valid (i.e. providing sufficient data), rejected or related studies (i.e. abstracts of studies that were not time-series studies but not obviously other study designs either). Keywords in the reference manager records detail the status of the papers following this process.

Step 2 - Extraction of data

Each 'valid' paper was then read in detail and the appropriate data recorded on data extraction forms. From these forms the data were entered into the Access databases. The forms served as a record of what data were extracted and a place to record essential information that was used in the standardization of the data. Each form is divided into two parts, study information and estimate information. Study information includes the Reference Manager id number, title, authors and full reference of the study. Estimate information includes details about the health outcome and pollutant being studied plus other data items required to standardize the effect estimates.

Step 3 - Data entry and standardization

Each APED Access database comprises a series of tables that hold the relevant data, together with a series of Visual Basic programs that manage and manipulate the data so that effect estimates standardized to 10μg/m^3 can be calculated. Access forms control the data entry process.

CATEGORIZATION OF OUTCOME, AGE AND POLLUTION

The published time series literature does not observe conventions for reporting results, which leads to a great variety of categorization of outcomes and age groups. In order to have a consistent approach to the classification of these outcomes for meta-analysis we assigned outcomes to outcome categories. We first listed all the outcomes (diagnoses, ICD codes, symptoms), age-groups and pollutants as reported in the studies and entered into the database. We then assigned each outcome/disease/age group to a smaller number of outcome and diagnostic categories based on a consideration of clinical coherence and numbers of estimates. This process was informed by a frequency distribution by age and diagnosis obtained from a dataset of daily mortality and hospital admissions for the West Midlands conurbation.

The panel outcomes considered in this review were lung function, respiratory symptoms and medication for respiratory problems. Lung function measures were Peak Expiratory Flow (PEF), Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 second (FEV_1). Symptoms were categorized as Lower Respiratory Symptoms (LRS) and Upper Respiratory Symptoms (URS). LRS were sub-classified into those in which there was mention of breathlessness, wheezing, asthma or other breathing discomfort (generically termed "dyspnoea")(LRS-D), and other respiratory symptoms, such as cough or phlegm (LRS-O). In the event, there were sufficient studies for meta-analysis only of LRS-O. Other lung function measures, such as ΔPEFR or FEV_1/FVC, were not available in sufficient numbers to meta-analyze.

The pollutant variables could generally be analysed as reported in the papers. However, in some cases less conventional size ranges (e.g. PM_{13}) or averaging times (e.g. 6 hr ozone) were encountered and these were absorbed into the main categories, which were as follows: PM_{10}, $PM_{2.5}$, $PM_{2.5-10}$, black smoke, sulphate , TSP(all particulate measures were 24 hr average), nitrogen dioxide (1 hr, 24 hr), ozone (1 hr, 8 hr, 24 hr), sulphur dioxide (24 hr) and carbon monoxide (1 hr, 8 hr, 24 hr).

ANALYSIS

Lag selection

It is common for time series studies to investigate the effects of pollution measured on the same day, or days prior to, the health event occurring. Studies vary in their selection of 'lags' analysed and presented. Hence the lag selected for this analysis was based upon the following algorithm: if only one lag estimate was presented (either because only one lag was examined or only one was presented in the paper) this was recorded as the author-selected lag. If estimates for more than one lag were presented, we chose the estimate mentioned by the author in the abstract or emphasized in the presentation of the results or discussion. If the author did not indicate a preference, or an a priori basis for choice of estimate, we chose one based firstly on the smallest p value, and then on the size of the estimate, irrespective of direction. We adopted this policy because most papers explicitly or implicitly select the most significant or sometimes largest association. However to avoid introducing additional bias we applied these criteria irrespective of the direction of the association.

In panel studies there is less variation in the lags analysed and/or presented. For consistency with time series studies the following selection criteria were followed where possible: where a choice of estimates was possible for lung function measurements, morning result and pollutant lagged 1 day was selected, followed by evening lag 1. Morning lag 0 was excluded, unless it was all that was reported. Symptoms were grouped into upper respiratory, lower respiratory (not dyspnoea - e.g. cough) and lower respiratory (dyspnoea – e.g. wheezing). Within each of these categories, the most significant estimate was selected where there was a choice. This meant that these meta-analyses were based on a varied mixture of cough, phlegm, wheeze and other lower respiratory symptoms, depending on which was most significant. For medication use (generally bronchodilator) lag 1 was also chosen. Symptom and medication use incidence was analysed separately from prevalence.

City selection

It is common in time series studies for the same cities to be studied more than once, either using different or overlapping time periods or even using the same time periods but employing different statistical techniques. Therefore, it was necessary to decide whether or not to use all estimates irrespective of the city/time period studied or to select just one estimate per city for analysis. We decided, for the main analysis, to select one estimate per city in order not to overweight a meta-analysis with more than one estimate from a city.

This policy required a systematic approach to the selection of estimates when two or more estimates were available from a single city. In selecting the estimate we gave priority to one from a planned multicity study because this might be less prone to publication bias and more likely to have benefited from a protocol-driven approach to analysis. Otherwise, we chose the most recent estimate on the assumption that this was more likely to have employed more advanced statistical techniques and to have used the most recently available data. The selection policy was not influenced by the direction, size or statistical significance of the chosen effect estimates.

The position for panel studies was somewhat different. Since panel studies use groups of individuals we allowed estimates from several panels from the same city so long as they were independent. Panels of subjects with chronic respiratory symptoms, clinical asthma or chronic obstructive pulmonary disease were categorized as "symptomatic". Those based on the general population (e.g. unselected samples of school children) as "unselected".

Where possible, estimates from the individual cities of multicity time series and panel studies were coded in APED. Hence, their estimates could be treated as individual city specific estimates. However, many multicity (time series and panel) studies did not report city specific estimates in a numerical format suitable for inclusion in a quantitative analysis, preferring to report their findings as summary estimates only or in graphical format. Summary estimates from all multicity studies (2 or more cities) are presented but not subjected to meta-analysis.

Estimation of summary effects and heterogeneity

The "meta" command as implemented in Stata Version. 9 (STB-38: sbe16; STB-42: sbe16.1: Stephen Sharp, London School of Hygiene and Tropical Medicine, UK and Jonathan Sterne, United Medical and Dental Schools, UK) was used to calculate summary fixed and random effects estimates and to estimate the

heterogeneity between effect estimates. Forest plots of individual estimates were produced using the graphics facilities in Stata.

Analysis of publication bias

Publication bias may manifest itself as an association between effect size and study precision. The funnel plot is a simple scatter plot of study effect against study precision (Sterne & Egger 2001). Estimates from smaller studies tend to be scattered more widely than those of larger studies due their relatively greater random variation. In the absence of bias the plot resembles an inverted symmetrical funnel. An asymmetrical funnel plot suggests that there is an excess of small studies with estimates biased in a particular direction. Publication bias is a common reason for such a pattern, though there may be other explanations. In our presentation of funnel plots we have used the inverse of the variance rather than the standard error as a measure of precision since this increases the visual contrast between studies of higher and lower power.

The funnel plot is assessed subjectively. Two statistical tests were employed to help assess objectively the evidence for asymmetry in the plots. Egger's linear regression test regresses the standardized effect estimate against the inverse of the standard error (Egger et al. 1997). A non-zero intercept provides evidence that the funnel plot is asymmetric. Begg's test is an adjusted rank correlation method to examine the association between the study estimates and their variances (Begg & Mazumdar 1994). Sterne et al have shown that in circumstances where there are reasonable numbers of studies in the meta-analysis, including a number of large studies, the Begg's test can be too conservative. We have therefore tended towards the Egger test of asymmetry when the p values for the two tests differed considerably. We employed the trim-and-fill method to adjust the summary estimate for bias (Duval & Tweedie 2000). This method removes small studies until symmetry in the funnel plot is achieved - recalculating the centre of the funnel before the "removed" studies are replaced together with their "missing" mirror-image counterparts. A revised summary estimate is then calculated using all of the original studies, together with the hypothetical "filled" studies. This method provides an indication of the possible impact of publication bias upon the size and precision of the summary effect estimates. We applied this adjustment irrespective of whether there was evidence of bias from the Begg or Egger test.

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Appendix 2 Project management

To manage and deliver the project objectives and outcomes a project management group oversaw and monitored the progress of the research. The project management group was made up from the research partnership members and associated parties.

Project Management Group:

Project Manager:	Nigel Jenkins	Sussex Air Quality Partnership
Lead Researcher:	Dr Heather Walton	King's College London

Project management group members:

Dr Matt Kearney	Department of Health
Dr Gary Fuller	King's College London
Simon Ballard	Sussex Air Quality Partnership/Chichester District Council

Invited group members:

Paul Clift	airTEXT London and Chair of Air Pollution Research in London (APRIL) – Health
Dr Kirsty Smallbone	University of Brighton
Sheila O'Sullivan	East Sussex Downs and Weald PCT/ Rother and Hastings PCT
Dr Angela Iverson	Surrey and Sussex HPU