COPD and environmental risk factors other than smoking

9. Outdoor air pollution

Author : P N Lee
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1. Papers identified

The procedures described in "COPD and risk factors other than smoking. 1. Identifying Relevant Papers" were carried out to identify papers (and reviews) that were relevant to outdoor air pollution, except that, as the number of papers obtained already approached 100, the "secondary references" stage was not attempted. Indoor air pollution is considered to be covered by heating and cooking and by ETS, considered elsewhere.

2. General approach

The literature is very substantial and at this stage all that has been done is to give little more than a very broad summary of the type of material available and the consistency of the conclusions.

3. Views from overall reviews

A number of the general review papers refer to the possible role of outdoor air pollution in COPD. While many of these papers consider, or seem to consider, that the evidence of a relationship is good[1-7] some are more cautious[8-13]. However, it is not always clear whether authors are referring to evidence of an association or of a causal relationship.

4. Views from more specific reviews

More relevantly, a number of review papers have been identified that concern themselves particularly with effects of air pollution. Some are more wide ranging[14-18] but most are concerned with respiratory effects or COPD [19-25]. A few quotations from these review papers are given below:

"Epidemiologic studies suggest that air pollution plays an important role in the exacerbation and in the pathogenesis of chronic respiratory diseases". (Baldacci and Viegi, 2002[20])

"Air pollution is an important etiological factor for many chronic respiratory disorders, such as bronchial asthma and COPD". (Del Donno et al, 2002[21])

"Epidemiological studies have consistently shown an association between particulate air pollution and not only exacerbations of illness in people with respiratory disease but also rises in the numbers of deaths from cardiovascular and respiratory disease among older people. Meta-analyses of these studies indicate that the associations are unlikely to be explained by any confounder, and suggest that they represent cause and effect". (Seaton et al, 1995[18])

"Overall, there is evidence that air pollution is one of the major environmental risk factors for the occurrence and/or the exacerbation of chronic respiratory conditions". (Viegi and Baldacci, 2002[24])

"While smoking has been demonstrated to cause and aggravate COPD and bronchial asthma, the influence of air pollution, suspected to have hazardous environmental effects since the historical episodes of severe air pollution such as the London Smog, on the prevalence of airway diseases remains unclear. This is due, in part, to changes over time in the nature of the air pollutants concerned. There have been no consistent findings on the effects on airway diseases of air pollutants at levels currently observed in developed countries". (Sasaki et al, 1998[19])

5. Short-term effects of air pollution

There are a substantial number of papers that correlate variation in pollutant levels, typically on a daily basis, to variation in hospital admission or mortality from COPD or respiratory conditions more generally. Studies conducted in North America[26-36], Europe[37-44], Asia[45-47] and Australia[48,49] have consistently shown a significant relationship, with many of the studies adjusting for a range of potential confounding variables (e.g. temperature, humidity, wind, day of week, season, influenza epidemics) using complex

statistical models. Many of these studies look at a wide range of pollutants (e.g. ozone, black smoke, PM_{10}, $PM_{2.5}$, SO_2, NO_2 and CO) and a variety of health endpoints. Two review/meta-analysis papers[50,51] consider the relationship between particulate pollution and daily mortality. I do not propose to discuss this short-term variation evidence further, other than to note that it has been suggested that although sudden increases in pollution levels (particularly in "smogs") may be associated with clearly increased mortality from COPD, those dying may be mainly those who would have died shortly from COPD anyway.

6. Long-term effects of air pollution

6.1 Mortality studies

Dockery et al (1993)[52] carried out a 14-16 year prospective study in six US cities in which measurements were made of total particles, fine particles, SO_2, sulfate particles, aerosol acidity and ozone. After adjustment for age, smoking and other variables, death rates from cardiopulmonary disease were 37% higher (95% CI 11%-68%) in the most polluted city than in the least.

Hoek et al (2002)[53] carried out a prospective study from 1986 to 1994 in the Netherlands. Long-term exposure to traffic-related air pollution (black smoke and NO_2) was estimated for the 1986 home address. Cardiopulmonary mortality, after adjustment for age, smoking and other variables, was related to living near a major road (RR 1.95, 95% CI 1.09-3.52) and, less consistently, with the estimated ambient background concentration (1.34, 0.68-2.64). There were only 27 respiratory deaths.

Hospers et al (2000)[54] followed up 2008 inhabitants of three communities in the Netherlands for 30 years. There were 60 deaths from COPD (combined primary and secondary diagnoses). After adjustment for age, smoking and other risk factors, those who had an urban residence had a non-significantly lower risk of death (0.54, 0.26-1.09).

Meyer et al (2002)[55] used the National Mortality Followback Survey, a nationally representative sample of US deaths in 1993, to compare 1279

decedents from COPD and 11524 decedents from other causes. After controlling for age, sex and race, they found no association between dying from COPD and metropolitan residence.

Pope et al (2002)[56] carried out a 16 year prospective study based on the American Cancer Society CPS II study, which enrolled approximately 1.2 million adults in 1982. Risk factor data collected for about 500000 of the adults was linked with air pollution data for metropolitan areas throughout the US and combined with vital status and cause of death data up to the end of 1998. Fine particle and sulfur oxide-related pollution were associated with cardiopulmonary mortality. Each 10-$\mu g/m^3$ elevation in fine particulate air pollution was associated with a 9% increase in risk (95% CI 3% to 16%), after controlling for age, smoking and other variables. Measures of coarse particle fraction and total suspended particles were not consistently associated with mortality. Results were not presented specifically for COPD mortality. (See also review 1231 for detailed comments on this publication.)

Salinas and Vega (1995)[57] carried out an ecological study within the Metropolitan Area of Santiago, Chile. A clear pattern in the risk of COPD death was found, with SMRs highest in the most polluted areas, regardless of socioeconomic and living conditions.

Samet et al (2000)[58] carried out a study of fine particulate air pollution and mortality in 20 US cities in 1987-1994. Pollutants studied included PM_{10}, ozone, CO, SO_2 and NO_2. After taking into account potential confounding by other pollutants, they found consistent evidence that PM_{10} is associated with the rate of death from all causes and from cardiovascular and respiratory illnesses. The relative risk of death from cardiovascular and respiratory causes increased 0.68% (95% CI 0.20% to 1.16%) for each 10 $\mu g/m^3$ increase in PM_{10}. There was weaker evidence that ozone increases increased death rates during the summer. Other pollutants were not significantly related to the mortality rate.

Naess et al (2007)[59] described a 6 year follow-up study of all inhabitants of Oslo aged 51-90 with data on NO_2, PM_{10} and $PM_{2.5}$ available for the 470 neighbourhoods in which they lived. All the indicators of air pollution were linked to COPD mortality, with an apparent linear relationship. These analyses were based on 1452 COPD deaths.

Of the eight studies cited, many have limitations. The three large US studies involving detailed measurement of multiple pollutants[52,56,58] do not report results specifically for COPD, only with cardiorespiratory mortality, as is true for the smaller Netherlands study[53]. Of the studies that do involve COPD mortality[54,55,57], one is ecological[57] and two[54,55] have a weak exposure indicator (urban/rural residence). Only one study[59] has both COPD mortality data and detailed pollutant measurements.

6.2 Comparison of specified areas with low and high levels of air pollutants

12 papers describe comparisons of areas with low and high levels of air pollutants, but do not have mortality as the endpoint. Mainly they present results consistent with high pollution levels being associated with significantly increased prevalence of COPD or symptoms related to it, or reduced lung function[60-68]. However, two studies[69,70] show no differences between the areas compared and one, conducted in Japan and China[71], reported that prevalence of obstructive lung disease was higher in rural than in residential areas, after adjustment for age, smoking and other variables.

6.3 General population studies in which levels of specific pollutants were measured

Seven papers[72-78] describe the results of population studies to which levels of specific pollutants were measured.

Abbey et al (1993)[72] and Euler et al (1987)[73] described a prospective study in Seventh Day Adventist nonsmokers in which COPD symptoms were linked to ambient concentrations of TSP, ozone and SO_2 at their residence. Associations were found for TSP and ozone.

Karakatsani et al (2003)[74] described a case-control study in Athens in which residential and occupational subject history was linked with geographical air pollution data on black smoke and NO_2. Cases were significantly more exposed than controls after adjustment for age, smoking and other factors.

Schikowski et al (2005)[75] carried out cross-sectional studies in the Rhine-River Basin of Germany, linking NO_2 and PM_{10} exposure assessed by measurements done in an 8 km grid, and traffic exposure by distance from the residential address, to COPD as determined by the GOLD criteria. COPD and pulmonary function generally were most strongly affected by PM_{10} and traffic-related exposure.

Schindler et al (1998)[76] related lung function to associated average exposure to NO_2 in eight areas of Switzerland (SAPALDIA Study). Differences in NO_2 exposure between subjects within community and between communities were both associated with NO_2 exposure.

Schwartz (1993)[77], a study in 53 urban areas in the USA, found that, other controlling for age, smoking and other variables a 10μg/m^3 increase in average TSP concentration was associated with a 5% (95% CI 2 to 12%) increased risk of chronic bronchitis and a 6% (2 to 11%) increased risk of a respiratory diagnosis by the examining physician. The association was evident in never smokers.

Sunyer et al (2006)[78], a study conducted in 21 centres in 10 countries in the EC from 1991-93 to 2001-02, found that the prevalence and new onset of chronic phlegm was significantly associated with traffic intensity and from outdoor NO_2, but only in females.

Generally, the results from this group of studies are consistent with some effect of air pollution, though the pollutants studied vary.

6.4 General population studies in which people living in urban and rural areas were compared

There are also quite a large number of studies in which COPD symptom prevalence or lung function has been compared in people living in urban and rural areas, often without any specific measurement of pollutants. Here the evidence is much less consistent. While some studies find higher COPD prevalence (or reduced lung function) in urban areas[79-87], some find no significant difference[88-96] and others, particularly in Asia[97-99] although also elsewhere[100], find higher COPD rates in rural populations.

7. Conclusions

The evidence relating to COPD to outdoor air pollution is quite extensive and difficult to interpret clearly. There is considerable variation in the detail of the exposure measurement, varying from extensive data completed on a wide range of pollutants to a simple comparison of residents of urban and rural populations. It is also clear that the nature of the major pollutant sources varies from region to region and over time. Add to this the variety of the indices of COPD used, and the difficulties of controlling for confounding variables, it is not surprising that a very clear answer cannot be obtained. However, there does appear to be considerable support to the idea that some air pollutants may increase the risk of COPD.

8. References

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