Long-term Exposure to Air Pollution and Chronic Bronchitis

A report by the Committee on the Medical Effects of Air Pollutants

Chairman: Professor Frank Kelly

Chairman of QUARK Subgroup on Chronic Bronchitis:
Professor Peter Burney

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Foreword

In this report we evaluate the epidemiological evidence linking long-term exposure to ambient air pollution and chronic respiratory morbidity with the aim of calculating the likely number of people affected in the UK. To undertake this task we established a working group to review the substantial body of literature available. To avoid double counting of effects in quantification, the working group focused on chronic bronchitis and assessed the non-lethal effects of long-term exposure to air pollution on the lung in terms of symptoms, ie cough and phlegm.

I am extremely grateful to the working group members and the secretariat who, led by Professor Peter Burney, performed this detailed work and produced several draft reports for COMEAP to consider. Having completed this task, the working group concluded that the evidence of an association between chronic bronchitis and long-term exposure to air pollution was inconsistent and therefore not sufficient to infer a causal relationship in the UK today.

Although concluding that the evidence base is not sufficiently robust to link long-term exposure to ambient air pollution and chronic respiratory morbidity, the working group was able to estimate that for up to 18% of those individuals reporting chronic phlegm in 2010, the symptom was possibly due to ambient air pollution exposure. Further, it was of interest to see that some longitudinal studies reviewed in this report observed a change in symptoms following a reduction in levels of particulate pollution, potentially reflecting both remission of symptoms and a reduction in new cases of the disease.

Ambient air pollution is increasingly being linked to a range of human conditions. However, as highlighted in this report, important gaps in our knowledge remain and uncertainties exist. In the case of chronic bronchitis, which affected nearly 4.5 million individuals in the UK in 2010, more detailed and well-controlled epidemiological studies are required.

Professor Frank Kelly
Chair of the Committee on the Medical Effects of Air Pollutants

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Contents

Executive Summary

The Committee on the Medical Effects of Air Pollutants (COMEAP) was asked to consider the evidence linking long-term exposure to ambient air pollution and chronic obstructive pulmonary disease (COPD) and to advise on the likely number of people affected in the UK. Members of the subgroup on the Quantification of Air Pollution Risks (QUARK) reviewed the epidemiological evidence on the topic and prepared this report, which has been endorsed by COMEAP.

COPD is a term that refers to a group of lung diseases including chronic bronchitis, chronic airway obstruction and emphysema. The condition is characterised by airflow obstruction and persistent cough and phlegm. Confirmation of COPD is achieved using measurements of lung function. COPD is the third leading cause of death worldwide and, in the UK, 3 million people are estimated to have the disease. Each year COPD accounts for 30,000 deaths in the UK, representing 23% of all respiratory deaths, and it also results in 130,000 emergency admissions to hospital. Tobacco smoking is the major cause of COPD worldwide.

In deciding which aspects of COPD to put into the assessment, COMEAP has taken into consideration an understanding of the disease and the availability of robust data on which to assess effect sizes and the need not to count effects twice. Although a case can be made for focusing on measures of lung function based on their objective measurement and close association with mortality (from both respiratory and non-respiratory causes, even in lifelong non-smokers), COMEAP has decided not to adopt this approach, principally on the grounds that the association of mortality (and of hospital admission in later stages of COPD) with air quality has already been taken into account by COMEAP (1998, 2009, 2010) based on a much more substantial body of evidence. Therefore using the prevalence of low lung function as an additional 'cost' would be to count the same effect twice. However, COPD is often associated with symptoms of chronic bronchitis (chronic cough and phlegm production) and these are associated with disability, commonly assessed in surveys, and only loosely associated with lung function. COMEAP has therefore opted to assess the non-lethal effects of long-term exposure to air pollution on the lung in terms of the symptoms of chronic bronchitis (cough and phlegm).

The identification of chronic bronchitis was standardised in the first instance by the British Medical Research Council questionnaire (MRC, 1960), in which the condition is defined by the reporting of cough and phlegm on most days during at least three consecutive months for more than two years. The MRC's questions were later introduced (with some modifications) into other respiratory symptom questionnaires used in epidemiological studies reviewed in this report.

Chapter 2 of the report presents COMEAP's assessment of the relevant epidemiological evidence. We examined a number of cross-sectional and longitudinal studies published worldwide that investigated the relationship between long-term average concentrations of ambient air pollutants and chronic bronchitis/respiratory symptoms. The majority of the studies, especially

the more recent ones, focused on measures of exposure to particulate pollution. We identified some evidence of an association between the incidence or prevalence of chronic bronchitis (defined from reports of respiratory symptoms) and long-term exposure to particulate pollution. Further, some longitudinal studies reported changes in symptoms following a reduction in levels of pollution. These findings were identified in some well-conducted studies in Europe and the USA. However, the overall body of evidence of associations between chronic bronchitis and long-term exposure to air pollution was inconsistent. The inconsistencies in the evidence along with our other observations regarding the studies considered are discussed in Chapter 2 of the report.

We conclude that whilst there is some epidemiological evidence of an association between the incidence or prevalence of chronic bronchitis and long-term exposure to air pollution (mainly particulate matter measured as PM_{10})[1], overall, the evidence is not sufficient to infer a causal relationship in the UK today.

We do not recommend that an association between long-term exposure to ambient air pollution and chronic bronchitis is included in core health impact assessments (HIA) because the evidence considered does not sufficiently establish causality. We recommend instead that only sensitivity calculations are undertaken. These may be used to define a range of estimates of the size of the possible effect of long-term exposure to ambient air pollutants on chronic bronchitis in the UK, on the assumption that the relationship is a causal one. If the relationship is not causal, the best estimate is of no effect. Chapter 3 provides the results of our sensitivity calculations of the possible size of the effect of long-term exposure to particulate matter on chronic respiratory morbidity in the UK, along with the method and associated assumptions.

We recommend use of long-term average concentrations of particulate matter measured as PM_{10} in the sensitivity calculations. Further, quantification should be focused on the prevalence of chronic bronchitis rather than on the incidence of the condition. Some longitudinal studies reviewed in this report observed a change in symptoms following a reduction in levels of particulate pollution, potentially reflecting both remission of symptoms and a reduction in new cases of the disease, and the epidemiological evidence does allow calculations in terms of the incidence of chronic bronchitis to be undertaken. However these calculations are limited. First, problems remain with interpreting the seriousness of a disease 'case'. The studies do not distinguish between mild and severe cases. Second, the incidence of new cases needs to be offset against the rate of remission of other cases and the relation of each to air pollution. Both the assessment of incidence and the rate of remission are subject to error and it was felt that focusing on changes in the prevalence of chronic bronchitis was a simpler and more robust approach to quantification.

COMEAP addressed the following two questions on quantification in this report:

1. *Question on burden* (of current levels of anthropogenic PM_{10}): "What might be the number of cases of chronic bronchitis attributable to current levels of particulate pollution in the UK?"
2. *Question on impact* (of reducing anthropogenic PM_{10} concentrations by 1 $\mu g/m^3$): "What might be the change in the number of cases of chronic bronchitis as a result of reducing levels of particulate pollution in the UK?"

1 PM_{10} refers to the mass per cubic metre of particles of less than 10 μm (less than 10 millionths of a metre) diameter in the ambient air.

The sensitivity calculations produced answers to these questions at national (UK, England, Northern Ireland, Scotland and Wales) and regional levels. The inputs to the calculations are outlined below before a summary of estimated effects is provided.

For similar quantification exercises, we recommend use of a coefficient from the large cross-sectional study by Cai *et al* (2014) on chronic respiratory symptoms from the European Study of Cohorts for Air Pollution Effects (ESCAPE) project. We chose this particular study because it is based on European data (including from some studies reviewed in this report) and contemporary annual average PM_{10} concentrations. We used the coefficient from Cai *et al* (2014) for chronic phlegm in never-smokers: odds ratio (OR) 1.32 (95% confidence interval (CI) 1.02, 1.71) per 10 $\mu g/m^3$ increase in PM_{10}.

This risk estimate has the advantage of being statistically significant and very similar to the study's estimate (OR 1.35, 95% CI 0.97, 1.88, per 10 $\mu g/m^3$ increase in PM_{10}) for chronic bronchitis in never-smokers. We therefore focused our quantification of increased prevalence of chronic bronchitis in terms of the presence of chronic phlegm for at least three months of the year over at least two years.

Cai *et al* (2014) were unable to show the same proportional increase in chronic phlegm due to air pollution among smokers as they showed in non-smokers. We have therefore made the assumption that any increase among smokers would have been similar in absolute terms to the increase seen in non-smokers. We have done this by applying the same odds ratio (1.32) to the baseline prevalence of chronic phlegm in non-smokers (5% in England, Northern Ireland and Wales; 4.6% in Scotland) to the whole of the adult population aged 16 years and over. For this reason, the estimated effect on chronic phlegm attributable to PM_{10} and the baseline prevalence for chronic phlegm in never-smokers (≥16 years) will be applied to the whole population (≥16 years) regardless of smoking status. This is equivalent to assuming that exposure to air pollution causes the same absolute increase in symptoms among smokers and non-smokers rather than having a much larger (multiplicative) effect on symptoms among smokers.

Chapter 3 of the report discusses a number of other assumptions made during different stages of our quantification. In addition, we provide detailed discussion of the approach to quantification of effects when using an odds ratio and scaling on the log odds scale.

Our sensitivity calculations show that in 2010, over 722,000 cases of chronic phlegm in those aged 16 years and over could be attributable to anthropogenic PM_{10} concentrations in 2010 in the UK. This affects a little over 1% of the population. For comparison, the total number of people in the UK aged 16 years and over reporting chronic phlegm in 2010 was about 4,336,000. Our sensitivity analysis also shows that a 1 $\mu g/m^3$ reduction in anthropogenic PM_{10} concentrations in 2010 could lead to over 65,000 fewer cases of chronic phlegm. The table provides a breakdown of our estimates of the possible burden and impact of anthropogenic PM_{10} on the prevalence of chronic phlegm by regions and countries in the UK.

The evidence reviewed in this report does not provide a clear view about the likely severity and duration of the respiratory symptoms found to be associated with long-term exposure to ambient air pollution. The typical outcome definition – reported symptoms of cough and/or phlegm for more than three consecutive months of the year for two years – used in the epidemiological studies is imprecise and only provides a minimum indication of severity and duration. Clarity on the nature and duration of effects is important to ensure that impacts are correctly valued. Whilst the process of monetary valuation is outside the scope of this report, we have included some additional information in Chapter 3 to aid monetisation.

Estimated burden/impact of anthropogenic PM_{10} in 2010 on the prevalence of chronic phlegm in the UK in 2010 – results of sensitivity calculations

Country/region	Population weighted anthropo-genic PM_{10} ($\mu g/m^3$)	Baseline prevalence of chronic phlegm in never-smokers (%)[a]	Number/change in number of people (≥16 years of age) with symptoms		
			Total with chronic phlegm at baseline[b]	Chronic phlegm attributable to anthropo-genic PM_{10} (burden)	Benefit of a 1 $\mu g/m^3$ reduction in anthropo-genic PM_{10} (impact)
England[c]					
East of England	13.7	5.0	234,827	71,715	6,117
East Midlands	14.1	5.0	183,514	57,403	4,780
London	16.7	5.0	328,112	117,833	8,547
North East	11.4	5.0	104,092	27,198	2,711
North West	11.8	5.0	213,071	57,347	5,550
South East	12.7	5.0	344,517	98,717	8,974
South West	11.1	5.0	210,529	53,756	5,484
West Midlands	13.5	5.0	226,631	68,366	5,903
Yorkshire and the Humber	13.0	5.0	283,684	82,905	7,389
Northern Ireland	9.6	5.0	70,382	15,829	1,833
Scotland	9.3	4.6	195,552	42,901	5,115
Wales	10.0	5.0	123,065	28,690	3,206
All UK	12.7	4.9	2,517,977[d]	722,660[d]	65,609[d]

Notes

a Baseline prevalence (%) of chronic phlegm in never-smokers aged ≥16 years. Rates sourced from the 2010 Health Survey for England (HSE, 2011) and the 2010 Scottish Health Survey (Scottish Government, 2011). Baseline prevalence for England (5%) has been applied to all regions in England as analyses by St George's, University of London, indicate there is no statistically significant regional difference in the prevalence of chronic phlegm in never-smokers aged ≥16 years. There is little difference in the baseline prevalence between England and Scotland (5% vs 4.6%). On this basis, the baseline prevalence for England (5%) has also been applied to Northern Ireland and Wales.

b The total for chronic phlegm at baseline was estimated by applying the baseline prevalence in never-smokers to the whole population (≥16 years) regardless of smoking status.

c The total for chronic phlegm at baseline and the total burden/impact for England can be derived from the sum of the results for the regions of England.

d The total for chronic phlegm at baseline and the total burden/impact for the UK is the sum of the results for the regions/countries.

The calculations were done as a reduction from the baseline prevalence which includes the effects of air pollution.

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Chapter 1
Introduction

The purpose of this report is to assess the evidence linking long-term exposure to outdoor air pollutants with indices of morbidity relating to chronic respiratory morbidity, including chronic obstructive pulmonary disease (COPD). This is a longstanding condition characterised by a progressive and largely irreversible limitation to airflow, often with mucus hypersecretion and destruction of lung parenchyma. Before detailing the methods and findings of the hazard assessment, it is helpful to set the scene by providing a brief description of COPD and the evolution of the associated diagnostic labels, including chronic bronchitis.

Chronic respiratory morbidity is assessed in several different ways, and these identify overlapping conditions using different criteria. The understanding of this area is still based on the outcome of a symposium held in 1958 and published in 1959 (Fletcher *et al*, 1959). This distinguished four important conditions, among others: emphysema and three forms of non-specific lung disease – asthma, chronic bronchitis and irreversible obstructive lung disease. Emphysema was defined by histology and could not then be identified other than at post-mortem or, on rare occasions, if part of the lung had been removed and examined. This is still effectively true in epidemiological studies, though advances in radiology mean that individuals can be diagnosed more easily during their lifetime. Asthma (reversible airflow obstruction) and chronic (irreversible) airflow obstruction were identified by physiological tests, specifically by spirometry, and 'chronic bronchitis' by symptoms of chronic cough and phlegm. Later, the term COPD was applied to refer to the syndrome of irreversible airflow obstruction. Although COPD was originally defined physiologically, in practice, as few people have physiological tests, the term is used more widely and it is better to distinguish between chronic airflow obstruction (CAO) (a physiological abnormality) and COPD (a more heterogeneous group of conditions that include both chronic airway obstruction and chronic bronchitis).

Cigarette smoking is the major, worldwide, cause of CAO. The prevalence of the disease in the UK has declined as smoking has become less popular. Given that smoking involves inhalation of a mixture of gases and particles produced by the combustion of organic matter, it seems possible that exposure to air pollution, which contains rather similar toxicants albeit at much lower concentrations, might also be a cause of COPD. This inference is supported by studies of chronic bronchitis in urban areas of the UK during the 1950s and 1960s when an 'urban factor' that played a part in causing the disease was suggested. High concentrations of coal smoke containing high concentrations of particles and sulphur dioxide (SO_2) seemed an obvious candidate. How large a part was played by exposure to air pollutants was difficult to discover in a population in which cigarette smoking was widespread. Deciding how much of the reduction in COPD that has occurred in the UK in recent years is due to reductions in levels of air pollutants, as compared with the reduction in the prevalence of smoking, is also difficult.

Globally COPD is one of the most challenging public health problems. It is now the third leading cause of death worldwide, up from fourth in 1990 (Lozano *et al*, 2012). In the UK, 3 million people are estimated to have COPD, but only 900,000 have been diagnosed (NICE, 2010). Each year COPD accounts for 30,000 deaths, representing 23% of all respiratory deaths. COPD also results in 130,000 emergency admissions to hospital each year in the UK and, in 2008, the median length of stay was 5 days (interquartile range 3–10 days) (NICE, 2010). It has been estimated that COPD costs the UK healthcare system between £810 and £930 million, and an estimated 24 million working days are lost annually. The European Respiratory Society recently estimated the economic burden of lung disease across 28 member states of the European Union (ERS, 2013). COPD was estimated to cost the 28 EU countries 23.3 billion euros in direct costs[1], 25.1 billion euros in indirect costs[2] and 93 billion euros in the monetised value of disability-adjusted life-years (DALYs) lost, giving a total of 141.4 billion euros.

COMEAP is charged with providing the best data to enable assessment of the economic costs associated with air pollution in the UK. It has already provided evidence on the impact on all-cause mortality of long-term exposure to air pollution represented by fine particles (measured as $PM_{2.5}$ [3]) (COMEAP, 2009, 2010) and is now turning to the effects of air pollution on morbidity. In this report we assess the evidence that air pollution causes chronic respiratory morbidity (hazard), and provide a best estimate for the quantification of any effects (risk).

In deciding which aspects of COPD to put into the assessment, COMEAP has taken into consideration an understanding of the disease and the availability of robust data on which to assess effect sizes and the need not to count effects twice. Although a case can be made for focusing on measures of lung function based on their objective measurement and close association with mortality (from both respiratory and non-respiratory causes, even in lifelong non-smokers), COMEAP has decided not to adopt this approach, principally on the grounds that the association of mortality (and of hospital admission in the later stages of COPD) with air quality has already been taken into account by COMEAP (1998, 2009, 2010) based on a much more substantial body of evidence. Therefore using the prevalence of low lung function as an additional 'cost' would be to count the same effect twice. However, COPD is often associated with symptoms of chronic bronchitis (chronic cough and phlegm production) and these are associated with disability, commonly assessed in surveys, and only loosely associated with lung function. COMEAP has therefore opted to assess the non-lethal effects of long-term exposure to air pollution on the lung in terms of the symptoms of chronic bronchitis (cough and phlegm).

Chronic bronchitis has been defined as increased cough and phlegm, and is associated with asthma as well as with COPD. While it is not by itself associated with a substantially higher risk of death (Peto *et al*, 1983), it is associated with exacerbations of disease, incapacity and poor quality of life. The identification of chronic bronchitis was standardised in the first instance by the British Medical Research Council questionnaire (MRC, 1960; Holland *et al*, 1966) and subsequently the questions were introduced into other respiratory symptom questionnaires. In relation to the impact on health, the 2005 report of the cost-benefit analyses for the Clean Air for Europe

1 Primary care, hospital outpatient and inpatient care, drugs and oxygen.

2 Lost production including work absence and early retirement.

3 $PM_{2.5}$ refers to the mass per cubic metre of particles passing through the inlet of a size selective sampler with a transmission efficiency of 50% at an aerodynamic diameter of 2.5 μm; similarly, PM_{10} refers to the mass per cubic metre of particles of less than 10 μm diameter.

(CAFE) programme estimated (in monetary valuation) that chronic bronchitis was the next most important health outcome in relation to long-term exposure to air pollution second only to adult mortality (Hurley *et al*, 2005).

1.1 Scope of the report

Chronic bronchitis has long been associated with air pollution (Holland and Reid, 1965), though early reports relate to a time when the bulk of outdoor air pollution came from coal burning in domestic fires and when pollutant levels were very considerably higher.

This report reviews the epidemiological evidence linking long-term exposure to outdoor air pollution with chronic bronchitis. Although we have based our conclusions on the association with chronic bronchitis, we have also considered other related conditions. The review considers studies of long-term exposure to common ambient air pollutants: particulate matter (PM), nitrogen dioxide (NO_2), ozone (O_3) and sulphur dioxide (SO_2). Emphasis has been placed on pollutants and mixtures of greatest current relevance to the UK (ie traffic dominated rather than coal dominated). The report does not consider the toxicological evidence that might be used to identify the mechanisms by which air pollution might exert an effect.

The evidence will be used to determine whether long-term exposure to ambient air pollution is associated with chronic bronchitis and to assess the strength of evidence of a causal association. Subsequently it will be used to quantify the size of the effects identified.

The report is structured in two parts: the first part provides a hazard assessment (Chapter 2) and the second part addresses quantification (Chapter 3) of the effects identified in the hazard assessment.

1.2 Approach adopted

1.2.1 Assessment of 'hazard', 'burden' and 'impact'

'Hazard', 'burden' and 'impact' are all ways of assessing the consequences of air pollution on health. The *hazard* of a pollutant is its capacity to cause harm, including illness. The *burden of disease* due to the pollutant is the amount of the current disease that can be attributed to past and current exposure to the pollutant. These assessments need to make large assumptions about past exposures and about the persistence of effects of exposures at different ages. The *impact of policies on disease* is a measure of what would happen if levels of exposure to air pollutants were to be changed.

1.2.2 Incidence or prevalence of disease?

The incidence of disease is the number of new 'cases' of a disease, usually in a year, divided by the number of people at risk of getting the disease (usually this is simply the number of people who do not yet have the disease). The prevalence of disease at a particular time is the number of people with the disease as a proportion of the total population.

All other things being equal, prevalence will increase if incidence increases. However, prevalence will also depend on how quickly people with the disease are removed from this category either because they die or because they get better.

In looking at the causes of disease, measurements of incidence are generally preferred. This is because they measure the onset of new disease, whereas prevalence will also be influenced by factors that extend life but do not cure the disease. It would be perverse to suggest that an effective treatment that prolonged life was a 'cause' of disease, even if it increased its prevalence. For these reasons, if studies of suitable quality are available, hazard assessment generally relies upon studies of incidence.

If, on the other hand, we are looking at the 'burden of illness' attributable to a risk factor such as outdoor air pollution, we only need to know the net effect on prevalence and this is easier to measure and generally more precisely estimated as it depends on a single measurement.

The situation is more complicated when looking at the impact of a change in policy or of new policies. It is relatively simple to estimate the impact of a policy on disease prevalence directly, using evidence from cross-sectional studies. However, the impact of a policy on prevalence estimated in this way reflects composite effects on both incidence and persistence (or remission). These may be quite different in their time-course; separating them, if feasible, may give insights into *when* changes in prevalence may occur (following a policy change) that are not possible through estimates of prevalence directly. Also, for new policies, effects on prevalence in one location may not reflect the balance of incidence/persistence elsewhere, and this may affect both the transferability of relationships from cross-sectional studies and the estimation of impacts if the same policy were introduced in another setting. There are therefore some good reasons in principle to estimate the impact of a policy on incidence and on persistence/remission separately because these are direct estimates of how future events are affected. Doing so also allows different weights to be applied to these different outcomes.

In practice, implementation requires access to information that is accurate enough to be a reliable guide: there is a trade-off between the gains in principle from estimating incidence/persistence and the feasibility of achieving these gains in practice. Complicating factors include the reliability with which 'new cases' of the disease or condition can be identified, the availability of suitable studies of disease incidence to allow quantification (typically cross-sectional studies will be more numerous, being easier to perform), and the availability of suitable background rates of incidence and persistence/remission in the target population. A further advantage of relying upon measures of prevalence is that any misclassification of disease state at the beginning of the period of observation will bias the estimates of incidence and remission more than the estimate of the change in prevalence. We weighed general considerations such as these in assessing the evidence on chronic bronchitis specifically when developing a quantification approach for this report.

1.2.3 Literature search

A systematic literature search of PubMed (http://www.ncbi.nlm.nih.gov/pubmed) for papers published up to June 2012 was undertaken to support the assessment of the relationship between long-term exposure to common ambient air pollutants and chronic bronchitis. Details of the search procedures and criteria for inclusion of studies are provided in Appendix 1 to this report. Briefly, only epidemiological studies of samples of the general population which provided quantitative estimates of the association between chronic bronchitis (or chronic respiratory symptoms) and a measure of long-term exposure to outdoor air pollution, published in the English language, were included in the review. Relevant papers were identified using a two-stage process, with titles and abstracts of each citation scanned to remove irrelevant ones in the first

stage and full papers of possible citations reviewed at the second stage. Appendix 1 summarises all (48) relevant studies which form part of the review.

1.2.4 Disease definitions used

The identification of chronic bronchitis based on the MRC questionnaire (1960) is based on a positive answer to questions indicating the presence of cough and sputum on most days during at least three consecutive months for more than two successive years. In practice, many studies, though using similar questions, define chronic cough and phlegm using slightly different criteria. We have inevitably had to accept these alternative definitions when reviewing the literature and these will probably make relatively little difference providing that the same definitions are used consistently within a study. A few studies have reported on 'doctor-diagnosed' chronic bronchitis and it is far less likely that this relates closely to 'chronic bronchitis' as defined by the MRC questionnaire. The term has been used historically in a much broader sense to embrace chronic respiratory conditions and the attachment of the label to someone will depend to a great extent on current practice in the local health care system and on access to health care. We have therefore given less weight to studies of reported diagnoses.

1.2.5 Assessment of causality

Bradford Hill's (1965) characteristics of causal associations that can be judged from epidemiological evidence have been used to evaluate the causal nature of the epidemiological associations reported in the literature eligible for this review. These characteristics enabled the evidence to be graded according to the following categories, adopted from the 2010 American Thoracic Society (ATS) statement on novel risk factors and the global burden of COPD[1]:

a Evidence is **sufficient** to infer a causal relationship

b Evidence is **suggestive but not sufficient** to infer a causal relationship. There are two sub-categories:

- sufficient evidence of an association
- limited/suggestive evidence of an association

c Evidence is **inadequate** to infer the presence or absence of a causal relationship (which encompasses evidence that is sparse, of poor quality, or conflicting)

d Evidence is **suggestive of no causal relationship**

1 The ATS classification is based largely on the 2004 US Surgeon General's report on the health consequences of smoking (http://www.cdc.gov/tobacco/data_statistics/sgr/2004/complete_report/index.htm, accessed March 2016).

Chapter 2
Hazard assessment
Can exposure to ambient air pollutants cause chronic bronchitis?

There is literature on the association of high levels of air pollution with chronic bronchitis (chronic cough and phlegm) from an earlier period when the great majority of the air pollution came from coal fires. This includes Holland and Reid's study of postal workers in England which showed higher rates of cough and phlegm and lower lung function in individuals in London where pollution levels were much higher than in the three county towns examined (Holland and Reid, 1965). At that time the levels of ambient air pollution were very much higher than they are today and had a different composition. In 1979, Holland *et al* critiqued the evidence and concluded that there were few reliable studies to support the existence of a substantial effect of air pollution at the lower levels prevailing at the time (Holland *et al*, 1979). Since then study methods have become much more sensitive in their ability to detect effects and many larger and better designed studies have been conducted. We have reviewed the more recent studies, which are relatively few.

2.1 Appraisal of the evidence: cross-sectional studies

A total of 36 cross-sectional studies form part of this assessment: see Appendix 1 for a summary of each study. A subset of the more influential studies is discussed in the paragraphs that follow.

In the Adventist Health and Smog (AHSMOG) study COPD symptoms were defined as any of the following: (i) chronic cough and/or sputum production (chronic bronchitis); (ii) physician-diagnosed asthma and a history of wheezing; (iii) physician-diagnosed emphysema and having shortness of breath when walking whether normal paced or hurried (Euler *et al*, 1987, 1988; Hodgkin *et al*, 1984). The authors reported that total suspended particulate (TSP) exposure (750 hours/year above 200 $\mu g/m^3$) was the best single surrogate representing the mixture of pollutants measured. Total oxidant exposure was also associated with respiratory symptoms, as was SO_2, but NO_2 was not. Inevitably, because of the unique definition in both exposure and outcome, comparison of the findings with other studies would be difficult.

Galizia and Kinney (1999) studied the residential histories of Yale freshmen and assigned them to those who had lived at least four years in counties with an average O_3 summer level of more than 80 ppb (exposed) or others who had not (unexposed). After adjustment for a number of potential confounders they found that chronic phlegm was more common in the exposed, but not significantly so (odds ratio (OR) 1.79; 95% confidence interval (CI) 0.83, 3.82), and that a less specific 'respiratory symptoms index' was significantly associated with exposure (OR 2.00, 95% CI 1.15, 3.46).

Zemp *et al* (1999) analysed data from the Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA). They found no association between O_3 and respiratory symptoms, but they found significant associations between PM_{10} and both chronic phlegm production (OR 1.35, 95% CI 1.11, 1.65) and chronic cough or phlegm (OR 1.27, 95% CI 1.08, 1.50) in never-smokers.

Sekine *et al* (2004) analysed cross-sectional data on respiratory symptoms and air pollution in Japan. In 1987, 5,682 women (30 to 59 years of age) were recruited from nine districts in the Tokyo metropolitan area. Symptoms were assessed by a questionnaire and included 'persistent cough', 'persistent phlegm' (cough or phlegm almost every day for three or more months a year, respectively) and breathlessness (breathing difficulty in walking *[on]* a flat road and not catching up with people of the same generation). The nine districts were classified into three groups, based on NO_2 (measured between 1990 and 1994) and suspended particulate matter (SPM, between 1987 and 1994) levels, with group 1 being the most polluted (mean NO_2 47–56 ppb, mean SPM 48–62 $\mu g/m^3$), group 2 being moderate (mean NO_2 38–46 ppb, mean TSP 38–46 $\mu g/m^3$) and group 3 being the least polluted (mean NO_2 24–36 ppb, mean TSP 28–39 $\mu g/m^3$). The prevalence of both persistent phlegm and breathlessness were significantly associated with the area of residence, with a significant concentration-response relationship. Compared with the least polluted group 3 districts, those living in group 1 districts had an OR of 1.78 (95% CI 1.26, 2.53) for persistent phlegm and 2.70 (95% CI 1.48, 4.91) for breathlessness.

Heinrich *et al* (2005) published a paper based on the nationwide German Health Survey 1998, which included data on respiratory health from 6,896 subjects aged 18 to 79 years collected between 1997 and 1999. Exposure was assessed by means of a questionnaire, which inquired whether the residential address was located at an extremely busy road or considerably busy side street (high traffic intensity), not busy side street (moderate) or on a street with no or very rare traffic (low). Adjusting for confounders, those subjects reporting high traffic intensity had an OR for ever having chronic bronchitis of 1.36 (95% CI 1.01, 1.83) compared with the low intensity reference group.

Schikowski *et al* (2005) reported on the Study on the Influence of Air Pollution on Lung Function, Inflammation and Aging (SALIA) that investigated both chronic bronchitis by physician diagnosis and chronic respiratory symptoms of 'chronic cough with phlegm production' and 'frequent cough' assessed by means of a questionnaire. The definition of the former was essentially equivalent to that of chronic bronchitis. In brief, an interquartile range (IQR) (16 $\mu g/m^3$) increase in five-year mean NO_2 was associated with a significant increase in the OR for chronic bronchitis according to a doctor's diagnosis (1.37, 95% CI 1.16, 1.62). A weaker association was observed in frequent cough with marginal statistical significance (OR 1.15, 95% CI 0.99, 1.33). There was no association between NO_2 and chronic cough with phlegm production, or between PM_{10} and any of the outcomes.

Sunyer *et al* (2006) reported cross-sectional data from the European Community Respiratory Health Survey (ECRHS) on the relation of chronic productive cough and other symptoms to outdoor NO_2 and $PM_{2.5}$ in 21 European sites. There was no association between the prevalence of chronic phlegm and levels of $PM_{2.5}$ (men: OR per $\mu g/m^3$ of 0.97, 95% CI 0.70, 1.35; women: OR per $\mu g/m^3$ of 0.99, 95% CI 0.85, 1.17) or levels of NO_2 (men: OR per 30 $\mu g/m^3$ of 0.95, 95% CI 0.44, 2.03; women: OR per 30 $\mu g/m^3$ of 1.22, 95% CI 0.56, 2.66).

Using the same questionnaire and including some of the same subjects, Orru *et al* (2009) reported on a much larger sample of participants in Tartu, Estonia. The modelled PM from exhaust was on a 40 m × 40 m grid and the authors reported an OR for chronic bronchitis per 1 $\mu g/m^3$ of PM (exhaust) exposure of 0.78 (95% CI 0.53, 11.44).

In a study that combined participants in the Melbourne ECRHS study (not included in the paper by Sunyer *et al*) with another cohort from Melbourne, Bennett *et al* (2007) reported a significant and protective cross-sectional association between $PM_{2.5}$ (per 1 μg/m³) and cough with phlegm in the morning of OR 0.28 (95% CI 0.08, 0.97).

Schwartz (1993) analysed data on doctor-diagnosed chronic bronchitis among 6,138 adults aged 30–74 years and recruited to the first US National Health and Examination Survey (NHANES I) in 1971–75. He found an OR of 1.07 (95% CI 1.02, 1.12) per 10 μg/m³ increase in annual TSP and of 1.11 (95% CI 1.02, 1.21) in people who had never smoked.

Scarlett *et al* (1995) found a linear increase in cough when transformed on to a logarithmic scale that was not statistically significant ($p = 0.10$) and a similar relation with phlegm that was significant ($p = 0.04$) with increasing levels of Black Smoke[1] in an analysis of 11,552 participants in the 1958 British Birth Cohort when they were aged 23 years in 1981. They found no association with SO_2.

Solomon *et al* (2003) undertook a cross-sectional analysis of 1,166 women living in 11 electoral wards in the UK. They defined a low exposure to Black Smoke as an exposure less than 50 μg/m³ and a high exposure as more than 120 μg/m³. They found no association between the exposure to Black Smoke and reports of a productive cough (relative risk (RR) of 1.0, 95% CI 0.7, 1.5).

Bentayeb *et al* (2010) examined 2,104 participants over the age of 64 years living in Bordeaux, Dijon and Montpelier (ie the 3C *[3 Cities]* study). They noted no association between usual cough and either PM_{10} (OR per μg/m³ of 1.01, 95% CI 0.96, 1.06) or NO_2 (OR per μg/m³ of 1.01, 95% CI 0.99, 1.04) but a significant increase with SO_2 (OR per μg/m³ of 1.23, 95% CI 1.11, 1.36). Similarly, they found no association between usual phlegm and NO_2 (OR per μg/m³ of 1.01, 95% CI 0.98, 1.04), but a positive association with SO_2 (OR per μg/m³ of 1.24, 95% CI 1.10, 1.39).

Nachman and Parker (2012) analysed data from 109,485 adults responding to the American National Health Interview Survey (NHIS) using responses to a question on doctor/health professional diagnosis of chronic bronchitis in the past 12 months and modelled data on exposure to $PM_{2.5}$. They reported an OR of 1.08 (95% CI 0.94, 1.24) adjusted for sex, age, smoking, urbanicity, health insurance, education, income, body mass index and exercise.

A Swedish study by Lindgren *et al* (2009) analysed data from 9,319 subjects aged 18 to 77 years from the county of Scania in 2000. Self-reported and geographical information system (GIS) derived traffic intensity, as well as modelled nitrogen oxides (NO_X) data, based on the year 2001 were obtained. COPD was defined as any self-reported physician-diagnosed COPD, chronic bronchitis or emphysema. Self-reported heavy traffic was significantly associated with COPD (adjusted OR 1.36, 95% CI 1.10, 1.67). Living within 100 m from a regional main road carrying 6–10 cars/min or more than 10 cars/min was also associated with a higher COPD risk, compared with those whose residence was only close to local roads (OR 1.57, 95% CI 1.15, 2.14, and OR 1.64, 95% CI 1.11, 2.41, respectively). There was a statistically significant trend in prevalence of COPD diagnosis with escalating NO_X levels, with the OR being 1.43 (95% CI 1.04, 1.95) for the highest category (>19 μg/m³) compared with the lowest (0–8 μg/m³). Chronic bronchitis symptoms followed similarly with a comparable magnitude of risk estimates: an OR for 6–10 cars/min of 1.24 (95% CI 0.93, 1.65); and an OR for more than 10 cars/min of 1.53

1 Black Smoke: non-reflective (dark) particulate matter, measured by the smoke stain method.

(95% CI 1.10, 2.13). Self-reported heavy traffic was not significantly associated with chronic bronchitis symptoms (adjusted OR 1.11, 95% CI 0.94, 1.31).

Cesaroni *et al* (2008) collected data from 9,488 adults aged 25–59 years living in Rome and compared self-reports of ever having had chronic bronchitis or emphysema with exposure to traffic and also to estimated particulate emissions and estimates of NO_2 levels derived from land use regression. None of these associations was significant and most were very close to one or less than one. The OR for the association with the highest quartile of NO_2 (50.3–62.6 $\mu g/m^3$) was 0.97 (95% CI 0.71, 1.31), and for the highest quartile of PM emissions was 1.05 (95% CI 0.77, 1.42).

There are in addition to these studies a number of studies that have not measured pollution levels directly but have looked at associations with traffic levels. These do not provide any data that could be used to assess a quantitative relation suitable for setting standards or concentration-response relationships, but they do provide some evidence relating to a possible hazard arising from traffic pollution. Oosterlee *et al* (1996), studying adults and children living in Haarlem, Netherlands, noted less chronic cough (OR 0.9, 95% CI 0.5, 1.4) and chronic cough with phlegm (OR 0.8, 95% CI 0.5, 1.4) in those living in busy streets. Heinrich *et al* (2005), described earlier, reported an increased prevalence of chronic bronchitis in those exposed to high volumes of traffic among participants in the 1998 German Health Survey (OR 1.36, 95% CI 1.01, 1.83). Karita *et al* (2004) found that reported frequent cough or phlegm was more common in Bangkok policemen who worked in more polluted areas (OR 1.27, 95% CI 1.01, 1.61) but not among those living in more polluted areas (OR 0.88, 95% CI 0.64, 1.20), but it was more common among the wives of policemen living in the more polluted areas (OR 1.53, 95% CI 1.10, 2.13). Garshick *et al* (2003) studied 5,654 male veterans living in Massachusetts and did not find any statistically significant link between residence less than 50 yards from a highway and cough or phlegm. Nuvolone *et al* (2011) found no association between COPD (reported diagnosis of emphysema or chronic bronchitis) and distance from roads in a study in Pisa and Cascina in northern Italy. Hazenkamp-von Arx *et al* (2011) reported increased levels of chronic cough (OR 2.88, 95% CI 1.17, 7.05) and chronic cough or phlegm (OR 2.40, 95% CI 1.01, 5.70) using questions similar to those used by the MRC questionnaire to define chronic bronchitis. Finally, Gundersen *et al* (2012) found a large excess of cough and phlegm associated with moderate and high levels of exposure to traffic among women, which was particularly marked among smokers and not found among men.

2.2 Summary of cross-sectional studies

Overall, there is relatively little recent information, even from cross-sectional studies, supporting a relationship or association between current levels of air pollution and symptoms of chronic bronchitis.

The results depend on slightly different definitions, but even given that drawback, the findings are inconsistent. There were clear associations between particle levels and symptoms compatible with chronic bronchitis in the AHSMOG study, NHANES I, SAPALDIA, Japanese study and, to some extent, the 1958 British Birth Cohort, but none in the German SALIA study, the French 3C study or the NHIS. The German Health Survey demonstrated a link with traffic intensity, but the Swedish Scania study did not.

Oxides of nitrogen (measured in different ways) were associated with symptoms in the Scania study and the SAPALDIA study and with a doctor's diagnosis of chronic bronchitis, but not with symptoms of chronic cough and phlegm in the SALIA study. No association between NO_2 and

symptoms of chronic bronchitis was reported in the AHSMOG study or with either usual cough or usual phlegm among elderly French participants in the 3C study, or in the ECRHS study, or with doctor-diagnosed bronchitis in the Italian study of Cesaroni *et al* (2008).

Cross-sectional studies of exposure to traffic and chronic bronchitis are similarly inconsistent in their results.

As already discussed, cross-sectional studies have limitations when assessing the risk of contracting a disease, and longitudinal studies are to be preferred.

2.3 Appraisal of the evidence: longitudinal studies

Although many epidemiological studies have been identified in the literature searches, the majority are cross-sectional in nature. The few available longitudinal assessments of cohorts of relevance will be familiar to many, and several had cross-sectional assessments which were discussed earlier in this report:

a AHSMOG: Adventist Health and Smog Study

b ECRHS: European Community Respiratory Health Survey

c SAPALDIA: Swiss Study on Air Pollution and Lung Disease in Adults

d SALIA: Study on the Influence of Air Pollution on Lung Function, Inflammation and Aging

e Melbourne Studies

f Sydney Road Tunnel Study

The majority of papers considered below are based on the AHSMOG cohort.

2.3.1 Series of papers from AHSMOG

The studies on the Californian Seventh Day Adventists cohort have made a major contribution to understanding the effect on health of long-term exposure to ambient air pollutants. The work focuses on subgroups drawn from the National Cancer Institute funded Adventist Health Study. This study enrolled individuals from 36,805 Seventh Day Adventist households in California.

Using data from a respiratory symptoms questionnaire, participants were classified as having none, possible or definite symptoms for chronic bronchitis, asthma (doctor diagnosed with history of wheezing), emphysema (doctor diagnosed with shortness of breath as the key criterion) or any or all of the above, which was termed 'airway obstructive disease' (AOD). The questionnaire, administered in 1977 and 1987, was developed originally by the MRC (1960) and modified for use by the US National Heart, Lung and Blood Institute (NHLBI). The health endpoints and disease definitions used were:

a Incidence of AOD symptoms, ie having symptoms in 1987 but not in 1977

b Incidence of chronic bronchitis symptoms was defined as having definite symptoms for the respiratory complex in 1987 but not in 1977. To be classified as having 'definite' chronic bronchitis, individuals must have reported symptoms of cough and/or sputum production on most days, for at least three months a year for more than two years

The prevalence of symptoms, the incidence of new cases of disease and the occurrence of a worsening of symptoms have been studied with regard to estimated levels of air pollutants at the subjects' home locations. In some instances – for example, the study by Abbey and colleagues on the effects of NO_2 (Abbey *et al*, 1993) – information from a separate personal exposure study was used to adjust NO_2 concentrations to include indoor sources as well as ambient concentrations.

Current thinking on the effects of both short- and long-term exposure to air pollutants has led to the conclusion that, at a population level, no thresholds of effect can be identified. A major corollary of this conclusion is that setting air quality standards that provide a guarantee of complete protection from adverse effects on health is impossible. Although the association with mean pollutant levels was analysed, the main analytical approach adopted in the AHSMOG studies relates effects to the estimated total hours of exceedance of specified concentrations of pollutants. This presentation of results stems from an examination of the degree of public health protection provided by California Air Quality Board standards at that time. We note that the concentrations of pollutants examined in this study are much greater than the current concentrations found in the UK: see Appendix 2.

The AHSMOG analyses have several virtues:

a The subjects' lifestyles are well studied and much information is available regarding, for example, education status, occupational history, exact home location and hours of freeway driving each day

b In the air pollution studies, subjects are required to have lived for at least 10 years within 5 miles of their current residence at the time of the study

c High response rates to questionnaire studies have been consistently achieved with the subgroups studied

d Sufficient variation of pollutant levels exists in the areas studied to allow meaningful between-area comparisons of effects

e Several different pollutants were considered

However, we have also noted areas of concern relating to these analyses:

a The reported associations may reflect exposure to higher levels of ambient air pollutants

b The relation between AOD and chronic bronchitis is unknown/unclear. The endpoint (AOD) had been derived using questionnaire data on doctor-diagnosed disease which could be regarded as being unreliable

c All such studies are subject to biases in reporting both symptoms and potential confounders. In this case this could include cigarette smoking which is forbidden among Seventh Day Adventists and may therefore be under-reported. We note that in other AHSMOG analyses of lung cancer mortality, a strong positive association with O_3 in males for both past-smokers and never-smokers was found (Abbey *et al*, 1999). To test the possibility of the under-reporting of smoking, the authors performed sensitivity analyses assuming a 10-fold greater risk for current smokers and 50% under-reporting in the top quartile of air pollution exposure. If this had occurred, it was calculated that the true relative risks would be overestimated by no more than 15%

d Whether smoking is a confounder in the AHSMOG studies depends on whether the (unreported) smoking correlates with air pollutant levels. We think that any such correlation is likely to be low. Consideration of the possible under-reporting of smoking raises a different question: "What is the nature of chronic bronchitis/AOD symptoms in this largely non-smoking cohort, and can that relationship be generalised to more 'typical' populations where the majority of chronic bronchitis is smoking related?"

For our present purposes we are using the AHSMOG studies to discover whether long-term exposure to various pollutants could have an association with certain endpoints relating to respiratory disease: for this purpose the AHSMOG studies are very important. Our general conclusions from this series of studies are as follow.

There is a consistent increase in symptoms of AOD, chronic bronchitis and severity of disease associated with all measures of particulate pollution (~35% increase per 42 days TSP above 200 $\mu g/m^3$; ~17% increase per 42 days PM_{10} above 100 $\mu g/m^3$; ~50% increase per 45 $\mu g/m^3$ increase in annual average $PM_{2.5}$; and an RR of 1.81, 95% CI 0.98, 3.25, p = 0.058) per 45 $\mu g/m^3$ increase in annual average $PM_{2.5}$) (Abbey *et al*, 1995a,b).

No evidence was reported of a statistically significant association between any of the symptoms and O_3, NO_2, SO_2 or sulphate (SO_4).

2.3.2 ECRHS (Sunyer *et al*, 2006)

Using data from participants of ECRHS, Sunyer *et al* (2006) investigated the associations between the prevalence and new onset (ie prevalence at follow-up among the subjects without the symptoms at baseline) of chronic bronchitis and urban air pollution. Nearly 7,000 people from 21 centres in 10 European countries were identified in 1991–93 and followed 8.9 years later. Data on various risk factors were collected using questionnaires. Two definitions of chronic bronchitis were used:

a Productive chronic cough (chronic cough and chronic phlegm for more than three months each year)

b Chronic phlegm alone

Concentrations of $PM_{2.5}$ from centre-level (background) locations and NO_2 at home level (in 1,634 households) were recorded. $PM_{2.5}$ and sulphur content at centre-level did not show any association with prevalence or new onset of chronic phlegm. Constant traffic was significantly associated with chronic phlegm at follow-up among females (OR 1.86, 95% CI 1.24, 2.77). Similar results were obtained with chronic productive cough as the endpoint.

The authors also reported that, among females, home outdoor levels of NO_2 (regarded as a surrogate for traffic exposure) were associated with the prevalence and new onset of chronic phlegm: an OR of 2.71 for >50 $\mu g/m^3$ vs <20 $\mu g/m^3$ of NO_2 (95% CI 1.03, 7.16).

The authors noted that based on only two surveys, they could not know to what extent changes between the surveys were permanent or whether they represented temporary fluctuations in response to current conditions.

2.3.3 Melbourne Studies (Bennett *et al*, 2007)

The Australian study of Bennett *et al* (2007), already mentioned, also reported results from a longitudinal analysis. They estimated an odds ratio for cough and phlegm in the morning of 1.28 (95% CI 0.70, 2.33) per μg/m^3 of daily average $PM_{2.5}$ over the previous 12 months adjusted for age, sex, use of β_2 agonists and corticosteroids, and smoking.

2.3.4 SAPALDIA (Schindler *et al*, 2009)

Schindler *et al* (2009) investigated whether reductions in ambient concentrations of PM_{10} could be associated with reductions in respiratory symptoms in the SAPALDIA cohort. Data from 7,019 adults from eight areas in Switzerland were used. Participants who were 18–60 years of age at baseline in 1991 were examined again in 2002, with data on respiratory symptoms and a range of covariates obtained using the ECRHS questionnaire. Annual average estimates of home outdoor PM_{10} concentrations were assigned to each participant for every year of the follow-up using a validated dispersion model. The exposure measure used in the analyses was the difference between the estimated average PM_{10} level outside a subject's home(s) in the 12 months before the second assessment in 2002 and the corresponding mean level in the 12 months before the first visit. On average, home outdoor levels of PM_{10} decreased by 6.2 μg/m^3. Several health endpoints were investigated, including:

a Regular cough (regular phlegm) – defined by a positive response to at least one of the following questions: "Do you usually cough (bring up phlegm from your chest) first thing in the morning?" and "Do you usually cough (bring up phlegm from your chest) during the day or at night?"

b Chronic cough or phlegm – defined as chronic cough and/or chronic phlegm, with 'chronic' being defined by the presence of the respective symptoms during at least three months in a year for at least two years

The estimated adjusted odds ratios for the symptom reported in 2002 for a 10 μg/m^3 reduction in PM_{10} exposure between the two surveys are shown in Appendix 1. In the entire sample, decreased PM_{10} is associated with reduced odds of persistent reports of all symptoms investigated, with a statistically significant reduction in the odds for regular cough. Reduced odds of new reports of regular cough, regular phlegm and chronic cough or phlegm were also statistically significantly associated with reductions in PM_{10}. In a subgroup (ie persistent non-smokers), decreased PM_{10} was significantly associated with reduced odds of persistent reports of regular cough, with chronic cough or phlegm, and also with new reports of regular phlegm and chronic cough or phlegm.

The detailed characterisation of exposure using a validated model that showed good average agreement between modelled and measured PM_{10} values across and within study areas is a particular strength of this study. However, there is a strong negative correlation between absolute PM_{10} concentrations and change in PM_{10} levels over the period of the study, with the greatest reductions occurring in areas (and at addresses) with the highest initial concentrations. This makes the reported associations difficult to interpret. If air pollution exposure at the start of follow-up is the important determinant of chronic bronchitis, then results suggest that individuals exposed to higher concentrations were at a reduced risk of developing new symptoms or more likely to have their existing symptoms remit. On the other hand, if air pollution around the time of ascertainment of symptoms is more important, the results are consistent with a reduction in risk, with a reduction in hazard. Results were only presented in relation to change in PM_{10} levels, not

absolute PM_{10} levels, so direct information on this point is not available. No pollutants other than PM_{10} were examined, so the contribution of other pollutants is unknown.

2.3.5 SALIA (Schikowski *et al*, 2010)

The SALIA study also included a follow-up survey. This was a study of German women aged over 55 years of age living in the Ruhr area, initially studied in the years 1985–94 and subsequently followed up in 2006–09 (the mean age was greater than 70 years at follow-up). Five-year mean exposure levels were assessed for PM_{10} and NO_2. During this period the mean exposure to PM_{10} declined from 46.6 to 26.9 $\mu g/m^3$ and the five-year mean concentrations of NO_2 declined from 38.1 to 27.9 $\mu g/m^3$. Changes in exposure were linked to changes in both chronic cough and chronic cough and phlegm, not just the symptom reports at the final time point (stratified into new or persistent reports) as in the SAPALDIA study.

A decline in PM_{10} was significantly associated with a decline in both cough and cough and phlegm. A decline in NO_2 was associated with neither.

2.3.6 Sydney Road Tunnel study (Cowie *et al*, 2012)

Cowie *et al* (2012) have reported on the change in symptoms reported when a road scheme in Sydney diverted traffic through a road tunnel. The scheme halved the exposure to traffic pollution in one area but led to no reduction in symptoms. On the other hand, symptoms increased around the vents from the tunnel even though measured air pollution levels remained essentially the same.

2.4 Summary of longitudinal studies

The longitudinal studies on balance are suggestive of (support) an association between particulate air pollution and chronic bronchitis, though the evidence is not overwhelming. The early AHSMOG study gave a clear and positive (statistically significant) answer above a certain threshold for particles, with less clear results (ie positive but not/borderline statistically significant) for the analyses using a continuous measure of particle concentrations, in a population that was largely free of the confounding effects of cigarette smoking. The study, however, belongs to an earlier period with a high level of exposure to ambient air pollutants and studied a subgroup of the general population in whom the pattern of chronic bronchitis was probably different (due to the low prevalence of smoking).

More recent studies from Europe have been in general supportive of a relationship between chronic respiratory symptoms and air pollution. Both SAPALDIA in Switzerland and SALIA in Germany have shown positive associations between reductions in particulate pollution and reductions in chronic bronchitis (as respiratory symptoms *[chronic cough and/or chronic phlegm]* that classically define the condition). On the other hand, neither ECRHS nor the Australian study by Bennett *et al* (2007) have shown clear, positive associations with particulate pollution, though ECRHS showed an association with traffic and the other analyses were probably too small to show any effect. The study by Cowie *et al* (2012) failed to show any change in symptoms in spite of a marked reduction in exposure to traffic-related pollutants. The observed decline in NO_2 in SALIA was associated (but only marginally) with attenuation in the prevalence of respiratory symptoms in the population of elderly women. Among females in ECRHS, home outdoor NO_2 was associated with the prevalence and new onset of chronic phlegm and chronic productive cough.

2.5 Additional publications

Since our assessment of the epidemiological evidence published up to June 2012, results for the relationship between long-term average concentrations of ambient air pollutants and chronic respiratory symptoms from the European Study of Cohorts for Air Pollution Effects (ESCAPE) project have been published (Cai *et al*, 2014). We provide below a summary of this study's results before presenting our overall assessment of the evidence considered in this report.

The large, cross-sectional ESCAPE study used data from five cohorts (Asthma-E3N, ECRHS, NSHD[1], SALIA and SAPALDIA) from nine European countries, including data from studies considered in this report, to investigate associations between air pollution and the prevalence of respiratory symptoms. Following a measurement campaign in 2008–11, land use regression models were used to derive annual average concentrations for a range of traffic-related air pollutants at participants' home addresses at the time questionnaires were administered within each cohort. Because the ECRHS and SAPALDIA cohorts predated the 2008–11 measurement campaign, back-extrapolation was used to estimate long-term average concentrations of NO_2 and PM_{10} for 1998–2002 and 2002, respectively. In addition to these measures of exposure, indicators of local traffic (intensity and loads) were also derived. Respiratory symptoms were assessed using questionnaires that included the MRC questions defining chronic bronchitis:

a Chronic bronchitis (cough and phlegm production first thing in the morning and/or during the day or at night for three months of the year for two or more years)

b Chronic cough (reported cough for three months of the year for two or more years regardless of reported phlegm or not)

c Chronic phlegm (reported phlegm for three months of the year for two or more years regardless of reported cough or not)

The SALIA cohort did not provide data in a form which allowed chronic phlegm (alone) to be determined.

A total of 15,279 (for NO_2) and 10,537 (for PM_{10}) participants were included in the main analyses for 1998–2011 (the most recent assessment period in each cohort). The mean age of participants ranged from 42.9 years in ECRHS to 71.5 years in SALIA. In the full population, there was no evidence of a statistically significant association between any air pollutant or indicator of exposure to traffic and the health outcomes examined. However, in never-smokers positive and statistically significant associations were identified with chronic phlegm: OR 1.32 (95% CI 1.02, 1.71) and OR 1.31 (95% CI 1.05, 1.64) for PM_{10} (per 10 $\mu g/m^3$ increase) and $PM_{10-2.5}$ (per 5 $\mu g/m^3$ increase), respectively. Although cohort-specific estimates to derive the combined effect for chronic phlegm and PM_{10} varied (ranging from an OR of 0.62 for SAPALDIA to an OR of 2.34 in the NSHD) this was no more than would be expected by chance ($I^2 = 0\%$). The greatest weight in the pooling was applied to the estimate from ECRHS. The estimate for chronic bronchitis and PM_{10} in never-smokers was similar (OR 1.35, 95% CI 0.97, 1.88) to that for chronic phlegm, though not statistically significant. All other associations with respiratory symptoms in never-smokers were positive but not statistically significant, including for $PM_{2.5}$ or $PM_{2.5}$ absorbance.

1 NSHD: National Survey of Health and Development.

Overall, this study provides limited evidence of a relationship between the current long-term average concentrations of ambient air pollutants and chronic respiratory symptoms in Europe.

2.6 Overall summary of the evidence

We note that the majority of the available studies, especially the more recent ones, have focused on measures of exposure to particulate pollution. Many studies have not examined the full range of ambient air pollutants and some studies considered only one pollutant. This limits the conclusions that could be drawn regarding the possible relationship between long-term exposure to ambient air pollutants and chronic bronchitis. Whilst our conclusions focus mainly on particulate matter, this does not imply the absence of an association between chronic bronchitis and other outdoor air pollutants. We are not, at present, able to comment on any possible associations relating to O_3 and SO_2 as the numbers of studies of these pollutants are insufficient. We have extended our conclusions to exposure to ambient NO_2 and to the mixture of traffic-related pollutants as these have also been examined in a number of studies reviewed in this report.

There are sufficient high quality studies showing an association between particulate air pollution and the incidence or prevalence of chronic bronchitis (chronic cough and/or phlegm). The strongest epidemiological evidence of an association comes from the Seventh Day Adventist (AHSMOG) studies in California based on data from the 1970s and 1980s, when ambient concentrations of air pollutants were higher than those experienced today by the UK population.

More recent data from Europe have provided less certain evidence of an association between the incidence or prevalence of chronic bronchitis and long-term exposure to ambient air pollution. Longitudinal studies from Switzerland and Germany support the presence of an association between reductions in particles (measured as PM_{10}) and reductions in chronic bronchitis (with disease definitions similar to that of the MRC questionnaire). However, it is difficult to interpret the findings from SAPALDIA: there is a strong negative correlation between absolute PM_{10} concentrations and change in PM_{10} levels over the period studied, with the greatest reductions occurring in areas (and at addresses) with the highest concentrations. This suggests that individuals exposed to higher concentrations were at a reduced risk of developing new symptoms or more likely to have remission of their existing symptoms. Additional data from ECRHS, another large longitudinal study, show no convincing association with particles (measured as $PM_{2.5}$), though they do show an association between the prevalence and onset of chronic phlegm and chronic productive cough and exposure to traffic and NO_2.

Although some of the longitudinal studies report separately on incidence and remission of disease, we believe that there is too little information on which to base a clear assessment of the nature of the changes reported. For example, in the SAPALDIA study there were measurements at only two time points and we have no information on the relationship between the levels of pollution and other conditions and symptoms at the time the individual participants were first assessed, nor between the two time points. The SAPALDIA study shows that the change in chronic respiratory symptoms as pollution levels (ie PM_{10}) fall is partly associated with a fall in incidence and partly due to remission of symptoms. This suggests that at least part of the symptoms associated with higher levels of particulate pollution is reversible. Nevertheless, it is difficult to know to what extent changes between the surveys were permanent changes or whether they represented temporary fluctuations in response to current conditions.

Cross-sectional studies are generally regarded as more prone to biases and confounding, but two national studies – in the USA (NHANES I) and the UK (1958 British Birth Cohort) – support the association between air pollution and respiratory symptoms, though these are based on data from over 30 years ago. Moreover the US study was based on a doctor's diagnosis of chronic bronchitis and the UK study showed associations with phlegm but not with cough and showed only a marginally significant result for the dose-response gradient. The large National Health Interview Survey in the USA did not show an association between $PM_{2.5}$ levels but was also based on evidence of doctor-diagnosed chronic bronchitis. For reasons stated earlier, we have chosen to give less emphasis to studies of doctor-diagnosed chronic bronchitis.

The inconsistency of the findings in some studies could be explained by residual confounding but raises the possibility that the associations reported are modified by either the levels or the precise nature of the measured pollution.

Finally, we note that there are several studies that have related more qualitative measures of exposure to traffic to chronic bronchitis. The majority of these can be interpreted as being supportive of an association between air pollution from traffic and the presence of chronic bronchitis (Heinrich *et al*, Germany; Karita *et al*, Thailand; Bayer-Oglesby *et al*, Switzerland; Lindgren *et al*, Sweden; Nuvolone *et al*, Italy; Hazenkamp von Arx *et al*, Switzerland; Gundersen *et al*, Norway), though some have not shown the expected association (Schikowski *et al*, Germany; Oosterlee *et al*, Netherlands; Cesaroni *et al*, Italy; Cowie *et al*, Australia). Although these findings give some support to the view that air pollution increases the risk of chronic bronchitis, they are not useful for quantification of the effects of specific pollutants.

The AHSMOG studies provide support for an association between the incidence and prevalence of chronic bronchitis (cough and/or phlegm) and long-term exposure to high concentrations of ambient air pollution. Whether a relationship exists at lower ambient concentrations of the pollution mixture examined in the AHSMOG studies is unclear. More recent studies of lower concentrations of ambient air pollution have provided less convincing evidence of an association with the incidence or prevalence of chronic bronchitis (or respiratory symptoms related to this condition). It may be that it is more difficult to demonstrate associations with chronic bronchitis at lower ambient concentrations because of a number of methodological issues; for example, a lack of statistical power, inaccuracies in the exposure assessment and unresolved confounding are all more critical where effects are small. In addition, epidemiological studies have often failed to find a threshold concentration (ambient concentration, assumed to be related to exposure) associated with endpoints such as death and hospital admissions. These findings have led to the default assumption that population level thresholds for responses to air pollutants do not exist: it might be fairer to say that, where tested, none has been identified by modern epidemiological techniques. Furthermore, 'no-effect' thresholds that might be identifiable for individuals are obscured when studying groups in which there are always likely to be some individuals with a very low threshold, which leads to any 'no-effect' threshold being very low for a population (Watt *et al*, 1995).

We conclude, in the terms set out at the beginning of this document, that whilst there is some epidemiological evidence of an association between the incidence or prevalence of chronic bronchitis and long-term exposure to air pollution (mainly particulate matter measured as PM_{10}), overall the evidence is suggestive but not sufficient to infer a causal relationship in the UK today.

There is also some evidence of an association between NO_2 and chronic bronchitis and of a link between qualitative measures of exposure to traffic-related air pollutants and chronic bronchitis.

Again, we interpret these epidemiological associations as suggestive but not sufficient to infer a causal relationship. Whether these associations with NO_2 are due to this pollutant itself is unclear.

2.7 Recommendations for quantification

We do not recommend that an association between long-term exposure to ambient air pollution and chronic bronchitis is included in core health impact assessments (HIA). As discussed earlier, it is our view that the evidence considered does not sufficiently establish causality to justify inclusion of this outcome in core HIA regarding long-term exposure to air pollution. We recommend instead that only sensitivity calculations are undertaken. These may be used to define a range of estimates of the size of the possible effect of long-term exposure to ambient air pollutants on chronic bronchitis in the UK, on the assumption that the relationship is a causal one. If the relationship is not causal, the best estimate is of no effect. We recommend use of long-term average concentrations of particulate matter measured as PM_{10} in these sensitivity calculations.

Whether to focus quantification on the incidence or prevalence of chronic bronchitis has been considered. The longitudinal studies show that the change in symptoms of the condition as levels of particulate pollution fall is partly associated with a fall in the incidence of new cases and partly due to remission of symptoms. This suggests that at least some of the symptoms associated with higher levels of particulate pollution are reversible, and that this may need to be taken into account in quantification. The available evidence does allow calculations in terms of the incidence of chronic bronchitis (defined according to the MRC questionnaire) to be undertaken but: (i) problems remain with interpreting the seriousness of a 'case'; (ii) logically, remission and its relationship to air pollution also need to be taken into account; and (iii) doing either or both of (i) and (ii) is difficult because little is known about the proportions of the population in which the disease would remit or new disease might develop. Focusing on the prevalence of chronic bronchitis was felt to be a simpler and more robust approach to quantification, and this would not separate the specific components of new and remitting disease. In Chapter 3 of this report we discuss further the health outcome to be used in quantification.

Whilst we have concluded that the evidence is "suggestive but not sufficient to infer a causal relationship" between chronic bronchitis and air pollution, this does not imply that endpoints with a similar grading in future hazard assessments would necessarily be recommended for quantification in sensitivity analyses. For both core and sensitivity calculations, any uncertainties would need to be appropriately described.

Chapter 3
Health impact assessment
Quantification of chronic bronchitis impacts associated with exposure to particulate air pollution in the UK

3.1 Quantification questions

The following two questions on quantification have been addressed:

1. *Question on burden* (of current levels of anthropogenic PM_{10}): "What might be the number of cases of chronic bronchitis attributable to current levels of particulate pollution in the UK?"
2. *Question on impact* (of reducing anthropogenic PM_{10} concentrations by 1 $\mu g/m^3$): "What might be the change in the number of cases of chronic bronchitis as a result of reducing levels of particulate pollution in the UK?"

The sensitivity calculations presented in this report produced answers to the above questions at national (UK, England, Northern Ireland, Scotland and Wales) and regional levels.

3.2 Methods

Quantification of health impacts associated with exposure to air pollution follows the impact pathway approach illustrated in Figure 1. The schematic figure describes the main elements of the pathway. Other aspects, eg population size and background prevalence rate of the health effect, are also needed at particular stages of the quantification.

For the sake of completeness, Figure 1 includes elements that are not immediately relevant to this report (stages 1, 2 and 3, demand for some polluting activity to pollutant dispersion). The quantification presented in this report therefore starts at stage 4. Quantification at stages 4, 5 and 6 in the figure, from exposure of the population to quantification of health effects, takes the following general form:

$$I = C_i \times P_a \times P_r \times R \times CRF$$

where
- I = impact (a measure of the annual impact on chronic bronchitis)
- C_i = annual average pollutant concentration for pollutant i
- P_a = population exposed
- P_r = fraction of the population at risk within this age group
- R = background prevalence rate (eg cases per 1,000 population at risk)
- CRF = concentration response function (change in prevalence per unit concentration for those at risk)

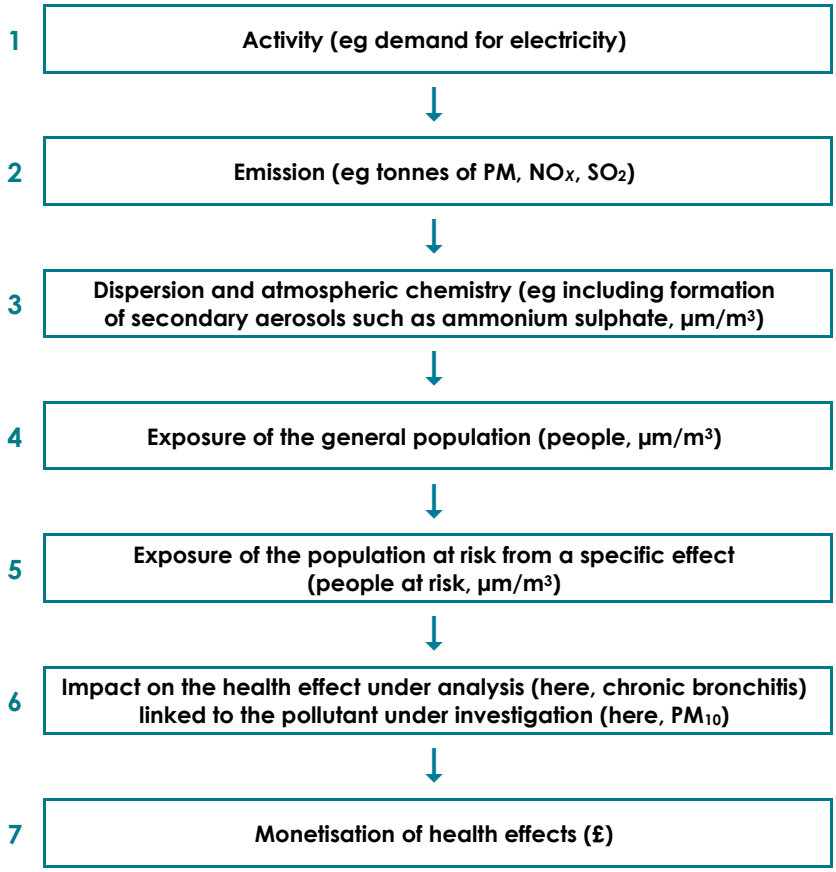

Figure 1: Representation of the impact pathway for chronic bronchitis associated with exposure to PM_{10} arising from emission of particles and their precursors

Stage 7 on monetisation may address a variety of elements, including the medical costs incurred through ill health, loss of productivity among workers and loss of amenity through premature death and being ill (pain, suffering, inconvenience, etc). Clarity on the nature of effects is therefore important to ensure that impacts are correctly valued. So, for monetisation, the following additional information is needed:

a As far as practicable, a precise definition of impact in terms of nature, severity and duration

b Value per case

We do not assign monetary values in this report but have ensured that our approach is suitable to link with information available for monetary valuation.

Air pollution epidemiology has not provided a precise definition of the impact of air pollution on chronic bronchitis. This leads to uncertainty in any valuation that is discussed further below.

3.2.1 Data

The following sections describe the data obtained for each of stages 4 to 6 of the pathway. The order is a little different to that shown in the pathway as some measurements are dependent on others lower down in the figure; for instance, the response function used will determine how the air pollution needs to be measured and expressed.

3.2.1.1 Coefficient

In Chapter 2 of this report we noted that the available evidence does allow calculations in terms of the incidence of chronic bronchitis (measured using the MRC (1960) questionnaire) to be undertaken. However, there are important limitations. These measurements do not distinguish between mild and severe cases. Furthermore, a full description of the effects of air pollution would also need to take account of the effects that changes in air pollution have on remissions in disease as well as on the inception of new disease. Focusing on the prevalence of chronic bronchitis and changes in prevalence was felt to be a simpler and more robust approach to quantification, even though this would not separate the specific components of new and remitting disease.

We have not attempted meta-analysis of the epidemiological studies reviewed in this report because of the diversity of outcome definitions and measures of exposure to air pollution. Of the epidemiological evidence considered, the large cross-sectional study from the ESCAPE project on the prevalence of chronic respiratory symptoms (Cai *et al*, 2014) is the best source of coefficients for use in quantification because it is based on European data and contemporary annual average concentrations of air pollutants, including PM_{10}. We recommend use of the coefficient for chronic phlegm in never-smokers from the ESCAPE study in quantification:

odds ratio 1.32 (95% CI 1.02, 1.71) per 10 $\mu g/m^3$ increase in PM_{10}

This has the advantage of being statistically significant and very similar to the study's estimate for chronic bronchitis in never-smokers (OR 1.35, 95% CI 0.97, 1.88, per 10 $\mu g/m^3$ increase in PM_{10}). Chronic phlegm implies chronic cough also, whether or not chronic cough was reported separately. We have used this risk estimate in the sensitivity analyses presented in this chapter.

3.2.1.2 Baseline prevalence data

Data on the proportion of never-smokers aged 16 years and over and the prevalence of chronic phlegm in the same age group have been sourced from the Health Survey for England 2010 (HSE, 2011). The survey asks a number of questions dealing with cough and phlegm. Prevalence of chronic phlegm in never-smokers is the basis of the coefficient to be used in quantification.

The percentage of the population aged 16 years and over that was classified as never-smokers was 42.7% (Table 1). Table 2 indicates that 5.15% of never-smokers in this survey brought up phlegm on most days for as many as three consecutive months of the year. Accounting for the way the sample had been selected (Ramyani Gupta, 2014, personal communication), the estimate derived for the English population is 5.0% (95% CI 4.2, 5.8).

Table 1: Fraction of the population (≥16 years) who have never smoked

Whether ever smoked cigarette/cigar/pipe?	Whether ever smoked cigarettes?			Total
	Not applicable	Yes	No	
Refused	14	0	0	14
Don't know	9	0	0	9
Not applicable	26	0	0	26
Yes	1,556	2,972	267	4,795
No	3,576	0	0	3,576
Total	5,181	2,972	267	8,420

Table 2: Responses among never-smokers (≥16 years) to survey questions

Bring up phlegm most days as much as 3 consecutive months each year?	Frequency	Percentage
Don't know	1	0.03
Not applicable	3,188	89.15
Yes	184	5.15
No	203	5.68
Total	3,576	100.00

Data from the 2010 Scottish Health Survey (Scottish Government, 2011) provide a similar, but lower rate, again among never-smokers aged 16 years and over only, of 4.6% (95% CI 3.2, 6.0).

Cai *et al* (2014) were unable to show the same proportional increase in chronic phlegm due to air pollution among smokers as they showed in non-smokers. We have therefore made the assumption that any increase among smokers would have been similar in absolute terms to the increase seen among non-smokers. We have done this by applying the same odds ratio (1.32) to the baseline prevalence of phlegm in non-smokers (5% in England, Northern Ireland and Wales; 4.6% in Scotland) to the whole of the adult population aged 16 years and over. For this reason, the estimated impact on chronic phlegm attributable to PM_{10} and the baseline prevalence for chronic phlegm in never-smokers (≥16 years) will be applied to the whole population (≥16 years) regardless of smoking status. This is equivalent to assuming that exposure to air pollution causes the same absolute increase in symptoms among smokers and non-smokers rather than having a much larger (multiplicative) effect on symptoms among smokers.

The coefficient will also be applied to those aged 16–40 years, that is to those below the lowest mean age of the ESCAPE cohort data (approximately 40 years; Cai *et al* (2014) reported a mean age range of 42.9–71.5 years). We think it is unlikely that air pollution is any less likely to cause chronic bronchitis symptoms in those aged 16–40 years than in those aged over 40 years. No further extrapolation will be made to apply the coefficient to those under 16 years of age. The evidence linking air pollution and respiratory symptoms in the under 16 years age group has not been reviewed, and we believe that respiratory symptoms observed in children might not be chronic and may be different from those experienced by adults.

Whether it is appropriate to apply the baseline rate for England to other parts of the UK, ie Northern Ireland, Scotland and Wales, has been considered. The weighted baseline rate for chronic phlegm in never-smokers (≥16 years of age) from the 2010 Scottish Health Survey was 4.6% (95% CI 3.2, 6.0). This is slightly lower, but similar to, the 5% figure for England, and suggests that applying the 2010 Health Survey for England rate to the rest of the UK might be a reasonable approximation. The sensitivity analyses presented in this report made use of the two rates for chronic phlegm described in this paragraph.

3.2.1.3 Concentration and population data

Table 3 provides the population-weighted annual mean concentrations of PM_{10} for 2010 that were used in quantification. The concentration data are based on the pollution climate mapping (PCM) model for a 1 km^2 resolution. Full details of how PM_{10} concentrations were modelled, including the estimation of population-weighted anthropogenic PM_{10}, are reported by Stedman (2014). Although Stedman (2014) refers to $PM_{2.5}$ concentrations in the UK, the method

used is directly applicable to PM_{10}. Population data for 2010 for the total population and the population aged 16 years and over (the age group for which the response function is specified) are shown in Table 4[1].

Table 3: UK population-weighted PM_{10} concentration for 2010 by country/region

Country/region	Total	Non-anthropogenic PM_{10} ($\mu g/m^3$)	Anthropogenic PM_{10} ($\mu g/m^3$)
England			
East of England	16.8	3.1	13.7
East Midlands	17.2	3.1	14.1
London	19.9	3.2	16.7
North East	14.1	2.7	11.4
North West	14.7	2.9	11.8
South East	15.9	3.2	12.7
South West	14.4	3.3	11.1
West Midlands	16.3	2.9	13.5
Yorkshire and the Humber	16.0	3.0	13.0
Northern Ireland	12.9	3.3	9.6
Scotland	12.4	3.0	9.3
Wales	13.2	3.2	10.0
All UK	15.8	3.1	12.7

Table 4: UK population totals for 2010 by country/region

Country/region	Population	Population at risk (≥16 years)
England		
East of England	5,793,910	4,696,543
East Midlands	4,527,845	3,670,271
London	8,095,539	6,562,244
North East	2,568,280	2,081,848
North West	5,257,119	4,261,421
South East	8,500,289	6,890,334
South West	5,194,402	4,210,582
West Midlands	5,591,687	4,532,621
Yorkshire and the Humber	6,999,366	5,673,686
Northern Ireland	1,781,822	1,407,639
Scotland	5,146,651	4,251,134
Wales	3,008,934	2,461,308
All UK	62,465,844	50,699,631

1 The population weighting of concentration carried out with the PCM model was based on the distribution of the UK population in 2001. Using these results with 2010 population data for those aged 16 years and over assumes the same population distribution applies. This assumption does not add significantly to other uncertainties affecting the analysis.

The calculation below has been set out as if the whole of the UK had the same concentration of anthropogenic PM_{10}. Conceptually, where this is not the case, separate calculations need to be performed for each grid square with its own anthropogenic PM_{10} concentration and adult population, followed by adding up the results. Where we assume that the baseline prevalence is the same across the UK, it is arithmetically equivalent to produce an average of the grid concentrations across the UK weighted by population and use this weighted average in one calculation rather than performing many calculations in each grid square[1]. The 12.7 $\mu g/m^3$ PM_{10} value quoted in Table 3 is in fact a population-weighted mean.

3.3 Analysis

3.3.1 Preferred method

This section demonstrates the use of odds ratios to quantify effects on health. For the purpose of illustration, this section calculates at the level of the UK as a whole. Further results, presented below, provide a regional breakdown and a result for the UK derived from adding the regional results.

The epidemiological studies examining the effect of air pollution on chronic bronchitis and phlegm are based on subjects answering 'yes' or 'no' to a series of questions. In these studies, the outcome variable is binary (yes/no), whereas the key exposure, annual average PM_{10} pollution, is a continuous measure. The relation of a binary outcome to a continuous variable is analysed using logistic rather than linear regression. Logistic regression assumes a linear relation between the continuous variable (here, annual average PM_{10} pollution) and the log (natural logarithm) of the odds of the binary outcome variable (here, yes or no to the relevant symptoms). The odds are the ratio of the probability of having the outcome to the probability of not having it.

The linearity in the log odds scale[2] allows us to estimate the probability of reporting symptoms at different concentrations of annual average PM_{10}. The steps involved are set out below, illustrated using the example of the relation of chronic phlegm to PM_{10} exposure.

As already shown, the baseline annual prevalence of chronic phlegm is 5.0% in never-smokers aged 16 years or older, with 95.0% of people not having symptoms. The odds are the ratio of the number of people having symptoms to the number of people not having symptoms, ie 5.0/95.0 (or, equivalently using proportions, 0.050/0.95). Thus, in numbered steps:

1 Baseline probability of reporting chronic phlegm (P_b) = 0.050

2 Baseline odds of reporting chronic phlegm (O_b) = $P_b/(1 - P_b)$ = 0.050/0.95 = 0.0526

1 Population weighting also assumes a linear relationship between concentrations and effects across areas. Strictly, this does not apply as there is a logarithmic relationship between PM_{10} and chronic phlegm. However, logarithmic relationships are approximately linear for small increments. So this may not matter if the differences between concentrations in different areas are small.

2 While in some circumstances, the odds ratio can be assumed to be equivalent to a relative risk, this approximation is only valid when the background risk is small. Where the background prevalence of chronic phlegm is 5% (as here) the odds ratio will overestimate the risk ratio by about 11%. However, for large concentration increments as used in burden calculations, scaling exposure concentrations on a linear rather than logarithmic basis, as has been done in the past, can give very inaccurate estimates.

3 Baseline log odds of reporting chronic phlegm
= ln $[P_b/(1 - P_b)]$ = ln 0.0526 = –2.944 (for use later)

Earlier we noted also that the effect of pollution on reporting of chronic phlegm has been estimated as an odds ratio of 1.32 for a 10 μg/m^3 increase in annual average PM_{10}, ie people exposed to annual average PM_{10} that is 10 μg/m^3 higher than another group would, on average, have 1.32 times the odds of reporting chronic phlegm, other things being equal. If the assumptions of this model are correct, this relationship will hold whatever the baseline level of pollution.

It is a basic property of logs that a constant odds ratio of 1.32 is equivalent to a constant difference on the log odds scale of ln 1.32, ie 0.278, so

4 Change in log odds for a 10 μg/m^3 increase
= ln 1.32 = 0.278

5 Change in log odds per μg/m^3 increase (slope of the logistic regression)
= 0.278/10 = 0.0278

We are now in a position to derive the change in log odds for a concentration change. This could be a predicted concentration change as a result of a new air pollution reduction policy (an impact calculation). However, here we show the example of calculating the burden of chronic phlegm as a result of the 2010 levels of PM_{10} associated with anthropogenic emissions.

The baseline log odds already include the effect of 2010 levels of pollution. Therefore, to calculate the burden of 2010 pollution, we need to subtract the 2010 level of anthropogenic PM_{10} (Table 3) to work out the proportion of the 2010 burden of chronic phlegm that would be avoided without 2010 levels of pollution. To do this we multiply the slope from step 5 by the concentration change (–12.7 μg/m^3).

6 New change in log odds for a 12.7 μg/m^3 decrease in PM_{10}
= 0.0278 × –12.7 = –0.353

This, in turn, gives us the log odds at the new lower concentration, ie the concentration 12.7 μg/m^3 below the baseline:

7 Log odds at new lower concentration of PM_{10}
= ln O_b + (–0.353) = –2.944 + (–0.353) = –3.297

Reversing the previous steps by taking the antilog of the figure from step 7 and then converting the resulting odds back to a probability by reversing step 2, gives the proportion of subjects with symptoms of chronic phlegm at the new lower concentration of PM_{10}:

8 Odds of reporting chronic phlegm at new lower concentration of PM_{10} ($O_{-12.7}$)
= exp(–3.297) = 0.0370

9 Probability of reporting chronic phlegm at new lower concentration of PM_{10}
= $O_{-12.7}/(1 + O_{-12.7})$ = 0.0357

In other words, the new prevalence of chronic phlegm without the burden of 2010 levels of anthropogenic PM_{10} is predicted to be 3.57% rather than 5.0%.

Expressing the burden in terms of the numbers of people with chronic phlegm associated with particulate air pollution requires multiplying the prevalence by the size of the relevant population at risk, in this case the UK adult population of 50,699,631 (Table 4). We apply this to the whole adult population of the UK because we assume that the increase will affect smokers and non-smokers to the same extent on an absolute rather than proportional scale.

10 Total with chronic phlegm at baseline
= 0.050 × 50,699,631 = 2,534,982

11 Total with chronic phlegm in the absence of anthropogenic PM_{10}
= 0.0357 × 50,699,631 = 1,809,977

12 Subtracting from the baseline, gives the current annual burden of people in the UK with chronic phlegm associated with PM_{10}
= 2,534,982 – 1,809,977 = 725,005 individuals

In this example we have illustrated the method by ignoring the effects of local variations. When we use the same principles to work out the effects taking account of these variations, we obtain the slightly lower figure of 722,660 cited below in Table 5 and the executive summary, based on a more disaggregated analysis than was appropriate for this illustration of the methods used.

For the purpose of comparison, Table 6 provides data on the proportion of the population aged 16 years and over reporting chronic phlegm in 2010, as well as the total number of people reporting these symptoms. The data do not take account of an individual's smoking status. We estimated that about 4,336,000 people in the UK aged 16 years and over reported chronic phlegm in 2010, with 722,660 cases attributable to anthropogenic PM_{10} in 2010 (Table 5). Results accounting for regional variation in anthropogenic PM_{10} concentration and the lower rate of chronic phlegm reported for Scotland are shown in Table 5. These refinements to the analysis make a small difference to the overall results shown above.

Results are also given for the marginal benefit of reducing anthropogenic PM_{10} concentrations in each region. These are calculated by subtracting results based on 2010 anthropogenic PM_{10} concentrations from those for a scenario where concentrations in each region are reduced by 1 $\mu g/m^3$.

Table 5: Estimated burden/impact of anthropogenic PM_{10} in 2010 on the prevalence of chronic phlegm in the UK in 2010 – results of sensitivity calculations

Country/region	Population weighted anthropo-genic PM_{10} ($\mu g/m^3$)	Baseline prevalence of chronic phlegm in never-smokers (%)[a]	Number/change in number of people (≥16 years of age) with symptoms		
			Total with chronic phlegm at baseline[b]	Chronic phlegm attributable to anthropo-genic PM_{10} (burden)	Benefit of a 1 $\mu g/m^3$ reduction in anthropo-genic PM_{10} (impact)
England[c]					
East of England	13.7	5.0	234,827	71,715	6,117
East Midlands	14.1	5.0	183,514	57,403	4,780
London	16.7	5.0	328,112	117,833	8,547
North East	11.4	5.0	104,092	27,198	2,711
North West	11.8	5.0	213,071	57,347	5,550
South East	12.7	5.0	344,517	98,717	8,974
South West	11.1	5.0	210,529	53,756	5,484
West Midlands	13.5	5.0	226,631	68,366	5,903
Yorkshire and the Humber	13.0	5.0	283,684	82,905	7,389
Northern Ireland	9.6	5.0	70,382	15,829	1,833
Scotland	9.3	4.6	195,552	42,901	5,115
Wales	10.0	5.0	123,065	28,690	3,206
All UK	12.7	4.9	2,517,977[d]	722,660[c,d]	65,609[d]

Notes

a Baseline prevalence (%) of chronic phlegm in never-smokers aged ≥16 years. Rates sourced from the 2010 Health Survey for England (HSE, 2011) and the 2010 Scottish Health Survey (Scottish Government, 2011). Baseline prevalence for England (5%) has been applied to all regions in England as analyses by St George's, University of London, indicate there is no statistically significant regional difference in the prevalence of chronic phlegm in never-smokers aged ≥16 years. There is little difference in the baseline prevalence between England and Scotland (5% vs 4.6%). On this basis, the baseline prevalence for England (5%) has also been applied to Northern Ireland and Wales.

b The total with chronic phlegm at baseline was estimated by applying the baseline prevalence in never-smokers to the whole population (≥16 years) regardless of smoking status.

c The total for chronic phlegm at baseline and the total burden/impact for England can be derived from the sum of the results for the regions of England.

d The total for chronic phlegm at baseline and the total burden/impact for the UK is the sum of the results for the regions/countries.

The calculations were done as a reduction from the baseline prevalence which includes the effects of air pollution.

The higher figure of 725,005 cited in Section 3.3.1 was provided to illustrate the methods. The figure of 722,660 given in this table is to be preferred as it is based on a more disaggregated and hence detailed analysis.

Table 6: Estimated number of cases of chronic phlegm in the UK in those aged ≥16 years, irrespective of smoking status

Country/region	Baseline prevalence, irrespective of smoking status (%)	Number of people with chronic phlegm at baseline, irrespective of smoking status
England		
East of England	7.85	368,679
East Midlands	8.49	311,606
London	6.4	419,984
North East	11.39	237,122
North West	9.65	411,227
South East	6.92	476,811
South West	7.45	313,688
West Midlands	10.86	492,243
Yorkshire and the Humber	9.96	565,099
Northern Ireland	8.46	119,086
Scotland	9.69	411,935
Wales	8.46	208,227
All UK	8.55	4,335,707

Notes

Rates sourced from the 2010 Health Survey for England (HSE, 2011) and the 2010 Scottish Health Survey (Scottish Government, 2011).

The average of the rates for regions in England has been used for Northern Ireland and Wales.

3.4 Discussion of results of quantification

The analyses demonstrate the quantification of an increased prevalence of chronic bronchitis, defined as the presence of chronic phlegm for at least three months of the year over at least two years, associated with exposure to PM_{10} in the UK. Overall, it is estimated that PM_{10} could have increased the prevalence by 722,000 cases in 2010, affecting a little over 1% of the population. Further, a 1 $\mu g/m^3$ reduction in anthropogenic PM_{10} in 2010 is estimated to reduce the prevalence of chronic phlegm by approximately 65,000 cases (2.6%). This conclusion must be seen in the context of the decision to recommend this impact for sensitivity analysis only. As discussed earlier, it is our view that the evidence considered does not sufficiently establish causality to justify inclusion of this outcome in core health impact assessments regarding long-term exposure to air pollution. The sensitivity calculations may be used to define a range of estimates of the size of the possible effect of long-term exposure to ambient air pollutants on chronic bronchitis in the UK, on the assumption that the relationship is a causal one. If the relationship is not causal, the best estimate is of no effect.

Refinements could be made to this analysis – for example, through the identification of prevalence data at a regional scale; with the exception of Scotland, prevalence data represent the average from the Health Survey for England 2010 (HSE, 2011). However, comparing the prevalence data for Scotland with the data for England suggests that this would make relatively little difference to the final estimate. Further epidemiological research for the UK specifically seems appropriate, given the large number of people estimated to be potentially affected and the decision that the function should only be applied for sensitivity analysis. Further consideration could also be given to the decision to use the prevalence rate from never-smokers for the whole

population (including current smokers) to consider the consequences of any bias that this decision generates for the final results. It is noted, however, that assessment of biases should be performed in a holistic manner, considering all stages of the analysis including valuation, to consider whether, overall, the set of methodological choices made is likely to lead to overestimation or underestimation in the final results.

For the purpose of valuation, COMEAP has agreed to provide guidance regarding the nature of the impact to help inform this stage of the impact pathway (Figure 1). The epidemiological research is not precise in that the definition of the effect refers only to the presence of phlegm for three or more months a year over two consecutive years. It is important to emphasise that the definition used for epidemiological research is not the same as a clinical one in which the information used to make a diagnosis may be both more extensive and less standardised. The epidemiological definition provides a minimum indication of severity and duration but does not provide an indication of how debilitating the effects are. The importance of this question is indicated by the following results from Salomon *et al* (2012), providing estimates of disability-adjusted life-years lost (DALY scores) associated with having COPD and asthma (Table 7). For both diseases there is a significant spread in the DALY scores according to the severity of the disease. It may be anticipated that for some people the effect of exposure to PM_{10} may be to initiate disease at a mild level, whilst for others it may exacerbate disease to a higher level.

Table 7: DALY scores for chronic respiratory diseases from Salomon *et al* (2012)

Effect	DALY score
Asthma: controlled	0.009
COPD and other chronic respiratory disease (mild)	0.015
Asthma: partially controlled	0.027
Asthma: uncontrolled	0.132
COPD and other chronic respiratory disease (moderate)	0.192
COPD and other chronic respiratory disease (severe)	0.383

Ideally such variation in severity would be reflected in the valuation, though this requires additional information. Table 8 presents unpublished quality of life data from subjects with chronic bronchitis in the Burden of Obstructive Lung Disease (BOLD) initiative. These data (physical component scores) were derived from the short-form 12 (SF-12) health survey instrument and have been linked to COPD grades 1 (mild) moderate (grade 2) and severe (grades 3 and 4). Both in the UK (London) data and in the global data, there is a consistent finding that chronic bronchitis lies between moderate and severe COPD. Whilst the data have been adjusted for age, they have not been adjusted for co-morbidities. Despite this, the data show the relative position of the different conditions and provide a link to monetary valuation.

Table 8: Effects of age and disease status on quality of life (unpublished data from the Burden of Obstructive Disease (BOLD) initiative: P Burney, personal communication)

	Change in physical health scale (SF-12)	
	London (UK)	All available sites (unweighted)
No COPD	0 (reference)	0 (reference)
COPD (mild)	1.93 (–0.89, 4.74)	–0.03 (–1.57, 1.51)
Age / 10 years	–2.20 (–3.10, –1.30)	–1.57 (–3.44, –2.48)
COPD (moderate)	–4.45 (–8.07, –1.03)	–3.30 (–4.70, –1.90)
Chronic bronchitis	–6.23 (–10.87, –1.58)	–4.70 (–11.83, 4.95)
COPD (severe)	–15.69 (–23.44, –7.93)	–9.94 (–14.90, –4.97)

Chapter 4
Conclusions and research recommendations

The aim of this report was to evaluate the epidemiological evidence linking long-term exposure to ambient air pollution and chronic respiratory morbidity and to advise on the likely number of people affected in the UK. To avoid double counting of effects in quantification, COMEAP assessed the non-lethal effects of long-term exposure to air pollution on the lung in terms of symptoms, as chronic bronchitis.

Summaries of the epidemiological evidence considered along with discussion of the results of quantification have been provided in Chapters 2 and 3. Therefore, we have focused our conclusions on some key points to emerge during the process of preparing this report. This is followed by our recommendations for research.

In the first chapter of this report we noted the economic importance of this health outcome (chronic bronchitis) to health impact assessments (HIA) and cost-benefit analyses (CBA) regarding air pollution in Europe: the effect of particulate matter on new cases of chronic bronchitis is the next most important health outcome after the effect of long-term exposure to $PM_{2.5}$ on mortality, and the most important among morbidity outcomes, in terms of monetised health benefits using methods that have previously been recommended elsewhere (Hurley *et al*, 2005). One reason COMEAP was asked to consider the evidence on chronic bronchitis was that this pollutant-outcome pair is not currently used in quantification in the UK, whereas it is elsewhere in Europe (Holland, 2014a,b; Hurley *et al*, 2005).

Our review of the evidence shows that whilst some cross-sectional and longitudinal studies reported associations between long-term exposure to air pollution and chronic bronchitis/respiratory symptoms, there is a lack of consistency in the overall body of epidemiological evidence. Recent recommendations by the World Health Organization (WHO, 2013) on concentration-response functions (CRF) for the relationship between chronic bronchitis in adults and long-term exposure to PM_{10} for use in HIA and CBA (eg Holland, 2014a,b) took some note of the less certain evidence regarding the health outcome. Our appraisal of the full body of evidence points to the need for further research to better understand the relationship between chronic bronchitis and current levels of air pollution, and the implications of reductions in concentrations of air pollutants for the condition in terms of its incidence, prevalence and remission.

The definitions of chronic bronchitis used in the epidemiological studies reviewed in this report were variable and were imprecise. In many studies the definition referred to reports of cough and/or phlegm for three months a year over two years. This definition provides limited

information about the duration and severity of the chronic respiratory symptoms. Some longitudinal data showed remission of symptoms, suggesting that the condition (chronic bronchitis) may be transient rather than one which remains once initiated. Whilst quantification exercises conducted elsewhere (Miller *et al*, 2011) focused on new cases of 'persistent' chronic bronchitis by taking account of remission, we opted to focus quantification on the prevalence of the disease. Our rationale behind this decision was that little is known about the proportions of the population in which the disease would remit or new disease might develop. Our approach to quantification did not separate the specific components of new and remitting disease.

The epidemiological evidence considered was suggestive of an association between long-term exposure to particulate pollution and chronic bronchitis, but not sufficient to establish causality to justify inclusion of this pollutant-outcome pair in core HIA. Our sensitivity analyses therefore estimated the size of the *possible* effect of particulate pollution (anthropogenic PM_{10}) on the prevalence of chronic bronchitis (in terms of chronic phlegm) in the UK. We estimated that over 722,000 cases of chronic phlegm in 2010 could be attributable to anthropogenic PM_{10} in 2010, and that a 1 $\mu g/m^3$ reduction in anthropogenic PM_{10} in 2010 could lead to over 65,000 fewer cases of chronic phlegm in 2010.

4.1 Research recommendations

Evidence regarding the possible effects of long-term exposure to common gaseous pollutants (O_3, SO_2 and, to a lesser extent, NO_2) on chronic bronchitis is sparse. Epidemiological studies investigating the effects of these pollutants, and of all pollutants (including particulate matter) controlled for the potential effects other pollutants, are needed.

Work to improve the link between the epidemiological definition of chronic bronchitis used in studies of air pollution and the monetary values applied to estimate economic costs of the condition attributable to ambient air pollution is also needed. The studies should attempt to improve understanding of the nature of the condition (symptom 'episodes') in terms of its severity and duration.

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Appendix 1
Summary of systematic literature search to support QUARK's assessment of the relationship between long-term exposure to outdoor air pollutants and chronic bronchitis

The search terms used in the final string are given in the table below.

Database used: PubMed (http://www.ncbi.nlm.nih.gov/pubmed). The terms were limited to the following search fields in PubMed: Title/Abstract. The search ran to 30 June 2012.

Pollutants	**Health**
air pollut*	chronic obstructive pulmonary disease
Ozone	COPD
O_3	chronic obstructive lung disease
sulphur dioxide	lung function
sulfur dioxide	pulmonary function
SO_2	spiromet*
nitrogen dioxide	chronic bronchit*
NO_2	cough
fine particl*	phlegm
fine particul*	breathless*
ultrafine particl*	dyspn*
ultrafine particul*	respiratory symptom*
total suspended particl*	emphysema
total suspended particul*	
TSP	
black smoke	
coarse particl*	
coarse particul*	
PM_{10}	
$PM_{2.5}$	
$PM_{10-2.5}$	
$PM_{2.5-10}$	
$PM_{1.0}$	

A total of 10,136 abstracts were identified. The criteria listed below were used to identify papers for inclusion in the review. A total of 48 papers of relevance to the work were identified; they are summarised in a series of tables in this appendix.

Sifting criteria

The following criteria were applied during various sifting stages.

Sift 1: titles and abstracts of each citation were scanned to remove irrelevant ones

a Include only peer-reviewed epidemiological studies of adults

b Include studies investigating the following outdoor air pollutants:

- particulate matter (PM_{10}, $PM_{2.5}$, Black Smoke, TSP, SO_4)
- nitrogen dioxide
- ozone
- sulphur dioxide
- 'traffic' mixture

c Include studies of long-term average air pollutant concentrations: preferably at least 12-month averages

d Include studies on the following endpoints of interest:

- prevalence of or change in chronic bronchitis/chronic respiratory symptoms, breathlessness (dyspnoea)

e Include only articles published in the English language

f Exclude epidemiological studies of asthmatic subjects

g Exclude epidemiological studies of short-term effects, eg time-series or panel studies

h Exclude experimental studies, eg chamber studies or animal studies

i Exclude studies of the following:

- indoor air
- occupational exposures
- industrial emissions
- volcanic emissions
- pharmaceutical products

j Exclude reviews

Sift 2: full papers of the remaining *possible* citations were sourced and assessed for eligibility against the following criteria

a Clear/useful definition of disease/health outcome must be stated

b Numerical estimate of effect (and estimate of precision) reported, ie odds ratios or relative risk per increment in air pollutant concentration

c Control for confounding factors (especially smoking of tobacco)

d Relevant air pollution exposure, ie as similar to exposure/mixture in the UK as possible

Searches were supplemented with papers identified from scanning reference lists of papers.

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
1 Abbey DE, Mills PK, Petersen FF, Beeson WL (1991) Long-term ambient concentrations of total suspended particulates and oxidants as related to incidence of chronic disease in California Seventh-Day Adventists. *Environ Health Perspect.* 94:43–50.			
Prospective cohort of 6,000 non-smoking Seventh Day Adventist adults in California in 1976 who resided within 5 miles of their current address for at least 10 years Self-reported data on chronic respiratory symptoms were collected from 3,914 using a questionnaire administered in 1977 and 1987 Air pollution profiles were generated based on zip code by month residence histories since 1966 using monitoring data from the three closest monitoring stations to each individual Exposure variables included various concentration thresholds and mean concentrations for TSP and O_3 (1973–77)	**Incidence of airway obstructive disease (AOD) symptoms** cases = 272 Defined as having none, possible or definite symptoms for each, or any or all of the following: chronic bronchitis, asthma (doctor diagnosed with history of wheezing), emphysema (doctor diagnosed with shortness of breath)	**TSP**	RR 1.36 (1.11, 1.85) for ≥1,000 h/y above 200 µg/m^3 Adjusted for age, education, sex, childhood colds, childhood AOD, possible symptoms in 1977, years smoked, years lived with a smoker and years worked with a smoker
		O_3	RR 1.02 (0.85, 1.29) for ≥500 h/y above 10 pphm (parts per hundred-million) – adjustment as above No statistically significant association when mean concentration analysed
	Incidence of chronic bronchitis symptoms cases = 234 'Definite' chronic bronchitis defined as having symptoms of cough, and/or sputum production on most days, for at least 3 months a year for more than 2 years	**TSP**	RR 1.33 (1.07, 1.81) for ≥1,000 h/y above 200 µg/m^3 Adjusted for age, education, sex, childhood colds, possible symptoms in 1977, years smoked and years lived with a smoker
		O_3	RR 1.20 (0.97, 1.52) for ≥500 h/y above 10 pphm – adjustment as above No statistically significant association when mean concentration analysed
2 Abbey DE, Petersen F, Mills PK, Beeson WL (1993a) Long-term ambient concentrations of total suspended particulates, ozone, and sulfur dioxide and respiratory symptoms in a nonsmoking population. *Arch Environ Health*. 48: 33–46.			
Subset (3,914) of a cohort of non-smoking Seventh Day Adventist adults (64% female; average age in 1977 of 55.9 years) living in Southern California who resided within 5 miles of their current address for at least 10 years were followed from 1977–87	**New cases of AOD** cases = 272 See Abbey *et al* (1991) for definition	**TSP**	RR 1.36 (1.11, 1.66), p < 0.01, for 1,000 h/y above 200 µg/m^3 Adjusted for age, sex, gender, education, frequency of childhood colds, childhood AOD, possible symptoms in 1977, years smoked, years lived with a smoker and years worked with a smoker

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
Self-reported data on chronic respiratory symptoms were collected using a questionnaire administered in 1977 and 1987 Air pollution profiles were generated based on zip code by month residence and work location history using monitoring data from the fixed-site monitoring stations Exposure variables included exceedance frequencies and excess concentrations greater than cut-off levels for the following pollutants (1973–77): TSP (60, 75, 100, 150, 200 µg/m^3); SO_2 (2, 4, 8, 14 pphm); and O_3 (10, 12, 15, 20, 25 pphm). Mean concentrations (1973–77) also analysed			In addition, RRs for mean concentrations of TSP, eg 60 µg/m^3, were reported. The RRs were positive and statistically significant at the 5% level, but no confidence intervals were reported
		SO_2	No statistically significant relationship found
		O_3	No statistically significant association found with either mean concentration or average annual exceedance frequencies for any cut-off
	New cases of chronic bronchitis cases = 234 See Abbey *et al* (1991) for definition	**TSP**	RR 1.33 (1.07, 1.65), $p < 0.05$, for 1,000 h/y above 200 µg/m^3 – adjustment as above In addition, RRs for mean concentration of TSP, eg 60 µg/m^3, were reported. The RRs were positive and statistically significant at the 5% level, but no confidence intervals were reported
		SO_2	No statistically significant relationship found
		O_3	No statistically significant association found with either mean concentration or average annual exceedance frequencies for any cut-off
	Change in symptom severity score (between 1977 and 1987) – all individuals	**TSP**	Statistically significant association found with average annual hours above 200 µg/m^3
		SO_2	No statistically significant relationship found
		O_3	No statistically significant relationship found with either average annual exceedance frequencies for any cut-off or for mean concentration
3 Abbey DE, Petersen FF, Mills PK, Kittle L (1993b) Chronic respiratory disease associated with long-term ambient concentrations of sulfates and other air pollutants. *J Expo Anal Environ Epidemiol.* 3:99–115.			
Study description as Abbey *et al* (1993a) 64% of the cohort was female, with ages in the cohort ranging from 27 to 95 years	**New cases of AOB symptoms** See Abbey *et al* (1991) for definition	**SO_4**	10-y mean concentrations and the exceedance frequency statistics failed to show a statistically significant association

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
(mean 56 years) in 1977 SO_4 (for 1977–87) was examined using mean concentrations, exceedance frequencies using cut-offs (6, 9, 12 and 15 µg/m^3) and excess concentrations Individuals who smoked between 1977 and 1987 were not included in the study. The proportions of smokers prior to 1977 and exposure to smoking in the home and workplace are reported Two-pollutant model analyses were conducted to test for possibility of surrogate effects – no numerical estimates were reported	**New cases of chronic bronchitis symptoms** See Abbey *et al* (1991) for definition		10-y mean concentrations and the exceedance frequency statistics failed to show a statistically significant association
	Change in symptom severity score (between 1977 and 1987)		No association with change in severity score for chronic bronchitis Statistically significant association for change in AOD severity score with average annual exceedance frequency above 6 µg/m^3, but not with the other cut-offs or mean concentrations
4 Abbey DE, Colome SD, Mills P, Burchette R, Beeson WL, Tian Y (1993c) Chronic disease associated with long-term concentrations of nitrogen dioxide. *J Expo Anal Environ Epidemiol.* 3:181–202.			
Cohort and study design as described earlier Cumulative NO_2 concentrations were estimated monthly for each participant using monitoring data from fixed-site monitoring stations according to residence and work location history. Data from a separate personal exposure study conducted in 650 people in southern California was used to adjust mean concentrations of NO_2 to include indoor sources as well as ambient concentrations Analyses used mean concentrations of NO_2 and exceedance frequencies (hours above cut-offs) for 5, 15, 20 and 25 pphm	**Development of new cases of definite symptoms of AOD**	**NO_2**	No statistically significant associations between any outcome and ambient mean concentrations of NO_2 or exceedance frequencies RR 1.26 (0.58, 4.33) per 5 pphm increase in average annual *adjusted* mean NO_2 concentration (1977–87). n = 1,831, cases = 139
	Development of new cases of definitive symptoms of chronic bronchitis		No statistically significant associations with ambient mean concentrations of NO_2 or exceedance frequencies No relationship with *adjusted* mean concentrations of NO_2 – negative coefficients found
	Persistent prevalence (having symptoms in 1997 and 1987)		Neither unadjusted or adjusted NO_2 showed a statistically significant positive association with this outcome for either AOD or chronic bronchitis

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	Change in symptom severity score		No statistically significant associations with ambient mean concentrations of NO_2 or exceedance frequencies and change in symptoms severity for AOD or chronic bronchitis No statistically significant associations reported between *adjusted* mean concentrations of NO_2 and change in symptoms severity for AOD or chronic bronchitis
5 Abbey DE, Ostro BE, Petersen F, Burchette RJ (1995a) Chronic respiratory symptoms associated with estimated long-term ambient concentrations of fine particulates less than 2.5 microns in aerodynamic diameter ($PM_{2.5}$) and other air pollutants. *J Expo Anal Environ Epidemiol.* 5:137–59.			
A subset of the prospective cohort previously analysed by Abbey *et al*: 1,868 adults who lived at least 80% of the months between 1966 and 1986 in areas close to selected airports throughout California. The participants were followed between 1977 and 1987 Description of data collection on chronic respiratory disease and outcome definitions are given above $PM_{2.5}$ concentrations were estimated using visibility data from nine airports, 1966–86. Analyses were conducted using mean concentrations and exceedance frequencies (20, 30 and 40 µg/m^3) Analyses were also conducted to determine whether other pollutants were acting as a surrogate for $PM_{2.5}$	**New cases of AOD** n =1,588, cases = 135	**$PM_{2.5}$**	RR 1.46 (0.84, 2.46) for 45 µg/m^3 increase in mean concentration (for 1966–77) – not statistically significant at the 0.05 level. Adjusted for age, gender, education, childhood AOD, possible symptoms in 1977 No statistically significant associations reported with exceedance frequencies
	New cases of chronic bronchitis symptoms n = 1,631, cases = 117		RR 1.81 (0.98, 3.25), p = 0.058, for a 45 µg/m^3 increase in mean concentration. Adjusted for age, gender, education, childhood colds, years smoked in past and possible symptoms in 1977 Analysis by type showed that only the 'cough with sputum' type (vs cough only) was statistically significant, p < 0.03 RR 1.41, p < 0.05, with 4000 h/y mean concentrations above 20 µg/m^3. No increase in RRs when the higher concentration cut-offs were used
	Change in symptom severity score (between 1977 and 1987)		Mean concentration was significantly associated, p ≤ 0.05, with change in severity score for AOD and chronic bronchitis The exceedance frequencies for each cut-off was significantly, p < 0.05, associated with AOD. For chronic bronchitis, only the cut-off for 20 µg/m^3 was statistically significant

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
6 Abbey DE, Hwang BL, Burchette RJ, Vancuren T, Mills PK (1995b) Estimated long-term ambient concentrations of PM_{10} and development of respiratory symptoms in a nonsmoking population. *Arch Environ Health.* 50:139–52.			
3,914 Californian Seventh Day Adventist non-smoking adults – 64% female. Average age in 1977 of 56 years (cohort age range 27–95 years) PM_{10} formed indirectly using monitored TSP for the years 1973–87 Mean concentrations and exceedance frequencies using various concentration cut-offs (40, 50, 60, 80 and 100 µg/m³) were examined	**Development of definite symptoms of AOD** n = 3,236, cases = 275	**PM_{10}**	Regression coefficients were not statistically significant for mean concentration or for exceedance frequencies below 80 µg/m³. It was statistically significant, $p < 0.05$, above 80 µg/m³ RR 1.17 (1.02, 1.33), $p < 0.05$, for an increase of 1,000 h/y in average annual exceedance frequency above 100 µg/m³
	Development of new cases of definite chronic bronchitis symptoms n = 3,237, cases = 239		Regression coefficients were not statistically significant for mean concentration or for exceedance frequencies below 100 µg/m³ RR 1.17 (1.01, 1.35), $p < 0.05$, for an increase of 1,000 h/y in average annual exceedance frequency above 100 µg/m³. Adjusted for age, gender, education, years smoked, years lived with a smoker, possible symptom in 1977, and childhood colds When analysed by type, RR for chronic productive cough 1.21 (1.02, 1.44) and for cough only 1.16 (0.96, 1.40) for an increase of 1,000 h/y in average annual exceedance frequency above 100 µg/m³
	Change in symptom severity score		Positive and statistically significant, $p < 0.05$, association between severity score for AOD and exceedance frequency of ambient concentrations of PM_{10} above 100 µg/m³. For bronchitis, $p = 0.06$ for the same exceedance frequency
7 Abbey DE, Lebowitz MD, Mills PK, Petersen FF, Beeson WL, Burchette RJ (1995c) Long-term ambient concentrations of particulates and oxidants and development of chronic disease in a cohort of non-smoking Californian residents. *Inhal Toxicol* 1:19–34.			
Cohort of 6,340 non-smoking Seventh Day Adventist (age range 27–95 in 1977; 64% female) residents of California who	**Development of AOD** Number of new cases = 272	**TSP**	RR 1.36 (1.11, 1.66) for 42 days/y above 200 µg/m³ TSP Adjusted for age, education, sex, childhood colds, childhood AOD, possible symptoms in 1977, years

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
resided for 10 years or longer within 5 miles of their present neighbourhood 3,914 individuals completed a respiratory symptom questionnaire in both 1977 and 1987 Pollutants measured: TSP (1973–87); PM_{10}, estimated from site/seasonal-specific regressions on TSP; $PM_{2.5}$ (1967–87) estimated from airport visibility data; SO_4 (1977–87); O_3, NO_2 and SO_2 (1973–87) Measures of exposure used in analyses: excess concentrations and exceedance frequencies above a number of cut-offs as well as mean concentrations, and mean ambient concentrations adjusted for time spent indoors Though not shown in this table, results from analyses using cut-offs for exceedance frequencies and of multi-pollutant analyses are available			smoked, years lived with a smoker and years worked with a smoker
		PM_{10}	RR 1.17 (1.02, 1.33) for 42 days/y above 100 µg/m^3 PM_{10}
		$PM_{2.5}$	RR 1.46 (0.48, 2.46) for average annual increase 45 µg/m^3 $PM_{2.5}$ Number of new cases = 135 – those with $PM_{2.5}$ data
		SO_4	RR 1.43 (0.88, 2.26) for average annual increase 7 µg/m^3 SO_4
		NO_2	No statistically significant associations found
		SO_2	No statistically significant associations found
		O_3	RR 1.04 (0.86, 1.25) for 500 h/y above 10 pphm O_3
	Development of chronic bronchitis Number of new cases = 234	**TSP**	RR 1.33 (1.07, 1.65) for 42 days/y above 200 µg/m^3 TSP Adjusted for age, education, sex, childhood colds, possible symptoms in 1977, years smoked and years lived with a smoker
		PM_{10}	RR 1.17 (1.01, 1.35) for 42 days/y above 100 µg/m^3 PM_{10}
		$PM_{2.5}$	RR 1.81 (0.98, 3.25) for average annual increase 45 µg/m^3 $PM_{2.5}$ Number of new cases = 117 – those with $PM_{2.5}$ data
		SO_4	RR 0.96 (0.58, 1.55) for average annual increase 7 µg/m^3 SO_4
		NO_2	No statistically significant associations found
		SO_2	No statistically significant associations found
		O_3	RR 1.02 (0.83, 1.25) for 500 h/y above 10 pphm O_3

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
8 Sunyer J, Jarvis D, Gotschi T , Garcia-Esteban R, Jacquemin B, Aguilera I, *et al* (2006) Chronic bronchitis and urban air pollution in an international study. *Occup Environ Med.* 63:836–43.			
Follow-up study (in 2000–02) of adult subjects (3,232 males and 3,592 females) who participated in ECRHS I (in 1991–93) which investigated the association between the prevalence and new onset of chronic bronchitis and urban air pollution. Participants were from 21 centres in 10 European countries Health and covariate data were collected using questionnaires. Two definitions of chronic bronchitis were used: (i) productive chronic cough for chronic cough and phlegm (more than 3 months each year), and (ii) chronic phlegm alone. The outcomes of interest were prevalence at follow-up and new onset (prevalence at follow-up among the subjects without the symptoms of chronic bronchitis at baseline) Annual means for $PM_{2.5}$ (centre-level background locations), and its sulphur content, were derived. NO_2 was also monitored – home outdoor and indoor for 1,634 participants – for 14 days in 16 centres. This was repeated 6 months later in 659 households New onset *during* the follow-up: chronic phlegm was 4% (4.5% in males and 3.5% in females); chronic productive cough was 1.2% in males and 1.1% in females Prevalence at the *end* of follow-up: chronic phlegm was 6.9% in males and 5.3% in females)	**Prevalence (at follow-up) and new onset chronic phlegm**	**Traffic**	None (ref) 1 Seldom: for males 1.25 (0.82,1.93); females 1.23 (0.77, 1.96) Frequent: for males 1.26 (0.82, 1.95); for females 1.46 (0.92, 2.31) Constant: for males 0.88 (0.56, 1.38); for females 1.86 (1.24, 2.77)
		Centre-level $PM_{2.5}$ (µg/m³)	Males 0.97 (0.70, 1.35); females 0.99 (0.85, 1.17)
		Centre-level sulphur content (µg/m³)	Males 1.00 (0.70, 1.44); females 1.00 (0.85, 1.17)
		NO_2	The association with NO_2 was statistically significant among females but not among males (for IQR change). In females OR 2.71 (1.03, 7.16) (>50 µg/m³ vs <20 µg/m³)
	New onset of chronic phlegm or chronic productive cough	**Centre-level $PM_{2.5}$ (µg/m³)**	No association observed
		Centre-level sulphur content (µg/m³)	No association observed
	Prevalence of chronic productive cough at follow-up	**NO_2**	OR in females for a 30 µg/m³ change 1.87 (0.99, 3.42) and 2.93 (1.14, 7.49) for IQR change (>50 µg/m³ vs <20 µg/m³)
		Constant traffic	OR 2.70 (1.07, 7.12) in females

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
9 Orru J, Jõgi R, Kaasik M, Forsberg B (2009) Chronic traffic-induced PM exposure and self-reported respiratory and cardiovascular health in the RHINE Tartu Cohort. *Int J Environ Res Public Health*. 6:2740–51.			
ECRHS survey of 2,460 adults aged 25–45 years from Tartu (Estonia) in 1993 who were followed-up in 2000–01. The follow-up in Tartu and six other ECRHS centres comprised the RHINE cohort (The Respiratory Health in Northern Europe). At follow-up, complete data from 1,684 adults (mean age at follow-up = 35 years) from Tartu were available Annual modelled local traffic induced exhaust PM outside participants' homes. Mean (max) of PM exhaust: 0.10 (0.83) µg/m^3. Mean (max) of local traffic induced PM_{10}: 0.76 (7.40) µg/m^3	**Chronic bronchitis** (prevalence at follow-up): "Do you cough up phlegm in this way almost every day for at least 3 months every year? And if so, have you had periods of this kind for at least 2 years in a row?"	**PM exhaust**	OR 0.78 (0.53, 11.44) per 1 µg/m^3 increase All ORs adjusted for gender, age, BMI and smoking
	Cough (prevalence at follow-up): "Have you been woken by an attack of coughing at any time in the last 12 months?"		OR 1.01 (0.28, 3.64) per 1 µg/m^3 increase
	Breath shortness (prevalence at follow-up): "Have you been woken by an attack of shortness of breath at any time in the last 12 months?"		OR 2.92 (0.46, 18.65) per 1 µg/m^3 increase
10 Schindler C, Keidel D, Gerbase MW, Zemp E, Bettschart R, Brändli O, *et al*; SAPALDIA Team (2009) Improvements in PM_{10} exposure and reduced rates of respiratory symptoms in a cohort of Swiss adults (SAPALDIA). *Am J Respir Crit Care Med*. 179:579–87.			
Data from 7,019 SAPALDIA participants (mean age 41.4 years, range 18–60 years in 1991) from eight areas in Switzerland were used to investigate whether decrements in ambient concentrations of PM_{10} could be associated with reductions in respiratory symptoms Participants were examined in 1991 (baseline) and in 2002 Data on respiratory symptoms and a range of covariates were obtained using the ECRHS questionnaire. A remission rate of	**Regular cough** Defined by a positive response to at least one of the following questions: "Do you usually cough (bring up phlegm from your chest) first thing in the morning?" and/or "Do you usually cough (bring up phlegm from your chest) during the day or at night?" New reports: subjects without symptom reports in 1991	**PM_{10}**	ORs per 10 µg/m^3 decrement in PM_{10} *Entire sample* New reports 0.77 (0.62, 0.97) Persistent reports 0.55 (0.39, 0.78) *Persistent non-smokers* New reports 0.86 (0.63, 1.19) Persistent reports 0.28 (0.14, 0.60) ORs adjusted for baseline variables (sex, age, level of education, Swiss citizenship, BMI, parental smoking, parental history of asthma/atopy, early respiratory infection, smoking status, pack-years, daily number of

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
>50% in symptoms was reported, with lower rates reported in persistent smokers for regular cough, regular phlegm, chronic cough or phlegm and wheeze. Symptom prevalence was highest among persistent smokers Annual average estimates of home outdoor PM_{10} concentrations were assigned to each participant for 1990 and 2000 using a validated dispersion model. Annual average PM_{10} concentrations between these years were estimated using fixed site measurement data for 1990–2000 and residential histories of participants. The exposure measure used in the analyses was the difference between the estimated average PM_{10} level outside the subject's home(s) in the 12 months before the second assessment in 2002 and the corresponding mean level in the 12 months before the first visit Home outdoor levels of PM_{10} decreased on average by 6.2 µg/m^3	Persistent reports: subjects with symptoms reports in 1991		cigarettes, years since smoking cessation, passive smoking in general/at work, occupational exposure to airborne irritants), season of each interview and smoking status at follow-up
	Regular phlegm Definition given above – see regular cough New reports: subjects without symptom reports in 1991 Persistent reports: subjects with symptoms reports in 1991		ORs per 10 µg/m^3 decrement in PM_{10} *Entire sample* New reports 0.74 (0.56, 0.99) Persistent reports 0.82 (0.52, 1.33) *Persistent non-smokers* New reports 0.70 (0.49, 0.99) Persistent reports 0.87 (0.43, 1.84) Adjustment – see above
	Chronic cough or phlegm Defined as chronic cough and/or chronic phlegm, with 'chronic' being defined by the presence of the respective symptoms during at least 3 months a year for at least 2 years New reports: subjects without symptom reports in 1991 Persistent reports: subjects with symptoms reports in 1991		ORs per 10 µg/m^3 decrement in PM_{10} *Entire sample* New reports 0.78 (0.62, 0.98) Persistent reports 0.67 (0.40, 1.15) *Persistent non-smokers* New reports 0.71 (0.52, 0.99) Persistent reports 0.35 (0.16, 0.81) Adjustment – see above
11 Schikowski T, Ranft U, Sugiri D, Vierkötter A, Brüning T, Harth V, Krämer U. (2010) Decline in air pollution and change in prevalence in respiratory symptoms and chronic obstructive pulmonary disease in elderly women. *Respir Res*.11:113.			
4,874 women (approximate age 55 years) of a prospective SALIA cohort from the Rhur area, Germany, were first examined between 1985 and 1994. Lung function measurements were taken in a subset (n = 2,593) Follow-up was conducted in 2006–09; the	**Chronic bronchitis** Participants asked whether a physician had ever diagnosed chronic bronchitis and about respiratory symptoms Respiratory symptoms were asked	**PM_{10}**	Estimates and 95% CI (times 100): –0.17 (–4.37, 4.03) per 20 µg/m^3 /10 y
		NO_2	Estimates and 95% CI (times 100): 0.21 (–1.08, 1.50) per 10 µg/m^3 /10 y

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
mean age of the women was >70 years at follow-up. Completed questionnaires (in 2006) received from 2,116 surviving participants. Between 2007 and 2009, 706 women, with lung function measurements at baseline, were invited to extensive examinations. Of these 402 (aged 70–80 years) participated, with 395 having lung function tests The study investigated whether changes in the prevalence of respiratory symptoms and diseases are attenuated by a reduction in outdoor air pollutants Concentration data monitored at stations located nearest to the participant's home. Long-term exposure was characterised by 5-year mean concentrations of PM_{10} and NO_2: (i) for exposure at baseline: the 5-year mean of the year of the baseline examination (within 1985–94) and the preceding 4 years (ii) for exposure at follow-up, the means of the years 2002–06 Across the five study areas, the 5-year mean PM_{10} concentrations declined on average from 46.6 to 26.9 µg/m^3 (IQR range: 10 µg/m^3). For NO_2, the 5-year mean concentrations decreased in average from 38.1 to 27.9 µg/m^3 (IQR range: 12.2 µg/m^3) The individual change in exposure was	as "chronic cough with: (i) phlegm production (ii) for >3 month a year (iii) for more than 2 years" 'Chronic cough' and 'chronic cough with phlegm production' were also evaluated. The diagnosis of chronic cough with phlegm production was positive, when each of the answers categories (i), (ii) or (iii) was positive. This symptoms complex classically defines chronic bronchitis		
	Chronic cough	**PM_{10}**	Estimates and 95% CI (times 100): –8.17 (–14.54, –1.79), p < 0.05 per 20 µg/m^3 /10 y
		NO_2	Estimates and 95% CI (times 100): –1.15 (–3.25, 0.96) per 10 µg/m^3/10 y
	Chronic cough with phlegm production	**PM_{10}**	Estimates and 95% CI (times 100): –5.39 (–10.22, –0.57), p < 0.05 per 20 µg/m^3 /10 y
		NO_2	Estimates and 95% CI (times 100): – 0.87 (–2.41, 0.66) per 10 µg/m^3 /10 y
	Estimates from sensitivity analysis only including non-smoking women varied in an unsystematic way, with the effect for chronic cough being slightly stronger		

Table A1.1: Longitudinal studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
calculated as the difference between the baseline measurement and the measurement at follow-up. Generalised estimating equations (GEE) were used to determine the association between air pollution levels and the prevalence, and changes in prevalence, between respiratory symptoms at baseline and at follow-up. Analyses controlled for smoking behavior. Passive smoking, social status (school education) and exposure to indoor air pollutants were excluded from the final model as they did not change estimates by more than 10%			
12 Barakat-Haddad C, Elliott SJ, Pengelly D (2012) Health impacts of air pollution: a life course approach for examining predictors of respiratory health in adulthood. *Ann Epidemiol.* 22(4): 239–49.			
Participants were between 6 and 8 years of age in 1978 in Hamilton, Ontario, Canada. Participants were followed-up 30 years later, and a questionnaire was used to collect health data in adulthood. 395 individuals (mean age 36 years) completed the survey between August 2005 and February 2007. The study assessed the relationship between childhood exposure to air pollution and respiratory health in adulthood. Mean age of respondents was 36 years	Two health outcomes were examined: (i) diagnosed with at least one respiratory condition in adulthood (asthma or chronic bronchitis or chest conditions, eg pneumonia or lung infections) (ii) persistent respiratory symptoms (ie persistent morning/day/night cough or phlegm or wheeze for as many as 3 months in a row each year	Exposure to TSP, SO_2 and $PM_{3.3}$, in 1983–84 in neighbour-hood of residence in childhood	ORs for the health outcomes in adulthood *Persistent respiratory symptoms in adulthood* TSP (> median, 50 µg/m^3): 0.56 (0.23, 1.34) $PM_{3.3}$ (> median, 52 µg/m^3): 1.26 (0.42, 3.81) SO_2 (> median, 11.7 ppb): 1.03 (0.39, 2.71) ≤ median concentration used as the reference in logistic regression analyses *Diagnosis of any respiratory condition* TSP (> median, 50 µg/m^3): 0.50 (0.11, 2.19) $PM_{3.3}$ (> median, 52 µg/m^3): 0.84 (0.19, 3.68) SO_2 (> median, 11.7 ppb): 1.43 (0.41, 4.94) ≤ median concentration used as the reference in logistic regression analyses

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
13 Lan SP and Shy C (1981) Effect of air pollution on chronic respiratory disease in the New York City metropolitan area, 1972. *Environ Health Perspect*. 42: 203–14.			
In 1972, a questionnaire was administered to parents of children attending elementary school in one of four areas. Data from 5,416 white residents were analysed to determine if air pollution was associated with chronic respiratory disease. About a third of residents in each area were aged <18 years	Reported respiratory symptoms were classified into different levels of severity, with level IV (cough and phlegm for more than 3 months a year) and level V (cough and phlegm accompanied by shortness of breath for more than 3 months a year) used to define chronic bronchitis according to the MRC questionnaire	Paper reports concentrations, by site (A–C) for 1971 and 1972. Site A had lower levels of TSP than sites B and C. Annual geometric mean for site C in 1971 was 78.4 µg/m^3. Site A was the low exposure community No direct measurements were obtained for site D, which was located next to site B. Monitoring data for site B were used to indicate pollution exposure for individuals in site D	Site A used as the basis for comparison in analyses ORs for smokers, by sex *Site B/site A* Males 0.99 (0.61, 1.64) Females 1.43 (0.65, 2.10) *Site C/site A* Males 0.84 (0.56, 1.52) Females 1.02 (0.56, 1.84) *Site D/site A* Males 0.98 (0.61, 1.61) Females 1.18 (0.60, 1.92) ORs for non-smokers, by sex *Site B/site A* Males 2.79 (0.57, 4.16) Females 6.18 (0.41, 12.01) *Site C/site A* Males 1.30 (0.38, 3.28) Females 4.18 (0.33, 10.37) *Site D/site A* Males 1.50 (0.43, 3.30) Females 4.14 (0.34, 10.24) Smoking and level of education of the head of the household were controlled for in the analyses

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
14 Hodgkin JE, Abbey DE, Euler GL, Magie AR (1984) COPD prevalence in nonsmokers in high and low photochemical air pollution areas. *Chest* 86 (6):830–38.			
Study of subset (n = 6,666 adults) of AHSMOG cohort examining the effect of photochemical pollution in California on the prevalence of COPD n = 4,379 for those from a high photochemical pollution area and n = 2,287 for those from a low photochemical pollution area. Of the 6,666, 77.7% (n = 5,178) had never smoked; none were current smokers as they had been excluded during the recruitment phase of the study; 1,482 were past-smokers The National Heart, Lung and Blood Institute respiratory symptoms questionnaire, in addition to other questions, was used to obtain data on the subjects	**Prevalence of 'definite' COPD** Based on having either: (i) 'Definite' chronic bronchitis: symptoms of cough and/or sputum production most days, for at least 3 months a year, for 2 years or more (ii) GP diagnosis of 'definite' asthma and history of wheeze (iii) GP diagnosis of emphysema and shortness of breath when walking or exercising	**Smog** Comparison of those living inside the South Coast Air Basin with those living outside the Air Basin	% increase in risk estimate for prevalence of 'definite' COPD = 15% (2, 35%), p = 0.03 For past-smokers, 22% (5, 43), p = 0.01 Adjusted for past smoker status, adverse occupational exposure, race, sex, age and years of education
15 Euler GL, Abbey DE, Magie AR, Hodgkin JE (1987) Chronic obstructive pulmonary disease symptom effects of long-term cumulative exposure to ambient levels of total suspended particulates and sulfur dioxide in California Seventh-Day Adventist residents. *Arch Environ Health*. 42:213–22.			
Data from 7,445 adults (≥25 years of age) of the Seventh Day Adventist cohort, enrolled in 1974, were used. Participants had lived in their 1977 residential area for at least 10 years in the greater metropolitan areas of Los Angeles and its border counties, San Francisco and San Diego A questionnaire which included questions from the National Heart, Lung and Blood Institute on respiratory symptoms was administered in 1977 109 individuals who indicated that they were currently smoking were excluded from the analyses. 5,539 (75.5%) never smoked,	**COPD symptoms** Based on either: (i) Symptoms of cough and/or sputum production on most days, for at least 3 months a year, for 2 years or more (ii) GP asthma diagnosis and history of wheeze (iii) GP diagnosis of emphysema and shortness of breath when walking either normal paced or hurried	**TSP**	RR 1.22, p < 0.0001, for 750 h/y above 200 µg/m^3 PM_{10} (25% of the study population was exposed to concentrations at or above this level) n = 6,472, cases = 1,023 Adjusted for occupational exposure, years lived with smoker, years worked with smoker, past smoker, sex, age, race and education
		SO_2	RR 1.18, p = 0.03, for 500 h/y above 4 pphm (104 µg/m^3) (13.3% of the study population was exposed to concentrations at or above this level) n = 6,350, cases = 1,003

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
1,498 (20.4%) were past-smokers and smoking history was unknown for 299 (4.1%) Pollutants studied: TSP and SO_2 using several concentration thresholds and exceedance frequencies for 1966–76 and 1973–76, with results reported for the latter. 11-year monthly residential zip code history and monthly interpolated pollution concentrations for each zip code were used to calculate each individual's 11-year cumulative hours and dosage above each concentration threshold for each pollutant			
16 Euler GL, Abbey DE, Hodgkin JE, Magie AR (1988) Chronic obstructive pulmonary disease symptom effects of long-term cumulative exposure to ambient levels of total oxidants and nitrogen dioxide in California Seventh-Day Adventist residents. *Arch Environ Health.* 43:279–85.			
7,445 Seventh Day Adventist non-smokers ≥25 years of age. For further details see Euler *et al* (1987) TSP, NO_2, SO_2 and total oxidants (1966–76 and 1973–76, with results reported for the latter) were examined using four concentration thresholds. 11-year monthly residential zip code history and monthly interpolated pollution concentrations for each zip code were used to calculate each individual's 11-year cumulative hours and dosage above each concentration threshold for each pollutant	**COPD symptoms** (as Euler *et al*, 1987)	**NO_2**	No statistically significant association with exposure above any of the four threshold concentrations. Lowest threshold analysed was 5 pphm, ie 94 µg/m^3
		Total oxidants	RR 1.20, p < 0.004, for 750 h/y above 10 pphm (196 µg/m^3) n = 6,482, cases = 1,026 In three-pollutant analyses, TSP exposure (above 200 µg/m^3 threshold) showed a statistically significant association, p < 0.01
17 Portney PR and Mullahy J (1990) Urban air quality and chronic respiratory disease. *Regional Sci Urban Econ.* 20:407–18.			
Data, in 1979, on illnesses (including respiratory) were obtained from 80,000 adults (≥17 years) using a questionnaire – adults were sampled in the 1979 US National Health Interview Survey	The presence or absence of eight major types of chronic respiratory diseases ranging from hay fever to emphysema. Analyses were conducted using the chronic respiratory disease	**O_3 and TSP**	Annual average of daily maximum ozone concentrations in 1979 was positively but insignificantly correlated with the likelihood of chronic respiratory disease, while TSP was both positively and significantly related to chronic respiratory diseases

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
The authors matched individuals for whom they had complete health and socioeconomic data to air pollution monitors	aggregated together as well as disaggregated into separate diseases. In one model the presence or absence of emphysema, chronic bronchitis, or asthma was analysed		When pollution data, averaged over the 6-year period (1974–79) were used rather than a single's year data, the precision of the estimated coefficient on ozone improved Analyses of the presence or absence of emphysema, chronic bronchitis and asthma did not suggest that ozone is associated with these conditions
18 Xu X and Wang L (1993) Association of indoor and outdoor particulate level with chronic respiratory illness. *Am Rev Respir Dis.* 148:1516–22.			
A sub-sample of adults, aged 40–69 years, from the Beijing Respiratory Health Study from three areas: Dongchen (residential area), Haidian (suburban area) and Shijinshan (industrial area). 44% of subjects reported that they had never smoked. Analyses were conducted in 1,576 never-smokers from the 3,606 adults who completed the survey (1 August and 30 September 1986)	**Chronic cough**: defined as cough for 3 or more months of the year **Chronic phlegm**: sputum production for 3 or more months of the year **Bouts**: increased cough and phlegm lasting for 3 weeks during the last 3 years **Bronchitis**: any history of physician-diagnosed bronchitis with at least one of the following symptoms: chronic cough, chronic phlegm, bouts of cough and phlegm, and wheeze **Shortness of breath (SOB)** when walking at own pace on level ground	Indicators for high, moderate and low outdoor particulate levels were used in the analyses 5-year (1981–85) mean TSP (μg/m^3): Industrial area: 449 Residential area: 389 Suburban area: 261 5-year (1981–85) mean SO_2 (μg/m^3): Industrial area: 57 Residential area: 128 Suburban area: 18	ORs for never-smokers adjusted for gender, age, education, occupational exposure to dusts, gases, or fumes, passive smoking, house crowding, annual income and indoor coal combustion *Cough* Moderate: 1.3 (0.8, 2.2) High: 2.0 (1.1, 3.5) *Phlegm* Moderate: 1.2 (0.8, 1.9) High: 1.6 (1.0, 2.8) *Bouts* Moderate: 1.1 (0.7, 1.9) High: 1.8 (1.0, 3.1) *Bronchitis* Moderate: 1.0 (0.6, 1.6) High: 1.9 (1.1, 3.2) *SOB* Moderate: 1.3 (0.7, 2.3) High: 1.6 (0.8, 3.1) Analyses controlling for indoor air pollution produced estimates which were smaller and statistically insignificant

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
19 Schwartz J (1993) Particulate air pollution and chronic respiratory disease. *Environ Res.* 62:7–13.			
Study of 6,138 adults aged 30–74 years from the NHANES I survey (recruited between1971 and 1975) who completed a detailed medical history questionnaire Pollutant studied: TSP (annual average concentration, calculated for the year preceding the examination). Mean of 85.5 µg/m^3	**Chronic bronchitis** Defined as a positive response to both: (i) "Doctor-diagnosed chronic bronchitis (ever)" (ii) "Do you still have chronic bronchitis?"	**TSP**	OR 1.07 (1.02, 1.12) for a 10 µg/m^3 increase in annual TSP concentrations ORs were adjusted for age, race, sex and smoking When analyses were restricted to never-smokers, TSP remained statistically significant OR 1.11 (1.02, 1.21)
	Respiratory illness Defined as a diagnosis by a physician coded as ICD 8 (460–519)		OR 1.06 (1.02, 1.10) for a 10 µg/m^3 increase in annual TSP concentrations When analyses were restricted to never-smokers, OR 1.07 (0.996, 1.15)
	Dyspnoea Defined as shortness of breath when hurrying on a level or walking up a slight hill		No association found – no estimates provided in the paper
20 Scarlett JF, Griffiths JM, Strachan DP, Anderson HR (1995) Effect of ambient levels of smoke and sulphur dioxide on the health of a national sample of 23 year old subjects in 1981. *Thorax*. 50:764–8.			
11,552 members of the 1958 British Birth Cohort study, 23 years of age in 1981, Black Smoke and SO_2 in 1981 For each pollutant, subjects were grouped into five exposure categories, based on ranked annual average concentrations of each county. A combined exposure (Black Smoke and SO_2) group was also analysed Other health outcomes analysed: asthma/wheezy bronchitis – based on responses to the following questions: (i) "Have you suffered from asthma or wheezy bronchitis since your 16th birthday?"	**Cough symptoms** A "yes" answer to either question: (i) "Do you usually cough first thing in the morning in winter?" (ii) "Do you usually cough during the day or night during the winter?"	**Black Smoke**	ORs adjusted for smoking, social class and sex (n = 8,961) 2–13 µg/m^3 : 1.00 13.1–18.7 µg/m^3 : 1.19 19.6–20.8 µg/m^3 : 1.12 21.0–25.8 µg/m^3 : 1.25 26.1–55.1 µg/m^3 : 1.16 p = 0.17 for linear trend using median concentration
		SO_2	ORs (n = 9,042) 7–36.4 µg/m^3: 1.00 36.7–42.7 µg/m^3: 1.21 43.0–50.5 µg/m^3: 0.96 52.0–59.3 µg/m^3: 0.99

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
and (ii) "Have you suffered from asthma or wheezy bronchitis in the past 12 months?"			60.9–87.7 µg/m^3: 1.03
	Phlegm symptoms A yes answer to either question: (i) "Do you usually bring up phlegm first thing in the morning in winter?" (ii) "Do you usually bring up phlegm during the day or night during winter?"	**Black Smoke**	ORs (n = 8,961) 2–13 µg/m^3: 1.00 13.1–18.7 µg/m^3: 1.36 19.6–20.8 µg/m^3: 1.34 21.0–25.8 µg/m^3: 1.48 26.1–55.1 µg/m^3: 1.20 p = 0.04 for non-linear trend using log of median concentration
		SO_2	ORs (n = 9,042) 7–36.4 µg/m^3: 1.00 36.7–42.7 µg/m^3: 1.15 43.0–50.5 µg/m^3: 0.94 52.0–59.3 µg/m^3: 1.12 60.9–87.7 µg/m^3: 1.03
	Combined exposure (Black Smoke and SO_2) group: phlegm symptoms increased with increasing exposure, but this was not statistically significant. No association between cough symptoms and the combined exposure variable		
21 Forsberg B, Stjernberg N, Wall S (1997) Prevalence of respiratory symptoms and hyperreactivity symptoms in relation to levels of criteria air pollutants in Sweden. *Eur J Pub Health*. 7: 291–6.			
Cross-sectional study of 6,109 adults in Sweden (approximately 53% female), aged 16–70 years (mean age around 44 years), which investigated associations between air pollutants (Black Smoke, SO_2 and NO_2) and respiratory symptoms from areas around 55 air quality monitoring stations in Swedish towns Pollutant measurements were collected between October 1989 and March 1990 (6 months). Correlations between pollutants were reported Respiratory symptom (nine analysed) data and details on confounders were collected	**Cough**: "During the last 3 months how often have you had the following symptoms: cough, allergic rhinitis/hayfever, asthma, eye irritation, throat irritation, nose irritation?" (never/rarely, sometimes, often) **Persistent cough: "**Do you have a cough for more than 2 weeks when you have a common cold?" **Phlegm**: "Do you cough up phlegm from your chest in the morning?"	Mean concentration (range): Black Smoke: 9 (4–17 µg/m^3) SO_2: 6 (2–16 µg/m^3) NO_2: 19 (9–32 µg/m^3) Upper quartile limits Black Smoke: 10 µg/m^3 SO_2: 8 µg/m^3 NO_2: 22 µg/m^3 Analyses used different air pollution categories (medium and high – ie third and upper	ORs adjusted for age, sex, parental asthma, daily smoking and self-reported vehicle exposure almost every day at work *Cough* Black Smoke medium: 1.24 (0.94, 1.47) Black Smoke high: 1.08 (0.80, 1.46) SO_2 medium: 1.24 (0.64, 1.62) SO_2 high: 1.48 (1.15, 1.90) Among men, residence in the third quartile of SO_2 – OR =1.87 (1.26, 2.79) NO_2 medium: 1.10 (0.82, 1.49) NO_2 high: 1.41 (1.07, 1.87) Among women, residence in the upper

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
using a postal questionnaire sent in March 1990		quartiles); the first and second quartiles were used as reference categories. Vehicle exhaust also examined	quartile of NO_2 – OR =1.49 (1.04, 2.13) Vehicle exhausts: 1.67 (1.25, 2.23) *Persistent cough* Black Smoke medium: 1.14 (0.93, 1.39) Black Smoke high: 1.17 (0.96, 1.43) SO_2 medium: 0.97 (0.80, 1.25) SO_2 high: 1.19 (0.99, 1.42) NO_2 medium: 0.96 (0.79, 1.17) NO_2 high: 1.08 (0.89, 1.32) Vehicle exhausts: 1.60 (1.30, 1.97) *Phlegm* Black Smoke medium: 1.09 (0.92, 1.29) Black Smoke high: 1.07 (0.90, 1.29) SO_2 medium: 1.17 (1.00, 1.37) SO_2 high: 1.18 (1.00, 1.38) Among women, the upper quartile of SO_2 – OR =1.34 (1.07, 1.67) NO_2 medium: 1.04 (0.87, 1.25) NO_2 high: 0.96 (0.88, 1.23) Vehicle exhausts: 1.36 (1.13, 1.65)
22 Galizia A and Kinney P (1999) Long-term residence in areas of high ozone: associations with respiratory health in a nationwide sample of nonsmoking young adults. *Environ Health Perspect*. 107: 675–9.			
A study conducted in 623 freshmen from Yale College (New Haven, CT) investigating the associations between lung function and chronic respiratory symptoms and individual long-term estimates of ozone exposure. The paper reported results from the first year of a 3-year study for 520 subjects (17–21 years) who reported never having smoked Health data were collected using a questionnaire which included questions on	**Phlegm:** "Do you usually bring up phlegm from your chest?"	**O_3**	OR 1.79 (0.83, 3.82), p = 0.14, for comparing respiratory symptoms in all subjects across ozone strata Analyses stratified by sex could not be performed as frequencies were too low for gender comparisons Control for a range of covariates including sex, race, parental education and maternal smoking was conducted

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
respiratory symptom and disease adapted from the ATS adult questionnaire 10-year average summer month (June–August) values for O_3 were derived using hourly concentration data from monitoring sites from 1981–90. Ozone exposure was analysed as a dichotomous variable derived by identifying individuals (based on residential histories) who lived at any time for at least 4 years in US counties with 10-year average summer concentrations of O_3 ≥80ppb. Subjects who met this criterion were assigned to the high exposure class	**Respiratory symptom index (RSI)** Symptoms included: cough ("Do you usually have cough?"), phlegm ("Do you usually bring up phlegm from your chest?"), wheeze ("Does your chest ever sound wheezy or whistling occasionally apart from colds?") A composite RSI was also constructed, with a value of one indicating any of the individual symptoms reported		OR 2.00 (1.15, 3.46), p = 0.01, for comparing respiratory symptoms in all subjects across ozone strata
23 Zemp E, Elsasser S, Schindler C, Künzli N, Perruchoud AP, Domenighetti G, *et al* (1999) Long-term ambient air pollution and respiratory symptoms in adults (SAPALDIA study). The SAPALDIA Team. *Am J Respir Crit Care Med.* 159:1257–66.			
SAPALDIA – multi-centre, cross-sectional study of 9,651 adults (49.2% male; aged 18–60 years) selected from eight sites in Switzerland in 1991. Participants were required to have lived in an area for at least 3 years to be eligible Annual average (SD) of measured air pollutants in 1991: SO_2 : 11.7 (7.1); range 2.5–25.5 µg/m^3 NO_2 : 35.6 (16.0); range 9.2–57.7 µg/m^3 PM_{10} (for 1993): 21.2 (7.4); range 10.1– 33.4 µg/m^3 O_3: 43.1 (9.5); range 31.5–55.2 µg/m^3 O_3 summer daytime: 92.0 (12.9); range 79.2–118.2 µg/m^3 O_3 excess: 1.21 (1.47); range 0.015–4.72 µg y/m^3 Respiratory symptom information was	**Chronic phlegm** Defined as a positive answer to the question: "Do you usually bring up any phlegm from your chest during the day, or at night, on most days for as much as 3 months each year?" and an answer of ≥2 to the question "For how many years have you brought up phlegm like this?"	**PM_{10}**	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence of chronic phlegm OR 1.35 (1.11, 1.65) Estimates adjusted for age, BMI, gender, parental asthma, parental atopy, low level of education and foreign citizenship
		NO_2	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence of chronic phlegm
		O_3	No association found with annual mean concentration. However, an association between chronic phlegm and excess ozone (see paper for definition) was found
	Chronic cough or phlegm	**PM_{10}**	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence OR 1.27 (1.08, 1.50)

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
collected using a modified version of the ECRHS questionnaire Only results for never-smokers have been summarised. Results for former and current smokers are also reported in the paper		**NO_2**	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence
	Chronic cough Defined as a positive answer to the question "Do you usually cough during the day, or at night, on most days for as much as 3 months each year?" and an answer of ≥2 to the question "For how many years have you coughed liked this?"	**PM_{10}**	OR 1.11 (0.88, 1.41)
	Breathlessness during the day "Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?"	**PM_{10}**	OR 1.48 (1.23, 1.78)
		NO_2	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence of chronic phlegm
	Breathless at night "Have you been awakened by an attack of shortness of breath at any time in the last 12 months?"	**PM_{10}**	OR 1.11 (0.92, 1.35)
	Breathlessness, day or night	**PM_{10}**	OR 1.33 (1.14, 1.55)
		NO_2	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence of chronic phlegm
	Dyspnoea on exertion "Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?"	**PM_{10}**	OR 1.32 (1.18, 1.46)
		NO_2	Positive association found for a 10 µg/m^3 increase in annual mean concentration and change in prevalence of chronic phlegm

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
24 Zhang J, Qian Z, Kong L, Zhou L, Yan L, Chapman RS (1999) Effects of air pollution on respiratory health of adults in three Chinese cities. *Arch Environ Health*, 54:373–81.			
A study assessing the effects of chronic exposures to high ambient air pollution on the prevalence rates of respiratory symptoms and illness in adults (n = 4,108) who resided in four districts (three urban, one suburban) of three large Chinese cities. All participants were <49 years of age, with the majority <40 years of age Health data were collected using an adapted ATS questionnaire	**Cough:** often coughs, either with colds or in the absence of colds **Phlegm:** bringing up phlegm or mucus from the chest with colds or in the absence of colds **Persistent cough and phlegm:** had both cough and phlegm from the chest for at least 3 months a year **Bronchitis:** ever diagnosed as having bronchitis by a physician	**Districts used as the indicator of exposure** Ambient pollution data (1985-1988) were used to calculate 4-year average concentrations of: TSP (μg/m^3) Guangzhou: 296 Wuhan suburban: 191 Wuhan urban: 406 Lanzhou: 1067 SO_2 (μg/m^3) Guangzhou: 110 Wuhan suburban: 19 Wuhan urban: 92 Lanzhou: 121 NO_X (μg/m^3) Guangzhou: 89 Wuhan suburban: 18 Wuhan urban: 78 Lanzhou: 92	ORs for cough and phlegm were highest in the Lanzhou district (ie the district that had the highest 4-year mean concentration for each pollutant considered) ORs for the Lanzhou district *Cough* Men: 2.78 (2.13, 3.64) Women: 5.14 (3.86, 6.85) *Phlegm* Men: 1.67 (1.26, 2.23) Women: 2.06 (1.47, 2.89) *Bronchitis* Men: 8.27 (5.39, 12.68) Women: 9.69 (5.50, 17.06) ORs adjusted for age, years of residence in present district, occupation, education, home coal use, smoking status and indoor ventilation device use ORs for the other areas were reported. These ORs were largely >1 for all outcomes in both men and women, with the exception of bronchitis in men in the Wuhan urban area. In terms of statistical significance, the ORs for phlegm and bronchitis in men and for phlegm in women in the Wuhan suburban area did not achieve significance
25 Solomon C, Poole J, Jarup L, Palmer K, Coggon D (2003) Cardio-respiratory morbidity and long-term exposure to particulate air pollution. *Int J Environ Health Res.* 13:327–35.			
Cross-sectional study of 1,166 women aged 45 years or older from 11 electoral wards in the UK. Participants lived within 5 miles of their address for at least 30 years	**Productive cough:** usually bring up phlegm first thing in the morning in both winter and summer	**Black Smoke** for the period 1966–97. Mean concentrations for each ward, by year intervals, were reported	RR for productive cough 1.0 (0.7, 1.5)

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
		Exposure analysed as a categorical variable: low pollution in place of residence (<50 µg/m^3) and high (>120 µg/m^3). The exposure categories were based on Black Smoke levels during 1966–69	
26 Kumar R, Sharma M, Srivastva A, Thakur JS, Jindal SK, Parwana HK (2004) Association of outdoor air pollution with chronic respiratory morbidity in an industrial town in northern India. *Arch Environ Health.* 59:471–7.			
A study conducted in 3,603 individuals (>15 years) from one industrial and one non-industrial area in Punjab State, northern India. The mean age of men and women was <40 years in both study and reference towns Health data were collected using questionnaires (for symptoms of chronic respiratory diseases listed in the MRC questionnaire) and lung function tests (collected for 2,953 individuals)	A subject was regarded as having **chronic respiratory symptoms** if they had cough, phlegm, breathlessness or wheezing for more than a month	**Residence in a town with poor air quality** Ambient pollution data were collected from each area over a period of 2 years: TSP, NO_X, SO_X and O_3. CO was measured from July 2000 to December 2001. PM_{10} was measured from January 2000 to December 2001 Mean concentration in the study and reference towns for 2000–01: PM_{10} (µg/m^3) Study town: 112.8 Reference town: 75.8 NO_X (µg/m^3) Study town: 27.4 Reference town: 7.4	Increased risk of having chronic respiratory symptoms was OR 1.5 (1.2, 1.8), p < 0.001, in the high vs low air pollution town OR adjusted for age, gender, education, income, occupation, ever smoking, passive smoking, type of cooking fuel use and migrant status

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
27 Sekine K, Shima M, Nitta Y, Adachi M (2004) Long term effects of exposure to automobile exhaust on the pulmonary function of female adults in Tokyo, Japan. *Occup Environ Med.* 61:350–57.			
Cross-sectional study of 5,682 females aged 30–90 years who lived in the Tokyo metropolitan area for 3 years or more in 1987 Questionnaire administered between July and August 1987 was used to assess the prevalence of respiratory symptoms	**Persistent cough:** for ≥3 months a year, cough almost every day **Persistent phlegm:** for ≥3 months a year, phlegm almost every day **Breathlessness:** breathing difficulty in walking a flat road and not catching up with people of the same generation	Subjects were divided into three groups by the level of air pollution. The roadside areas and areas behind the roads (18 areas in total) in nine districts were classified into three groups by the level of air pollution (mean NO_2 and mean SPM concentrations) **Group 1**: both NO_2 (mean 0.047–0.056 ppm) and SPM (mean 48–62 µg/m^3) concentrations were high. The daytime average traffic density (in 1990) exceeded 20,000 vehicles including 4,000 large vehicles in each district **Group 2**: both NO_2 (mean 0.038–0.046 ppm) and SPM (mean 38–46 µg/m^3) concentrations were moderate. The traffic density in the roadside areas was 10,000–20,000 vehicles, including, <3,000 large vehicles	ORs for symptoms compared with the status in group 3 (p value for trend) *Persistent cough* Group 3: 1.00 Group 2: 1.02 (0.70, 1.48) Group 1: 1.07 (0.67, 1.70) p = 0.788 *Persistent phlegm* Group 3: 1.00 Group 2: 1.51 (1.11, 2.04) Group 1: 1.78 (1.26, 2.53) p = 0.001 *Breathlessness* Group 3: 1.00 Group 2: 0.84 (0.47, 1.50) Group 1: 2.70 (1.48, 4.91) p = 0.001

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
		Group 3: both NO_2 (mean 0.024–0.036 ppm) and SPM (mean 28–39 µg/m^3) concentrations were low. The traffic density in the roadside areas in Ome City was 8,641 vehicles	
28 Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann HE, Krämer U (2005) Long-term air pollution exposure and living close to busy roads are associated with COPD in women. *Respir Res*. 6:152.			
4,757 women (approximate mean age of 55 years) from the Rhine-Ruhr area, Germany, were investigated in consecutive cross-sectional assessments between 1985 and 1994 to determine the effect of long-term exposure to air pollution on COPD, defined by lung function, and respiratory symptoms. Women were participants of the SALIA cohort study Questionnaire data were collected on health outcomes and risk factors. 40.1% of participants reported to be never-smokers (without environmental tobacco smoke) Pollutants studied: NO_2 and PM_{10} (derived from TSP using a 0.71 conversion factor) – medium-term exposure (annual mean concentration) and long-term exposure (5-year mean concentration) ORs presented for an IQR increase in PM_{10} (7 µg/m^3) and NO_2 (16 µg/m^3) exposure and for living nearer than 100 m from a road with heavy traffic compared with ≥100 m	**Chronic bronchitis** Participants asked whether a physician had ever diagnosed chronic bronchitis and about respiratory symptoms Respiratory symptoms were asked as "Chronic cough with: (i) phlegm production (ii) for >3 months a year (iii) for >2 years" 'Chronic cough' and 'chronic cough with phlegm production' were also evaluated. The diagnosis of chronic cough with phlegm production was positive, when each of the answers categories (i), (ii) or (iii) was positive Sample size of all women (n_1) = 4,205 Sample size of women living at least 5 years at their residence	**PM_{10}**	OR 1.00 (0.85, 1.18) for a 7 µg/m^3 IQR range increase in the annual PM_{10} concentration OR 1.13 (0.95, 1.34) for a 7 µg/m^3 IQR range increase in the 5-y PM_{10} concentration
		NO_2	OR 1.25 (1.00, 1.58), $p < 0.1$, for a 16 µg/m^3 IQR range increase in the annual NO_2 concentration OR 1.37 (1.16, 1.62), $p < 0.01$, for a 16 µg/m^3 IQR range increase in the 5-y NO_2 concentration
		<100 m from major road with 10,000 cars/day compared to >100 m	1.15 (0.89, 1.50)

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	(n_s) = 3,716 Women living less than 5 years at their residence were excluded from the analyses of 5-year means of air pollutants		
	Chronic cough with phlegm production n_1 = 4,237 n_s = 3,792	**PM_{10}**	OR 1.03 (0.8, 1.23) for a 7 µg/m³ IQR range increase in the annual PM_{10} concentration OR 1.11 (0.93, 1.31) for a 7 µg/m³ IQR range increase in the 5-y PM_{10} concentration
		NO_2	OR 1.11 (0.85, 1.45) for a 16 µg/m³ IQR range increase in the annual NO_2 concentration OR 1.22 (0.90, 1.64) for a 16 µg/m³ IQR range increase in the 5-y NO_2 concentration
		<100 m from major road with 10,000 cars/day compared to >100 m	1.07 (0.83, 1.37)
	Frequent cough n_1 = 4,262 n_s = 3,813	**PM_{10}**	OR 1.01 (0.93, 1.10) for a 7 µg/m³ IQR range increase in the annual PM_{10} concentration OR 1.05 (0.94, 1.17) for a 7 µg/m³ IQR range increase in the 5-y PM_{10} concentration
		NO_2	OR 1.13 (1.01, 1.27), $p < 0.05$, for a 16 µg/m³ IQR range increase in the annual NO_2 concentration OR 1.15 (0.99, 1.33), $p < 0.1$, for a 16 µg/m³ IQR range increase in the 5-y NO_2 concentration
		<100 m from major road with 10,000 cars/day compared to >100 m	1.24 (1.03, 1.49), $p < 0.05$

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
29 Bennett CM, Simpson P, Raven J, Skoric B, Powell J, Wolfe R, *et al* (2007) Associations between ambient $PM_{2.5}$ concentrations and respiratory symptoms in Melbourne, 1998–2005. *J Toxicol Environ Health A*. 70:1613–18.			
Two cohorts were recruited in Melbourne in 1998–99 and followed up in 2004–05. n = 1,600 at baseline; n = 1,446 at follow-up (442 of which were recruited from the ECRHS study in Melbourne). All participants completed the ECRHS questionnaire for both time intervals. Mean age at baseline 37.2 years (based on combined cohort; the ECRHS cohort was slightly older) Measured annual $PM_{2.5}$: Daily mean over the previous 12 months (based on a combination of baseline and follow-up): 6.8 µg/m^3 Daily mean over the 12 months prior to baseline: 6.5 µg/m^3 Daily mean over the 12 months prior to follow-up: 7.1 µg/m^3 Both individual mean level of average $PM_{2.5}$ and deviations from the mean were analysed to assess within-person and between-person effects	**Cough with phlegm in the morning**	**$PM_{2.5}$**	Within-person (longitudinal) OR 1.28 (0.70, 2.33) Between-person (cross-sectional) OR 0.28 (0.08, 0.97) ORs per 1 µg/m^3, adjusted for age and gender at baseline, use of β_2-agonist reliever medication, use of inhaled corticosteroids, smoking and year of data collection
	Cough in the morning		Within-person (longitudinal) OR 0.74 (0.47, 1.15) Between-person (cross-sectional) OR 0.21 (0.07, 0.62)
	Phlegm in the morning		Within-person (longitudinal) OR 1.55 (0.95, 2.53) Between-person (cross-sectional) OR 0.49 (0.16, 1.44)
	Shortness of breath on waking		Within-person (longitudinal) OR 1.34 (0.84, 2.16) Between-person (cross-sectional) OR 1.29 (0.46, 3.60)
30 Schikowski T, Sugiri D, Reimann V, Pesch B, Ranft U, Krämer U (2008) Contribution of smoking and air pollution exposure in urban areas to social difference in respiratory health. *BMC Public Health*. 8: 179.			
The study population comprised 4,874 German women aged 54–55 years at the time of baseline. Only data from women with successful spirometry and with complete questionnaire data about education and covariates in the current	**Frequent cough with phlegm production**	**PM_{10}**	OR 1.09 (0.85, 1.41) for an IQR range increase of 7 µg/m^3
		Distance to major road (<100 m) with >10,000 cars/day	OR 1.02 (0.68, 1.53)

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
analysis (n = 1,251) were used. This exclusion enabled comparison of the effects on lung function with effects on respiratory symptoms in the same study group The following outcomes were assessed using a questionnaire: chronic bronchitis and bronchial asthma diagnosed by a physician, frequent cough, and frequent cough with phlegm production as well as medication NO_2 and PM_{10} (scaled from TSP using a 0.71 conversion factor). 5-year mean values for exposure to PM_{10} and NO_2 were 49.4 µg/m^3 and 49.2 µg/m^3, respectively. The mean distance to the nearest road with more than 10,000 cars a day was 519 m	**Frequent cough**	**PM_{10}**	OR 1.06 (0.87, 1.28) for an IQR range increase of 7 µg/m^3
		Distance to major road (<100 m) with >10,000 cars/day	1.13 (0.83, 1.53)
31 Bentayeb M, Helmer C, Raherison C, Dartigues JF, Tessier JF, Annesi-Maesano I (2010) Bronchitis-like symptoms and proximity air pollution in French elderly. *Respir Med.* 104(6): 880–88.			
First baseline study conducted in 1999–2001. 2,104 elderly participants (≥65 years) from Bordeaux (selected from the 3 Cities study of Bordeaux, Dijon and Montpellier). 574 people were seen in 1999, 1380 in 2000 and 150 in 2001. 61% of the population were women. Mean age of 75 years Dispersion modelled pollution concentration at individuals' addresses for 1999–2001. Mean (min, max) in µg/m^3: PM_{10}: 23.1 (19, 51); NO_2: 28 (18, 72.2); SO_2: 7.5 (5, 13.7). Benzene, VOCs and CO were also examined Exposure analysed as a categorical (low vs high) variable, with the latter defined	**Usual cough**	**PM_{10}**	OR 1.01 (0.96, 1.06) per 1 µg/m^3 increase All ORs adjusted for age, sex, smoking, income of household, level of education, occupation, BMI and heart failure
		NO_2	OR 1.01 (0.99, 1.04) per 1 µg/m^3 increase
		SO_2	OR 1.23 (1.11, 1.36) per 1 µg/m^3 increase
	Usual phlegm	**NO_2**	OR 1.01 (0.98, 1.04) per 1 µg/m^3 increase
		SO_2	OR 1.24 (1.10, 1.39) per 1 µg/m^3 increase

Table A1.2: Cross-sectional studies of chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
according to the third quartile of the concentration distribution, and as a continuous variable (per 1 µg/m^3 increase). Only available results for the latter are summarised in this table Analyses were conducted by assigning to each subject the estimation of the mean exposure to air pollution in the year in which they had participated in the survey Furthermore, a sensitivity analysis was conducted in the sub-sample of individuals seen in 2000 and 2001 by taking into account 3-year and 2-year mean exposure to proximity air pollution			
32 Nachman KE and Parker JD (2012). Exposures to fine particulate air pollution and respiratory outcomes in adults using two national datasets: a cross-sectional study. *Environ Health*. 11:25.			
2002–05 data from the US National Health Interview Survey (48 US states) 124,375 adults ≥18 years of age. Data for 109,485 adults available for analyses Annual (modelled) $PM_{2.5}$ for 2002–05: mean 12.1 µg/m^3; max 27.5 µg/m^3	**Chronic bronchitis**: doctor/health professional diagnosis of the condition in the past 12 months 4.3% of the population had chronic bronchitis in the last year	**$PM_{2.5}$**	OR 1.08 (0.94, 1.24) per 10 µg/m^3 increase in $PM_{2.5}$. OR adjusted for sex, age group, smoking status, urbanicity, health insurance type, education, income, BMI and exercise Estimates for subgroups, defined by race/ethnicity, also reported

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
33 Nitta H, Sato T, Nakai S, Maeda K, Aoki S, Ono M (1993) Respiratory health associated with exposure to automobile exhaust. I. Results of cross-sectional studies in 1979, 1982, and 1983. *Arch Environ Health*. 48:53–8.			
Three cross-sectional studies conducted in 1979, 1982 and 1983, of female residents living close to major roadways in Tokyo. The women were aged 40+ years and lived for more than 3 years in one of the survey areas. Mean age of subjects was 48.9 years in 1979 and 49 years in 1982 and 1983	Prevalence of: **Chronic cough/phlegm** on most days for 3 consecutive months or more during the year **Shortness of breath** – grade 2, walk slower than people of same age on level ground	Distance of residence from the roadside in different years: 1979 (<20 m and 20–150 m) 1982 (<20 m, 20–50 m and 50–150 m) 1983 (<20 m and 20–150 m)	ORs adjusted for age, smoking status, years at residence, education, occupation type and type of home heating. Except for 1982, ORs are for <20 m vs 20–150 m *Chronic cough* 1979: 1.62 (1.07, 2.46) 1982: <20 m vs 50–150 m: 1.35 (0.88, 2.07) 20–50 m vs 50–150 m: 1.78 (1.20, 2.67) 1983: 1.45 (0.98, 2.13) *Chronic phlegm* 1979: 1.47 (1.03, 2.11) 1982: <20 m vs 50–150 m: 1.87 (1.31, 2.68) 20–50 m vs 50–150 m: 1.85 (1.30, 2.64) 1983: 1.26 (0.94, 1.70) *Shortness of breath* 1979: 1.41 (0.89, 2.24) 1982: <20 m vs 50–150 m: 1.42 (0.94, 2.15) 20–50 m vs 50–150 m: 0.76 (0.47, 1.20) 1983: 1.66 (1.12, 2.48)
34 Oosterlee A, Drijver M, Lebret E, Brunekreef B (1996) Chronic respiratory symptoms in children and adults living along streets with high traffic density. *Occup Environ Med*. 53(4):241–7.			
A sample of 673 adults and 106 children (0–15 years) living along busy traffic streets in the town of Haarlem and surrounding communities in the Netherlands	Definitions of health outcomes were not provided in the paper The questionnaires contained questions derived from the WHO, MRC and ATS questionnaires	Busy traffic streets were selected using traffic maps for NO_2 A control population, a street with little traffic was chosen in the same neighbourhood	ORs for adults Chronic cough in the past 2 years: 0.9 (0.5, 1.4) Chronic cough with phlegm in the past 2 y: 0.8 (0.5, 1.4)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
Questionnaires were posted to all occupants of homes in the sample in February 1991			Dyspnoea – occasionally (during walking): 1.8 (1.1, 3.0) ORs adjusted for age, sex, education, smoking, presence of an unvented geyser, presence of a gas cooker, home humidity, presence of pet animals, crowding and, when relevant, exposure to possible harmful air pollution at work. As to dyspnoea, adjustment for heart disease was included as well ORs for children also available
35 Nakai S, Nitta H, Maeda K (1999) Respiratory health associated with exposure to automobile exhaust. III. Results of a cross-sectional study in 1987, and repeated pulmonary function tests from 1987 to 1990. *Arch Environ Health*. 54:26–33.			
2,600 women aged 30–59 years from Tokyo who lived in the same residence for at least 3 years. A questionnaire was used to collect data on respiratory symptoms	**Chronic cough** for 3 or more months of the year **Chronic phlegm** for 3 or more months of the year **Breathlessness:** walk slower than most people of same age on level ground	Three zones defined based on proximity to roads: Zone A: <20 m Zone B: 20–150 m Zone C: a residential district of suburban Tokyo away from roads with heavy traffic	ORs adjusted for age, years at residence, job status, smoking habit, type of heater used in home and structure of house *Chronic cough* Zone A vs zone C: 2.18 (1.08, 4.42) Zone B vs zone C: 1.17 (0.58, 2.35) Zone A vs zone B: 1.87 (1.02, 3.42) *Chronic phlegm* Zone A vs zone C: 1.79 (1.07, 3.01) Zone B vs zone C: 1.29 (0.80, 2.08) Zone A vs zone B: 1.40 (0.88, 2.21) *Breathlessness* Zone A vs zone C: 1.16 (0.66, 2.04) Zone B vs zone C: 1.40 (0.87, 2.25) Zone A vs zone B: 0.83 (0.50, 1.38)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
36 Duki MI, Sudarmadi S, Suzuki S, Kawada T, Tri-Tugaswati A (2003) Effect of air pollution on respiratory health in Indonesia and its economic cost. *Arch Environ Health*. 58:135–43.			
Study of 16,663 pairs of junior high school students and their mothers (approximate mean age of 40 years) conducted in October 1996 and 1997. An Indonesian version of the ATS questionnaire was used	**Cough:** "Do you usually cough, even when you do not have a cold?" **Persistent cough:** "Do you usually cough 4 consecutive days or more a week during 3 months of the year?" **Phlegm:** "Do you usually bring up phlegm, even when you do not have a cold?"	See table 2 of the paper: NO_2 concentrations reported for each school in examined from eight areas: "The NO_2 concentrations in the Jabotabek and Cianjur areas were measured in 1994–1997, in Lampung in 1996–1997, and in Bandung in 1996. The badges were placed on a shelf 1–2 m above ground in the schoolyards for 24 h, during each of Indonesia's two seasons (rainy and dry), in alternate years (in October 1994/1996 and in April 1995/1997). During each measurement period, the badges were left in place for 3 consecutive days. The average NO_2 concentrations for these periods were used in the analysis." Living <20 m from a wide road (6 m wide or wider)	β (p value) for mothers' symptoms (n =16,633) *Cough* NO_2: 0.242 (0.118) Living <20 m from a wide road: 0.302 (0.056) *Persistent cough* NO_2: 0.053 (0.715) Living <20 m from a wide road: 0.375 (0.015) *Phlegm* NO_2: 0.356 (0.015) Living <20 m from a wide road: 0.166 (0.247)
37 Garshick E, Laden F, Hart JE, Caron A (2003) Residence near a major road and respiratory symptoms in US veterans. *Epidemiology*. 14:728–36.			
Cross-sectional study of 5,654 male veterans drawn from the general population of south-eastern Massachusetts between 1988 and 1992	**Chronic cough:** cough on most days for 3 consecutive months or more during the year	Residential address within 50 m of a major road compared with subjects living >400 m or more away	OR 1.24 (0.92, 1.68) All ORs adjusted for smoking, occupational dust and age
		Average daily traffic volume within 50 m of a major road	ORs ≥10,000 vehicles/day: 1.29 (0.87, 1.91) ≤10,000 vehicles/day: 1.21 (0.85, 1.72)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	Chronic phlegm: phlegm on most days for 3 consecutive months or more during the year	Residential address within 50 m of a major road compared with subjects living >400 m or more away	OR 1.18 (0.88, 1.56)
		Average daily traffic volume within 50 m of major road	ORs ≥10,000 vehicles/day: 1.40 (0.97, 2.02) ≤10,000 vehicles/day: 1.03 (0.74, 1.45)
38 Burr ML, Karani G, Davies B, Holmes BA, Williams KL (2004) Effects on respiratory health of a reduction in air pollution from vehicle exhaust emissions. *Occup Environ Med*. 61:212–18.			
Study examining changes in respiratory symptoms in residents of congested and uncongested streets in an area of north Wales following the construction of a bypass A baseline survey conducted in 1996–97 (386 subjects in congested streets and 435 in uncongested streets), with follow-up in April 1999 to February 2000. Mean age of participants at baseline was approximately 38 years. The bypass opened on 6 March 1998 165 subjects and 283 subjects in the congested and uncongested streets provided information before and after the opening of the bypass	**Winter cough:** a cough in the winter that occurs on most days for as much as 3 months each year **Winter phlegm:** similar definition as for winter cough	**Counts of heavy goods vehicles (HGVs)** Congested streets 1996–97: 74 1998–99: 39 Change: –46.9% **PM_{10} (µg/m³)** Congested streets 1996–97: 35.2 1998–99: 27.2 Change: –22.7% Uncongested streets 1996–97: 11.6 1998–99: 8.2 Change: –28.9% **$PM_{2.5}$ (µg/m³)** Congested streets 1996–97: 21.2 1998–99: 16.2 Change: –23.5% Uncongested streets 1996–97: 6.7 1998–99: 4.9 Change: –26.6%	Changes in the reporting of symptoms in individuals who completed questionnaires in 1996–97 and in 1999–2000. Difference in net percentage better (95% CI) – expressed as the improvement in congested streets minus the improvements in uncongested streets Winter cough: 1.5 (–6.2, 9.3) Winter phlegm: 0 (–0.7, 7.6)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
39 Karita K, Yano E, Tamura K, Jinsart W (2004) Effects of working and residential location areas on air pollution related respiratory symptoms in policemen and their wives in Bangkok, Thailand. *Eur J Public Health*. 14:24–6.			
530 policemen and their wives from Bangkok. Mean age of policemen and their wives was 37.8 and 36.1 years, respectively Health information was collected between December 1998 and 1999 using a questionnaire	Respiratory symptoms in policemen and wives were classified as: **Frequent cough:** positive response to questions regarding coughs occurring four to six times a day, for 4 or more days a week **Frequent phlegm:** two or more times a day, for 4 or more days a week **Breathlessness:** having to stop for breath when walking at own pace on the level	The residential addresses were divided into four areas determined by the distance from the city centre of Bangkok: <8 km in area H (heavily polluted) 8–15 km in area M (moderately polluted) 16–25 km in area L (less polluted) >25 km in area R (rural) The annual average PM_{10} levels were 80 µg/m^3 or more in area H, between 70 and 60 µg/m^3 in area M and less than 60 µg/m^3 in area L Residential area was treated as a continuous variable using the four strata (H = 3, M = 2, L = 1 and R = 0) and working area using the three strata (H = 3, M = 2 and L = 1), after checking for linearity	ORs for respiratory symptoms of frequent cough or phlegm *Policemen (husbands)* Residential area 0.88 (0.64,1.20) Working area 1.27 (1.01,1.61) *Policemen's wives* Residential area 1.53 (1.10,2.13) ORs were adjusted for age, residential area, education, smoking, domestic pets, working area, working years and history of dust exposure for policemen (only the first five variables for policemen's wives)
40 Heinrich J, Topp R, Gehring U, Thefeld W (2005) Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. *Environ Res*. 98:240–49.			
6,896 subjects, aged 19–79 years, of the German Health Survey 1998	**Chronic bronchitis:** based on the question "Which of the following diseases have you ever had?" The answering category was chronic bronchitis, eg coughing during the night without cold and phlegm in the morning most of the days for at least	**Traffic exposure at home address** Defined based on responses to the following question: "Is your home located at an extremely busy road, considerably busy side street, not busy side street, or on a	ORs for the association between traffic exposure at home address *Chronic bronchitis (ever)* Low (n = 4,448): 1 Moderate (n = 797): 0.94 (0.60, 1.46) High (n = 1,651): 1.36 (1.01, 1.83) statistically significant after adjustment for multiple testing

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	3 months a year for 2 successive years **Nocturnal coughing attacks** (past 12 months)	street with no or very rare traffic?" The first two and the last two categories were combined, so three categories representing low, moderate and high traffic intensity were created	*Nocturnal attacks of coughing (past 12 months)* Low (n = 4,448): 1 Moderate (n = 797): 1.05 (0.76, 1.45) High (n = 1,651): 1.24 (0.98, 1.57) ORs adjusted for age, gender, education, community size and pack-years
41 Bayer-Oglesby L, Schindler C, Hazenkamp-von Arx ME, Braun-Fahrländer C, Keidel D, Rapp R, *et al*; SAPALDIA Team (2006) Living near main streets and respiratory symptoms in adults: the Swiss Cohort Study on Air Pollution and Lung Diseases in Adults. *Am J Epidemiol.* 164:1190–98.			
Data from SAPALDIA conducted in 1991 (SAPALDIA 1) and 2002 (SAPALDIA 2) from a random adult population sample aged 18–60 years from eight areas in Switzerland. Of 9,651 participants examined in 1991, 8,047 subjects re-enrolled in the study in 2002	12-month period prevalence of: **Attacks of breathlessness:** "Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?" or "Have you been awakened by an attack of shortness of breath at any time in the last 12 months?" **Regular cough:** "Do you usually cough in the morning after getting up?" or "Do you usually cough during the day, or at night?" **Regular phlegm:** "Do you usually bring up any phlegm from your chest in the morning after getting up?" or "Do you usually bring up any phlegm from your chest during the day or at night?" Whether the effect estimates in 1991 differed from those in 2002 was also investigated	Proxy variables for traffic exposure: (i) Distance from the 1991 and 2002 home coordinates to the closest main street (major road) or highway (ii) Length of main street segments within a 200 m perimeter around the home (iii) Living within 20 m of a main street Regional background concentrations of PM_{10} in 1990 and 2000 were estimated by a dispersion model and assigned to each participant's geocoded addresses in 1991 and 2002, respectively. The modelled PM_{10} concentrations (mean: 22.6 µg/m^3) were validated against PM_{10} measurements (mean: 21.4 µg/m^3)	ORs for the entire sample (n = 12,994–12,999 observations from 8,553–8,555 subjects) *Distance to closest main street (per 100 m)* Attacks of breathlessness: 0.93 (0.85, 1.01) Regular cough: 0.96 (0.90, 1.01) Regular phlegm: 0.93 (0.87, 0.99) *Length of main street segments within 200 m (per 500 m)* Attacks of breathlessness: 1.13 (1.03, 1.24) Regular cough: 1.00 (0.94, 1.07) Regular phlegm: 1.06 (0.98, 1.13) *Living within 20 m of a main street* Attacks of breathlessness: 1.16 (0.99, 1.35) Regular cough: 0.96 (0.85, 1.09) Regular phlegm: 1.15 (1.00, 1.31) ORs adjusted for sex, age, education, nationality, active and passive smoking, current and past

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
			occupational exposures, atopy, early respiratory infections, family history of asthma and atopy, maternal smoking, BMI, regional PM_{10}, month of interview and area
42 Cesaroni G, Badaloni C, Porta D, Forastiere F, Perucci CA (2008) Comparison between various indices of exposure to traffic-related air pollution and their impact on respiratory health in adults. *Occup Environ Med.* 65:683–90.			
9,488 25–59-year-old adults from Rome who lived in the same place for at least 3 years before the interview Data were derived from the Italian Studies on Respiratory Disorders in Childhood and Environment (SIDRIA) study. A cross-sectional survey carried out between October 1994 and March 1995 in eight centres of northern and central Italy using standardised questionnaires	**Prevalence of 'ever' chronic bronchitis or emphysema** 4% of the study population reported chronic bronchitis or emphysema	Different indices of traffic-related air pollution: (i) Self-report of traffic intensity in the area of residence (traffic absent, low, moderate or high) (ii) Distance from busy roads (iii) Metres of high traffic roads within 200 m from home (iv) Area-based emissions of particulate matter (PM): average PM exhaust emissions at each subject's census block of residence, and a categorical variable defined as the quartiles of PM emissions (km/m^3) (v) Estimated concentrations of NO_2 (from a land-use regression model). 15% of subjects reported living in high traffic areas, 11% lived within 50 m of a high traffic road, and 28% in areas with estimated NO_2 greater than 50 $\mu g/m^3$	ORs for the association between environmental exposures and chronic bronchitis or emphysema (n = 397) ORs adjusted for age, sex, smoking habit and educational level *Self-reported traffic* Absent: 1.00 Low: 0.88 (0.64, 1.20) Intermediate: 1.04 (0.77, 1.40) High: 1.19 (0.84, 1.69) p for trend = 0.211 *Distance from high traffic roads* >200 m: 1.00 100–200 m: 0.89 (0.66, 1.20) 50–100 m: 0.69 (0.45, 1.05) <50 m: 0.94 (0.67, 1.31) p for trend = 0.278 *Metres of high traffic roads within 200 m from home* None: 1.00 Low (<416 m): 0.90 (0.63, 1.26) Medium (416–798 m): 0.75 (0.52, 1.07) High (>798 m): 0.94 (0.69, 1.29) p for trend = 0.285

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
			Quartiles of PM emissions 1st: 1.00 2nd: 0.96 (0.71, 1.30) 3rd: 0.90 (0.66, 1.23) 4th: 1.05 (0.77, 1.42) p for trend = 0.871 *Estimated NO_2 (quartiles, $\mu g/m^3$)* 1st: (21.0–37.3): 1.00 2nd: (37.3–47.3): 1.03 (0.77, 1.39) 3rd: (47.3–50.3): 0.90 (0.65, 1.23) 4th: (50.3–62.6): 0.97 (0.71, 1.31) p for trend = 0.624 ORs by smoking habit also reported
43 Lindgren A, Stroh E, Montnémery P, Nihlén U, Jakobsson K, Axmon A (2009) Traffic-related air pollution associated with prevalence of asthma and COPD/chronic bronchitis. A cross-sectional study in Southern Sweden. *Int J Health Geogr*. 8:2.			
Survey of 9,319 individuals aged 18–77 years of age which investigated the association between traffic-related air pollution and asthma and COPD	**Chronic bronchitis symptoms:** "Have you had periods of at least 3 months where you brought up phlegm when coughing on most days?" and, if so, "Have you had such periods during at least 2 successive years?"	Three different measures assessed at each participant's residential address in 2000: (i) Self-reported exposure to traffic (ii) Traffic intensity on the heaviest road within 100 m (iii) Modelled exposure to NOx (in 2001)	ORs for the association between chronic bronchitis symptoms and traffic *Heavy traffic* No: 1.00 Yes: 1.11(0.94, 1.31) *Heaviest road within <100 m* No heavy road: 1.00 <2 cars/min: 1.21 (0.98, 1.50) 2–5 cars/min: 1.30 (1.04, 1.62) 6–10 cars/min: 1.24 (0.93, 1.65) >10 cars/min: 1.53 (1.10, 2.13) *NOx ($\mu g/m^3$)* 0–8: 1.00 8–11: 1.05 (0.81, 1.38) 11–14: 1.12 (0.86, 1.46) 14–19: 1.06 (0.81, 1.39) >19: 1.55 (1.21, 2.00) p for trend <0.0001 ORs adjusted for age, sex and smoking

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	COPD/CBE (chronic bronchitis emphysema) diagnosis: "Have you been diagnosed by a doctor as having chronic bronchitis, emphysema or COPD?"		ORs for the association between COPD diagnosis and traffic *Heavy traffic* No: 1.00 Yes: 1.36 (1.10, 1.67) *Heaviest road within <100 m* No heavy road: 1.00 <2 cars/min: 1.04 (0.80, 1.35) 2–5 cars/min: 0.96 (0.72, 1.28) 6–10 cars/min: 1.57 (1.15, 2.14) >10 cars/min: 1.64 (1.11, 2.41) *NOx (µg/m^3)* 0–8: 1.00 8–11: 0.89 (0.63, 1.24) 11–14: 1.19 (0.86, 1.64) 14–19: 1.03 (0.74, 1.42) >19: 1.43 (1.04, 1.95) p for trend <0.010 ORs adjusted for age, sex and smoking
44 Nuvolone D, della Maggiore R, Maio S, Fresco R, Baldacci S, Carrozzi L, *et al* (2011) Geographical information system and environmental epidemiology: a cross-sectional spatial analysis of the effects of traffic-related air pollution on population respiratory health. *Environ Health*. 10:12.			
Survey of 2,062 subjects from the Pisa-Cascina area (central Italy) in the period 1991–93 Participants' mean age was 45.9 years for men (range 8–93 years) and 48.9 years for women (range 8–97 years). Children aged 0–14 years comprised 5% of the study sample	**COPD:** reported diagnosis of emphysema or chronic bronchitis **Chronic cough (or phlegm):** cough (or phlegm) apart from common colds for at least 3 months of the year for at least 2 years **Dyspnoea I+ grade:** shortness of breath when hurrying on level ground or walking up a slight hill (I grade dyspnoea) or when	Distances of houses from the main road – the sample was classified into three groups: (i) Highly exposed (people living within 100 m of the main road) (ii) Moderately exposed (people living between 100 and 250 m from the main road) (iii) Unexposed subjects (people living between 250 and 800 m from the main road)	ORs for associations between distance of residence to main road and *COPD, in males* <100 m: 1.80 (1.03, 3.08), p < 0.05 100–250 m: 1.21 (0.69, 2.13) *Dyspnoea, in males* <100 m: 0.88 (0.55, 1.41) 100–250 m: 0.86 (0.59, 1.53) *COPD, in females* <100 m: 1.60 (0.71, 3.59)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	walking on level ground with people of the same age (II+ grade dyspnoea)		100–250 m: 0.99 (0.39, 2.51) *Dyspnoea, in females* <100 m: 1.61 (1.13, 2.27), p < 0.01 100–250 m: 1.35 (0.95, 1.93) ORs adjusted for age, educational level, smoking habits, passive smoking exposure, occupational exposure, working position, number of hours spent at home and time of residence, calculated with subjects living between 250 and 800 m as the reference group
45 Hazenkamp-von Arx ME, Schindler C, Ragettli MS, Künzli N, Braun-Fahrländer C, Liu LJ (2011) Impacts of highway traffic exhaust in alpine valleys on the respiratory health in adults: a cross-sectional study. *Environ Health*. 10:13.			
1,581 adults (mean age, 41.7 years; age range 15–70 years) from a random sample of 10 communities along the Swiss alpine highway corridors were recruited in 2005. 46.5% of participants were men	Respiratory symptoms were defined based on positive responses to the following questions: **Regular cough:** "Do you usually cough first thing in the morning?" and/or "Do you usually cough during the day, or at night?" **Regular phlegm:** "Do you usually bring up any phlegm from your chest first thing in the morning?" and/or "Do you usually bring up any phlegm from your chest during the day, or at night?" **Chronic cough:** regular cough and an affirmative answer to "Do you cough like this on most days for as much as 3 months each year?" and an answer of	Traffic exposure defined as: (i) As living within 200 m of the highway (ii) As a bell-shaped function simulating the decrease of pollution levels with increasing distance to the highway Participants lived at a median distance of 924 m from a highway, and 12.5% (n = 197) lived within 200 m of a highway PM_{10} measurements at five highway locations in the study region ranged between 22 and 29 µg/m^3	ORs in all subjects for living within 200 m a highway Regular cough: 1.36 (0.72, 2.56) Regular phlegm: 1.19 (0.60, 2.38) Chronic cough: 2.88 (1.17, 7.05) Chronic cough or phlegm: 2.40 (1.01, 5.70) ORs were adjusted for sex, age, smoking status (current, former or never), pack-years of cigarettes smoked, BMI, community of residence and the binary variables exposure to environmental tobacco smoke (ETS), ETS exposure at work, current occupational exposure to vapours, gas, dust, fumes or aerosols, primary school education only, doctor-diagnosed asthma, maternal atopy and severe respiratory infection in

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
	"≥2" to the question "For how many years?" **Chronic phlegm:** regular phlegm and an affirmative answer to the question "Do you bring up phlegm like this on most days for as much as 3 months each year?" and an answer of "≥ 2" to the question "For how many years?"		early childhood Adjusted ORs for reported respiratory symptoms associated with 'living within 200 m of a highway', by asthmatic status, are also available
46 Cowie CT, Rose N, Ezz W, Xuan W, Cortes-Waterman A, Belousova E, *et al* (2012) Respiratory health before and after the opening of a road traffic tunnel: a planned evaluation. *PLoS One*. 7:e48921.			
2,978 adults and children participated in this longitudinal study. Approximately 70% of participants in each exposure zone were adults (age ≥18 years) Health measurements were taken in the year before the tunnel opened (2006) and in each of 2 years afterwards (2007 and 2008) A sub-panel of the cohort (n = 380) kept a 9-week diary of respiratory symptoms and lung function measurements	**Self-reported cough in the last 3 months** Other composite respiratory symptom variables examined were lower respiratory symptoms, severe lower respiratory symptoms and upper respiratory symptoms Composite variables were based on a "yes" answer to any question on an individual symptom which formed part of the category	Study of a road traffic intervention (new road tunnel opened in March 2007) Exposure zones: (a) A zone along the bypassed main road (predicted 'decreased exposure zone') (b) A zone around the tunnel feeder roads (predicted 'increased exposure zone') (c) A zone of 650 m radius around the tunnel's eastern ventilation stack ('stack zone') (d) A control zone Exposure zones 'a' and 'b' were defined using NO_2 contours from dispersion modelling data. The modelling estimated small changes in pollutant concentrations arising from redistribution of traffic	Modelled changes in *cough in the last 3 months* between the pre-tunnel year (2006) and each post-tunnel year (2007 and 2008) by zone, adjusted for the change in the control zone *2007 vs 2006* Reduced exposure zone: OR 0.8 (0.6, 1.1) Increased exposure zone: OR 1.5 (1.0, 2.2) Stack zone: OR 1.1 (0.8, 1.7) All adjusted for: age, age^2, asthma, smoker, and gas cooker or oven *2008 vs 2006* Reduced exposure zone: OR 0.9 (0.6, 1.3) Increased exposure zone: OR 1.2 (0.8, 1.9) Stack zone: OR 1.3 (0.8, 1.9) Adjusted for: age, age^2, gender, asthma, smoker, and gas cooker or oven

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
		Air pollutants (NO_X, NO, NO_2, PM_{10}, $PM_{2.5}$ and CO) were also measured from two fixed site stations near the ventilation stacks	
47 Gundersen H, Magerøy N, Moen BE, Bråtveit M (2012) Low traffic and respiratory symptoms among smoking females: the Hordaland Health Study. *Arch Environ Occup Health*. 67(4):189–98.			
16,412 individuals, aged 40–45 years, were invited to participate in the Hordaland Health Study. 4,595 men and 5,255 women formed the study population Participants were recruited from three municipalities in Hordaland County (Bergen), Odda, and Kvam Data from individuals in Bergen were collected between August 1998 and June 1999, and data from individuals in Odda and Kvam were collected in November 1997	**Self-report of daily cough (with and without sputum), chronic chough, chronic bronchitis and asthma** The health outcomes were based on a positive response to the following questions: "Do you have daily cough in periods?", "If yes, do you have cough with sputum?", "Have you had such cough as long as a period of 3 months in both last years?" and "Do you have or have you had chronic bronchitis?"	Proxies for air pollution: (i) Road vehicle traffic density (ii) Emission from industrial plants Vehicle traffic density in each electoral district was based on vehicle traffic counting in 2008 Vehicle traffic was classified into three categories based on the busiest road in the district: (i) Low traffic (<3,600 cars passing daily) (ii) Moderate traffic (3,600–18,000 cars passing daily) (iii) High traffic (>18,000 cars passing daily) In the municipality of Odda there were three industrial plants (located in two electoral districts) and in Kvam there was one industrial plant	ORs adjusted for occupational exposure, educational level, smoking habits, passive smoking, hay fever and indoor carpet. The low vehicle traffic density category was used as the reference in analyses *Women, daily cough* Vehicle traffic moderate: 2.19 (1.38, 3.39) Vehicle traffic high: 2.53 (1.57, 4.07) *Women, cough with sputum* Vehicle traffic moderate: 4.93 (1.98, 12.3) Vehicle traffic high: 4.87 (1.93, 12.3) *Women, chronic cough* Vehicle traffic moderate: 2.53 (1.14, 5.61) Vehicle traffic high: 2.44 (1.08, 5.50) *Men, daily cough* Vehicle traffic moderate: 1.37 (0.93, 2.01) Vehicle traffic high: 1.23 (0.82, 1.84) *Men, cough with sputum* Vehicle traffic moderate: 1.15 (0.72, 1.85) Vehicle traffic high: 1.10 (0.67, 1.80)

Table A1.3: Studies of proxy measures of traffic-related pollutants and chronic bronchitis and respiratory symptoms *(continued)*

Study description	Health outcome and definition	Air pollution exposure	Effect estimate (95% CI or p-value)
			Men, chronic cough Vehicle traffic moderate: 1.36 (0.76, 2.46) Vehicle traffic high: 1.34 (0.73, 2.48) Results of further analyses for smokers and non-smokers, by sex, are reported
48 Karakatsani A, Andreadaki S, Katsouyanni K, Dimitroulis I, Trichpoulos D, Benetou V, Trichopoulou A (2003) Air pollution in relation to manifestations of chronic pulmonary disease: a nested case-control study in Athens, Greece. *Eur J Epidemiol.* 18:45–53.			
Nested case-control from the European Prospective Study into Cancer and Nutrition (EPIC), Greece. Study participants were recruited into the study from early 1990 until 1996. Participants were aged between 34 and 70+ years Case series 1: 168 cases and 168 matched controls. Cases were defined by reported history of COPD, chronic bronchitis, emphysema or respiratory symptoms such as breathlessness, chronic cough and chronic phlegm production for at least 3 months a year for at least 2 years All 336 participants were interviewed for completion of a questionnaire and for conducting spirometry Case series 2 (84 cases) was a subset of series 1, defined on the basis of participants meeting clinical diagnosis of chronic bronchitis, emphysema or COPD, ie reporting chronic cough and chronic phlegm production for at least 3 months a year for at least 2 years and/or doctor-diagnosed chronic bronchitis or emphysema or COPD and/or FEV1/VC <88% (men) and 89% (women)	*See column 1*	Past 5 years (prior to interview) and 20 years NO_2 concentrations	OR per one quartile of NO_2, recent 5-y exposure Case series 1 (all): 1.18 (0.94, 1.49) Case series 2: 1.37 (1.05, 1.79) OR per one quartile of NO_2, recent 20-y exposure Case series 1 (all): 1.10 (0.84, 1.43) Case series 2: 1.31 (0.95, 1.79) ORs for NO_2, recent 5-y exposure for people exposed to the highest quartile vs all others Case series 1 (all): 1.46 (0.82, 2.59) Case series 2: 2.01 (1.05, 3.86) ORs for NO_2, recent 20-y exposure for people exposed to the highest quartile vs all others Case series 1 (all): 1.39 (0.73, 2.67) Case series 2: 1.46 (0.67, 3.19) Data on the size of the quartiles are not available

Appendix 2
Comparing the UK and AHSMOG study air pollution environments

A2.1 Particle composition

The AHSMOG study began in 1977 with follow-up of the cohort in 1987 and in later years. The cohort included Seventh Day Adventists from three major geographical areas in California[1]:

a South coast air basin (Los Angeles and eastward)

b San Diego metropolitan district

c San Francisco metropolitan district

d 13% random sample from the rest of California

Abbey *et al* (1995a) reported associations with $PM_{2.5}$ data for 1966–77, though data for 1966–86 were available. The authors stated that ambient $PM_{2.5}$ concentrations for the years 1966–77 were the most strongly related to adverse health effects. A relative risk of 1.81 (95% CI 0.98, 3.25; $p = 0.058$) per 45 $\mu g/m^3$ $PM_{2.5}$ for new cases of definite symptoms of chronic bronchitis in 1987 was reported[2].

The secretariat identified the following papers reporting particle composition data for Southern California: Hidy *et al*, 1975; Appel *et al*, 1978; Christoforou *et al*, 2000. Christoforou *et al* (2000) reported trends in fine particle concentrations and composition for Southern California for the period 1982–93. Professor Roy Harrison compared this with particle composition data from Birmingham for 2004–05. His feedback is given in Table A2.1 and in the paragraphs which follow.

Although not wholly up-to-date, the data from the Birmingham centre form the largest dataset to which Professor Harrison has access and the particle composition has not changed appreciably since then. Apart from Birmingham having a little less organic material and a little more sea salt, it is very similar to Southern California in 1982 and 1986 when viewing the percentages: see Table A2.1.

Since the data from Christoforou *et al* (2000) are for a period later than the 1966–77 $PM_{2.5}$ data from AHSMOG, papers reporting particle composition data for Southern California from an earlier period, ie the 1970s (Appel *et al*, 1978; Hidy *et al*, 1975), were examined to determine if they

1 http://www.llu.edu/public-health/health/ahsmog.page (accessed March 2016).

2 Abbey et al (1995a) indicated that 45 $\mu g/m^3$ was chosen as it spanned the range of concentrations experienced by the cohort and had sufficient numbers experiencing higher levels to avoid extrapolation.

could be compared with data from the Birmingham centre. It was not possible to make a comparison since data reported by Appel *et al* and Hidy *et al* were derived from a different particle size range (total suspended particles, TSP) and are classified differently according to composition.

The two samples in Figure 7 of the paper by Hidy *et al* (1975) which were collected in 1972 show a content of organic material of 24% and 43%, respectively. Sulphate is 4% and 13% and nitrate 5% and 26%, respectively, in the two samples. Ammonium appears to be about 4% and 10%, respectively. The sum of crustal and sea salt is 11% and 8%, respectively, while a category called 'transportation', which may be relatively close to Birmingham's 'trace species' category from the earlier papers, is 12% and 6%, respectively. Overall, despite the different size range and classification, these numbers fall within or close to the ranges seen in the later California data and the Birmingham centre data.

The second paper (Appel *et al*, 1978) shows various campaign-based sulphate and nitrate data as well as (Table II) network data for nitrate and sulphate as annual averages for 1968. These range from 5.0–8.8% of mass for nitrate and 7.2–11.1% for sulphate. These again appear likely to be in TSP, implying that they would represent a somewhat higher concentration within $PM_{2.5}$ which would bring the percentages quite close to those in the California 1982–93 and Birmingham centre 2004–05 data. Once again, it appears that bulk composition will not have changed markedly over the years.

The section which follows provides an overview of concentrations of air pollutants (including trends) in the UK and the AHSMOG study.

A2.2 Concentrations of ambient air pollutants

A2.2.1 UK

In April 2013, Defra published air quality statistics for the UK for the period 1987–2012: https://www.gov.uk/government/publications/air-quality-statistics (accessed 19 July 2013). The trend in annual concentrations for PM_{10} and O_3 are shown in Figure A2.1.

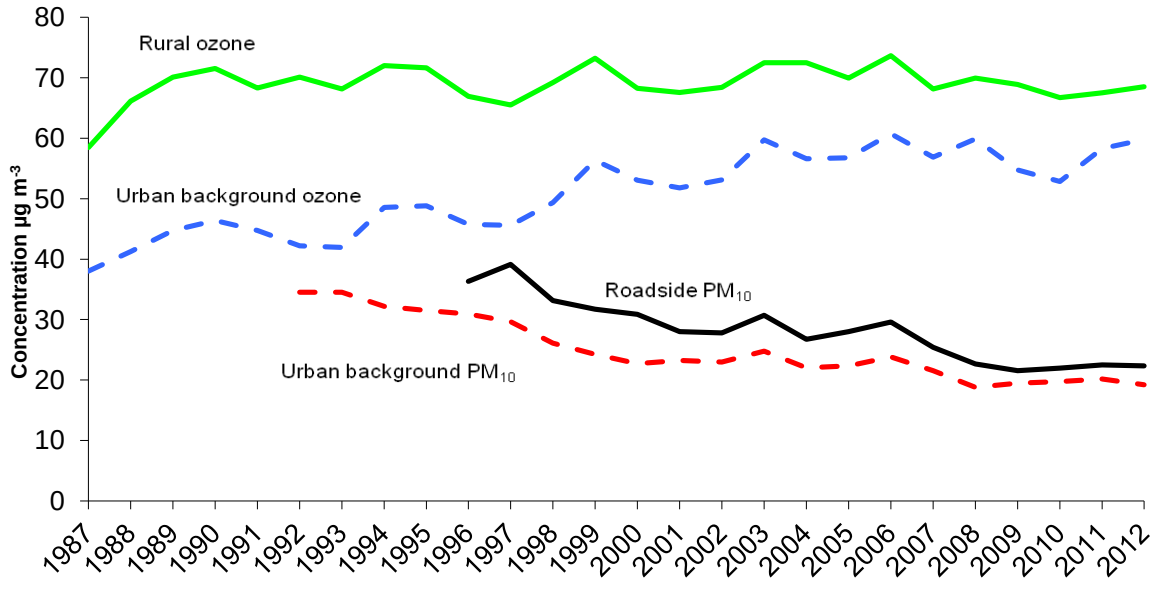

Figure A2.1: Annual levels of PM_{10} and ozone in the UK, 1987–2012

Table A2.1: Comparison of $PM_{2.5}$ composition between Southern California (1982–93) and Birmingham, UK (2004–05)

$PM_{2.5}$ mass	Organic material	Elemental carbon	SO_4^{2-}	NO_3^-	Cl^-	NH_4^+	Na^+	Crustal	Trace species
Southern California									
1982									
29.4	8.8	3.8	5.9	3.3	n/a	2.8	n/a	2.4	1.7
(n = 10)	(30%)	(13%)	(20%)	(11%)		(10%)		(8%)	(6%)
1986									
32.1	12.0	2.7	5.2	5.8	0.2	3.3	0.4	1.9	1.2
(n = 8)	(37%)	(8%)	(16%)	(18%)	(1%)	(10%)	(1%)	(6%)	(4%)
1993									
27.7	14.1	1.8	4.0	4.6	0.1	2.1	0.3	2.3	0.6
(n = 4)	(51%)	(7%)	(15%)	(17%)	(<1%)	(8%)	(1%)	(8%)	(2%)
BCCS – Birmingham centre									
2004–05									
15.8	3.8	1.6	2.2	2.1	0.4	1.4	n/a	1.3	
	(24%)	(10%)	(14%)	(13%)	(3%)	(9%)		(8%)	

Notes

The data from Southern California comes from Christoforou *et al* (2000) and are the average of 10, 8 and 4 sites sampled in 1982, 1986 and 1993, respectively. Data from a background site have been omitted. Data from Birmingham are from daily samples collected between 2004 and 2005 at a background site in the city centre.

In both datasets, organic material has been estimated from organic carbon measured by a thermal/optical technique multiplied by 1.4 to compensate for the presence of other elements. Different methods have been used to infer concentrations of crustal and trace species but these are relatively minor. Apparently poor mass closure for the Birmingham data is a consequence of the presence of bound water which is present under the conditions of weighing and is normally compensated for in the calculation.

Annual average concentration of PM_{10} in the UK in 2012:

a urban background = 19 μg/m^3

b roadside = 22 μg/m^3

Annual average concentrations of PM_{10} have remained relatively unchanged since 2008.

Annual concentrations of O_3 (maximum daily 8 hour mean) in the UK in 2012:

a urban background = 60 μg/m^3

b rural background = 69 μg/m^3

Defra's 2011 annual report on air pollution in the UK provides estimated annual mean background $PM_{2.5}$ concentrations in 2011: see Figure A2.2 taken from that report (Defra, 2012).

In addition, the time series of annual mean NO_2 and SO_2 concentrations are reported: see Figures A2.3 and A2.4 which were also taken from the report.

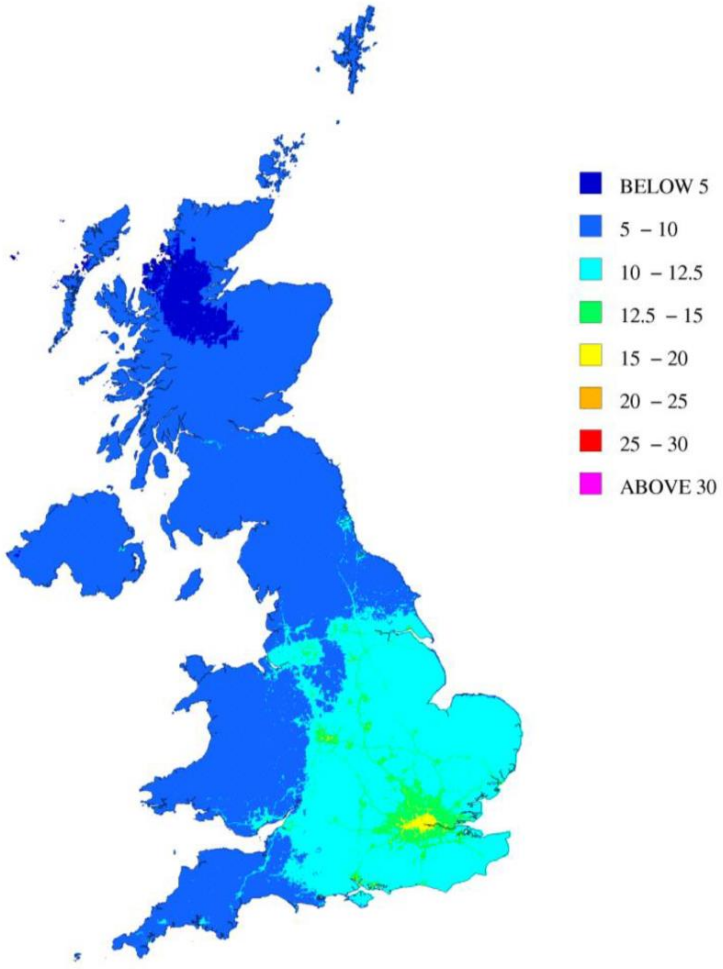

Figure A2.2: Annual mean background $PM_{2.5}$ concentration in 2011 (μg/m^3, gravimetric) (Defra, 2012)

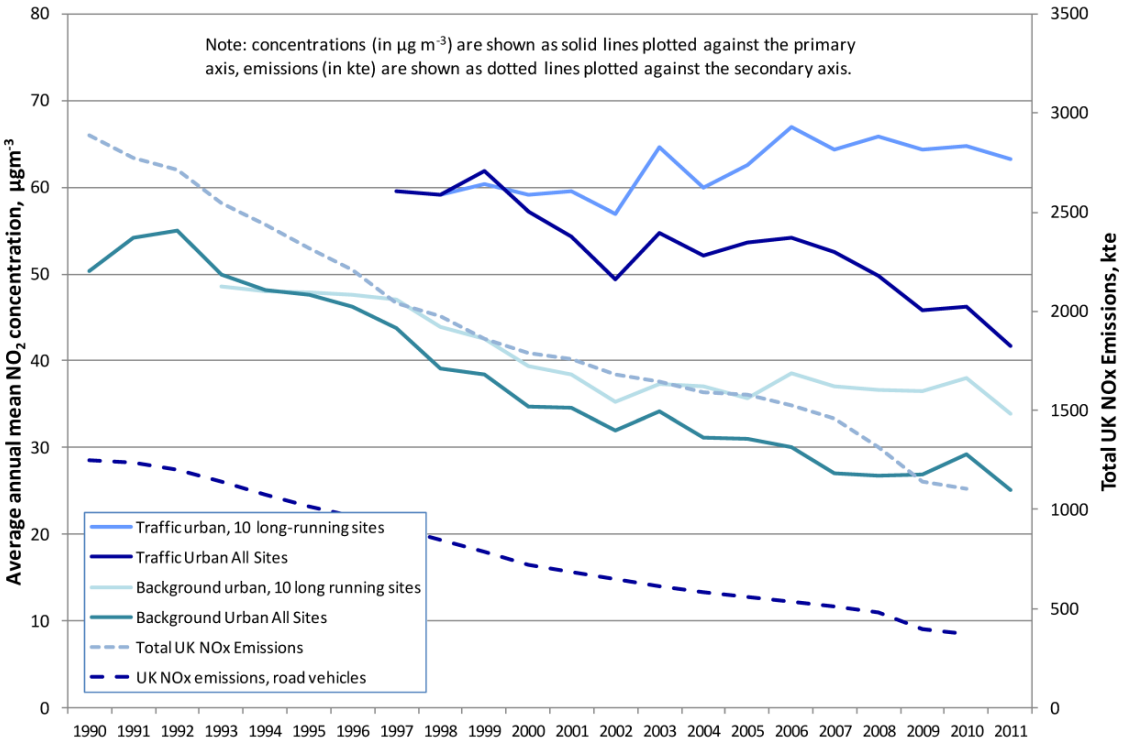

Figure A2.3: Average annual mean NO_2 concentration – background urban and traffic urban AURN sites (Defra, 2012)

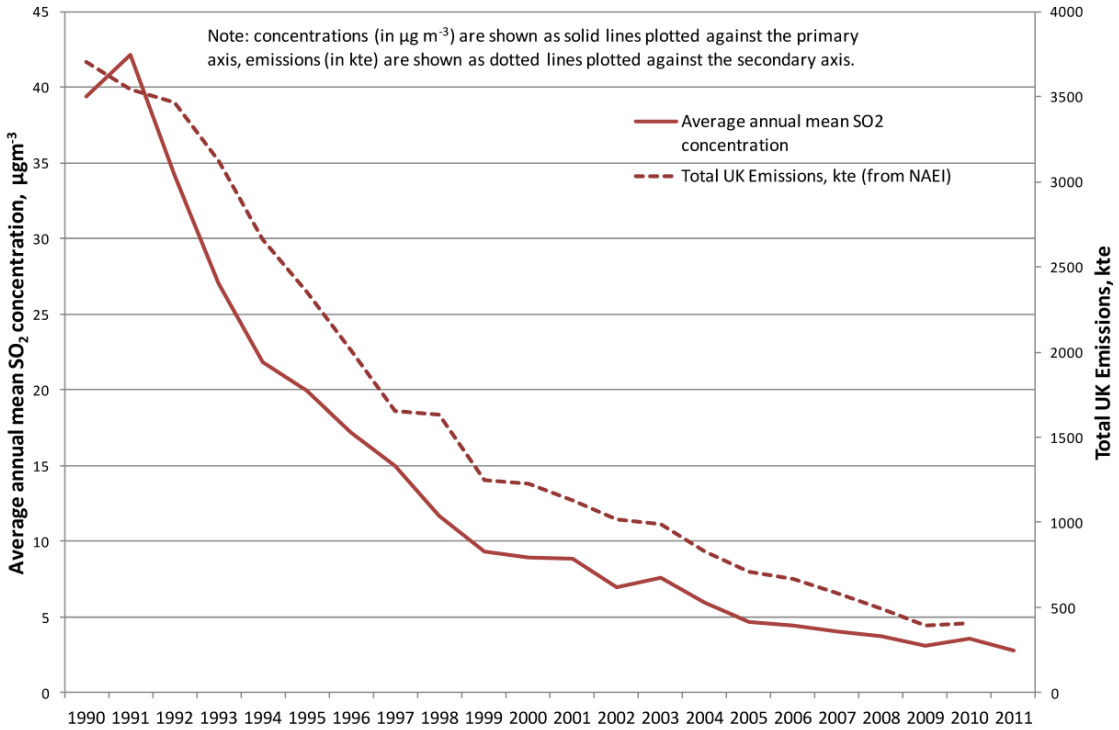

Figure A2.4: Average annual mean SO_2 concentration – all background urban AURN sites (Defra, 2012)

Dr Heather Walton previously did some work to explore the timing of a change in the composition of the UK air pollution mixture from coal to traffic dominated. John Stedman estimated that this change occurred early to mid-1970s and noted that there was still widespread use of coal-fired power stations into the 1970s.

Dr Walton also examined concentrations of TSP in the UK and noted that current data on this particle metric are unavailable. In order to make judgements about how high air pollution levels were in studies which measured only TSP, Dr Walton converted PM_{10} concentrations to TSP by using the following conversion: TSP = PM_{10} × 1.2. Using PM_{10} concentrations reported in the 2007 consultation draft of the UK Air Quality Strategy, the following mean concentrations of TSP were calculated:

a London: mean 31 μg/m³; max 53 μg/m³

b England not London: mean 26 μg/m³; max 42μg/m³

c Scotland: mean 24 μg/m³; max 26 μg/m³

Dr Walton noted that there was discussion of PM_{10} being 40% to 70% of TSP, ie a variable conversion. With caveats, the above give 'current UK' TSP levels (converted from the PM_{10} levels).

A2.2.2 AHSMOG

The concentrations of air pollutants examined in the AHSMOG studies were not always reported in the papers reviewed by the QUARK working group on chronic bronchitis. Only a few of the AHSMOG papers present graphically the distribution of average monthly mean concentrations of some pollutants. More recent papers based on the AHSMOG cohort do report long-term average concentrations of air pollutants, eg Abbey *et al* (1999) on mortality: see Table A2.2 for the period 1973–92 (1977–92 for SO_4).

Table A2.2: Descriptive statistics for estimated average ambient air pollutant values to censor date* for subjects in the AHSMOG cohort (taken from Abbey *et al*, 1999)

Pollutant	n†	Mean	Standard Deviation	Range‡	Interquartile Range
PM_{10} mean concentration in μg/m³	5,963	51.24	16.63	83.93	24.08
Days/year above 100 μg/m³ PM_{10}	5,991	31.08	32.48	178.84	42.63
Suspended sulfate (SO_4) mean concentration in μg/m³	5,070	7.24	2.55	32.11	2.97
Sulfur dioxide (SO_2) mean concentration in ppb	4,353	5.62	2.81	18.96	3.72
Ozone (O_3) mean concentration in ppb	5,893	26.11	7.65	43.91	12.03
Hours/year above 100 ppb O_3	5,893	329.61	294.51	987.97	551.10
Nitrogen dioxide (NO_2) in ppb	5,652	36.78	12.99	67.87	19.78

Definition of abbreviation: PM_{10} = inhalable particulates less than 10 μm.
* Except SO_4, 1977 to censor date.
† Number of subjects with 80% non-missing data.
‡ Maximum average value − minimum average value with average computed over entire time period. All minimum values were zero so that the ranges presented are maximum values. The zero values were assigned to a few individuals living in pristine areas remote from monitoring stations.

The concentrations of air pollutants investigated in the AHSMOG study are higher than the current levels of ambient air pollutants in the UK shown in the earlier paragraphs.

Correlations between ambient air pollutants in the AHSMOG study are shown in Table A2.3.

Table A2.3: Pairwise correlations of estimated mean 1977–87 concentrations of ambient pollutants for members of the AHSMOG respiratory symptoms cohort (n = 3914) (Abbey *et al,* 1995b)

	TSP	PM_{10}[a]	$PM_{2.5}$[b]	SO_4	O_3	SO_2	NO_2
TSP	1	0.95	0.86	0.69	0.72	0.61	0.46
PM_{10}		1	0.89	0.72	0.76	0.64	0.52
$PM_{2.5}$			1	0.30	0.62	0.47	0.25
SO_4				1	0.57	0.60	0.63
O_3					1	0.38	0.36
SO_2						1	0.85
NO_2							1

Notes

Correlations between $PM_{2.5}$ and other ambient concentrations are computed only for 1977–86 for individuals living in the vicinity of nine Californian airports, n = 1,868. Correlations of other pollutants are computed for the entire cohort, n = 3,914, April 1977 – April 1987.

a PM_{10} was indirectly estimated from TSP using site/season regression equations.

b $PM_{2.5}$ was indirectly estimated from airport visibility data.

A2.3 References

Abbey DE, Ostro BE, Petersen F, Burchette RJ (1995a) Chronic respiratory symptoms associated with estimated long-term ambient concentrations of fine particulates less than 2.5 microns in aerodynamic diameter ($PM_{2.5}$) and other air pollutants. *J Expo Anal Environ Epidemiol.* 5:137–59.

Abbey DE, Lebowitz MD, Mills PK, Petersen FF, Beeson WL, RJ (1995b) Long-term ambient concentrations of particulates and oxidants and development of chronic disease in a cohort of nonsmoking Californian residents. *Inhal Toxicol.* 7:19–34.

Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knusten SF, Beeson WL, Yang, JX (1999) Long-term inhalable particles and other air pollutants related to mortality in nonsmokers *Am J Respir Crit Care Med.* 159: 373–82.

Appel BR, Kothny EL, Hoffer EM, Hidy GM, Wesolowski JJ (1978) Sulfate and nitrate data from the California Aerosol Characterization Experiment (ACHEX). *Environ Sci Technol.* 12:418–25.

Christoforou CS, Salmon LG, Hannigan MP, Solomon PA, Cass GR (2000) Trends in fine particle concentration and chemical composition in southern California. *J Air Waste Manag Assoc.* 50:43–53.

Defra (2012) Air Pollution in the UK 2011. http://uk-air.defra.gov.uk/library/annualreport/index, accessed March 2016.

Hidy GM, Appel BR, Charlson RJ, Clark WE, Friedlander SK, Hutchison DH, *et al* (1975) Summary of the California aerosol characterization experiment. *J Air Pollut Control Assoc.* 25:1106–14.

Appendix 3
Membership lists

Membership of the Committee on the Medical Effects of Air Pollutants

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