EVALUATION OF HEALTH EFFECTS OF POLLUTION

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1. Introduction

Current initiatives to improve air quality in the Mexico City Metropolitan Area (MCMA) require estimation of the economic evaluation of the benefits gained from proposed programs. This document presents a review of the knowledge of health effects and more specifically a meta-analysis to summarise data available and obtain an estimate of exposure-response relations to be used to predict the number of health events that could be avoided by improving air quality.

This overview is restricted to particulate matter and ozone because these are the pollutants of more concern in this megalopolis. The first section presents an overview of the toxicology and exposure to air pollution, followed by a meta-analysis of published international and Mexican studies. The review was based on recent epidemiological studies of the association of acute and chronic exposures to particulate air pollution or ozone with increased morbidity and mortality. Specific health effects include acute effects on mortality, hospital emergency room visits, respiratory symptoms, restricted activity days, as well as the chronic effect on mortality and respiratory symptoms. To obtain an estimated average, studies were pooled using random effects models. These models take into account between study variability as a result from among sampling sites and the variance within the studies. Exposure- response curves are presented as increases in relative risks per $10\mu g/m^3$ in PM10 and 10 ppb in ozone.

2. General overview of air pollution and health

Anthropogenic air pollution has been a way of life for almost 500 years now. The industrial revolution introduced great strides in technology, society and services; however, it also initiated the production of huge quantities of pollutants emitted into the air with no notion of how they might affect health. At the time, smoke from burning coal was the major pollutant, but this was only the beginning of countless air pollutants which have since proven harmful to human health (Dockery and Arden Pope 1996). Since that time, many episodes have been recorded where elevated levels of pollutants have caused serious health effects in different populations. One of the most well-known cases occurred in London in December, 1952, when environmental conditions caused a 5-day accumulation of air pollution, especially sulphur dioxide and smoke, reaching 1500 mg/m^3 and resulting in an increase in the number of deaths to around 4000 for the period. In New York City in 1963, conditions similar to those occurring in London caused 400 deaths. These cities are not alone reporting such events. High levels of air pollution have been registered in Mexico City, Rio de Janeiro, Milan, Ankara, Melbourne, Tokyo and Moscow, to name only a few problematic cities (Dockery and Arden Pope 1996).

Since major cities frequently suffer episodes of severe pollution, they require special surveillance to protect the large number of individuals concentrated there and the important economic activities carried out therein. It is precisely due to the flourishing economic activity in these areas that the environment has been relegated to secondary importance. On the other hand, different diseases, from respiratory to cardiac ailments, in different degrees of severity from minor irritation to death, have been associated to exposure to air pollution (Dockery and Arden Pope 1996). Some of the more import toxic effects will be described in the following chapters of this report.

2.1 Sources of exposure

The majority of substances considered as environmental pollutants are produced through human activities such as the use of internal combustion engines (automobiles), power plants and industrial machinery. Because these activities are performed on such large scale, they are by far the major contributors of air pollution, with cars estimated as responsible for approximately 80% of today's pollution. Minor sources of pollution such as lawn mowers, cooking stoves, stationary diesel fuel tanks, heaters, gasoline stations, laundries, other cleaning services, etc. are currently being evaluated as well (Möller *et al.* 1994, Pooley *et al.* 1999).

All the exposure sources mentioned above can be classified as anthropogenic. Natural sources of pollution include soil erosion (the wind carries airborne particulate matter produced through erosion), evaporation of sea water (which carries with it various materials), volcanic eruptions and forest fires (which send toxic substances directly into the atmosphere) (Pooley *et al.* 1999).

2.2 Classification of environmental pollutants

We now know that air pollution is a complex mixture of a variety of substances produced by incomplete combustion reactions mainly resulting from anthropogenic activities but also through natural phenomena. Pollutants can be classified in a variety of ways. Table 1 shows some classifications based mainly on physical and/or chemical properties.

Table 1. **Classification of environmental pollutants**

1) Chemistry	
a) Inorganic	For example: sulphates (SO_4^{-2}), nitrates (NO_3^-), ammonium (NH_4^+), sulphur oxides (SO_x) and elemental carbon, which can form salts with: Fe, Mn, Zn, Pb, V, Cr, Ni, Cu, Co, Hg and Cd, and even with As and Se.
b) Organic	For example: benzene, 1-3 butadiene, polycyclic aromatic hydrocarbons, dioxins, CO and CO_2
2) Source	
a) Primary:	Pollutants are emitted directly into the atmosphere
b) Secondary:	Pollutants are emitted as supersaturated gasses and in the atmosphere become solid or react to form a different species (this phenomenon occurs mainly with polar compounds).
3) Physical Nature	
a) Dust	Particles produced by mechanical disintegration of solids.
b) Aerosol	Suspension of solids in the air, particles can be 1 nm to 2 μm in diameter, capable of remaining suspended in the air and moving easily.
c) Smoke	Material produced by the incomplete combustion of organic substances, generally of small particle size ($\leq$ 15μm).
d) Black Smoke	Non reflective particulate matter.
e) Vapor	Condensation product of evaporated material (iron oxides) and smoke.
4) Particle size	
Ultra fine particles (0.01-0.1 μm)	These are produced from supersaturated gasses such as SO_2, NH_3 and NO_x,
Fine particles (accumulation) (0.1-0.25 μm)	These are composed generally of SO_4^{-2}, NH_4^+ and NO_3^-, do not settle to the ground and are capable of travelling long distances.
Rapidly settling Particles (1-20 μm)	
Large particles (>20 μm),	Among these are the soil particles and some metallic salts with Al, Fe, Mn, Sr, Ca, Co and K

Source: Information from Möller *et al.* 1994, Wilson *et al.* 1996, Ghio *et al.* 1999, Pooley *et al.* 1999.

2.3 Toxicology of air pollutants

2.3.1 Relationship between the toxic effect and physical and chemical properties of air pollutants

Not all air pollutants have the same capacity for producing toxic effects, nor do they cause the same damage. It is a logical conclusion that the differences are due to the physical and chemical properties of these components. This report will briefly mention the properties as they relate to toxicity.

Beginning with the molecular aggregation state, substances in aerosol form have been shown to be more toxic than compounds in gaseous state. This is due to the fact that gaseous compounds are eliminated by the respiratory system much more easily than aerosols, which are rapidly deposited or absorbed. The particle size of an aerosol, between 1 nm and 2 μm, is easily deposited in the respiratory system (Wilson *et al.* 1996).

Particle size determines the extent to which the particles can penetrate into the respiratory system. Table 2 shows penetration ability of particles as a function of size. Once particles have entered the respiratory tract, depending on their size they can accumulate in different sites within the respiratory system. The major regions of accumulation are extrathoracic (nostrils and larynx), bronchial (trachea, bronchial and terminal bronchial) and alveolar (bronchiole and alveolar sacs). Up to 50% of particles smaller than 0.02 μm can be deposited in the lungs (ICRP 1996, Ghio *et al.* 1999).

Table 2. **Particle penetrability according to size**

Particle size	Region to which penetration can occur
> 11 μm	Captured in the nostrils, do not penetrate into the lower respiratory tract.
7-11μm	Nasal passage
4.7-7 μm	Larynx region
3.3-4.7 μm	Trachea and primary bronchial region
2.1-3.3 μm	Secondary bronchial section
1.1-2.1 μm	Terminal bronchial section
0.65-1.1 μm	Bronchioles
0.43-0.65 μm	Alveolar

Source: Information from Wilson *et al.* 1996 y Ghio *et al.* 1999.

Toxicity of environmental pollutants has also been related to chemical reactivity as acids or alkalis. The most studied compounds from each group are NH_3 and NH_4^+ (alkalis) and SO_2 and H_2SO_4 (acids). Of these, H_2SO_4 has been shown to be the most toxic. Both acids and bases can be found in the same region of the atmosphere where they combine to produce neutral species. However, when alkalis are present in greater abundance than acids, they tend to produce more severe toxic effects than when acid species dominate (Schlesinger *et al.* 1995, SUH 1995). In a 1995 German study of respiratory disorders, most were not attributable to the presence of acidic molecular pollutants (Brauer *et al.* 1995).

Another property of chemical elements, mainly the metals, is their ability to convert to other species by oxidation or reduction of other components present in the atmosphere or within the organism, itself (redox potential). This type of reactivity is associated with certain effects such as neutrophilic alveolitis, hypersensitivity reactions, increased lung infections and death. The subctance must be in solution for these oxidation-reduction reactions to occur, and for this reason, the more soluble salts have greater toxic potential. This solubility-toxic relationship persists as well for non-metallic compounds such as NH_4HSO_4, $(NH_4)_2SO_4$ and H_2SO_4 (Wilson *et al.* 1996, Ghio *et al.* 1999).

2.4 Toxic effects of air pollutants

Chemical compounds emitted into the atmosphere due to human activity or those compounds that are byproducts of the interaction of chemical emissions have been shown to have adverse effects on health. These effects, as discussed in this report, depend fundamentally on the nature of the compound in question, the concentration in the air and the time of individual exposure. Noxious health effects caused by air pollution can be classified as due to either chronic or acute exposure.

2.4.1 Health effects due to acute exposure to air pollutants

Toxic effects attributable to acute exposure to air pollutants vary widely and have been reported practically since the beginning of the industrial revolution where episodes of high levels of pollutants were associated with increases in diverse respiratory and heart diseases and death. These episodes have occurred on more than a single occasion in different parts of the world, especially in highly industrialised and/or populated areas (Ellison & Waller 1978, Holand *et al.* 1979, SMY 1979, Bates 1980).

The most studied toxic effect due to acute exposure to environmental pollutants is mortality. Many reports describe an increase in total mortality (not including accidental death) associated mainly with exposure to particulate matter (PM), ozone and sulphates. This association can be disputed, however, since the cause of death should be related to the route of exposure (Schwartz 1994[a], Dockery and Pope 1994).

A great number of studies report increases in mortality due to respiratory complications, and in this case, the mechanism obviously can be related to exposure to air pollution. Many reports also claim an increase in death due to cardiovascular ailments, which would implicate a mechanism with an indirect effect from air pollution. Both causes of death are associated with exposure mainly to PM, ozone and sulphates. Mortality attributable to exposure to air pollution occurs mainly in individuals who suffer from cardiac and/or respiratory diseases. Increased mortality in these groups occurs within 1 to 5 days following the hazardous exposure (Schwartz 1994[a], Wilson *et al.* 1996, Cropper, L. (1999).

Certain population groups are more susceptible than others to the effects of pollution, which has attracted the special attention of many researchers in the field. Individuals at the extremes of the life cycle, the elderly and infants, show increased mortality associated with exposure mainly to PM and sulphates. Although the mechanisms leading to death are the same as those causing toxic effects, these groups' biological defence mechanisms are less efficient than in the rest of the population.

Increased mortality due to exposure to air pollutants can also be associated to smoking habits. This phenomenon is likely due to the fact that smokers have a 30% decreased lung capacity compared to non-smokers of the same age (Wilson *et al.* 1996).

Besides mortality, a great number of acute conditions have been reported associated to exposure to air pollutants. Among these are diseases of the respiratory tract, both upper and lower, bronchitis, pneumonia, chronic obstructive pulmonary disease and cough with phlegm.

The proposed mechanism producing such diseases could be related to the ability of certain pollutants to produce systemic (NO_2) and local immunosuppression. In exposed animals (SO_4^{-2} and NO_3^-), a decrease in the affinity of macrophages for the Fc section of antibodies has been observed. Intuitively, in a human organism with diminished immune response, the capability to mount an adequate defence in a populated, urban environment, where exposure to multiple pathogens is high, would be unfavourable (Schlesinger *et al.* 1995. Ehrlich 1980).

Along this same line, many laboratory animal studies have evaluated the effects of pollutants on macrophages, one of the major cellular defence lineages present in the respiratory apparatus. Two types of effects have been observed. Exposure to certain pollutants (SO_4^{-2} ó NO_3^-, for example) causes a decrease in affinity for the Fc section of the immunoglobulins and limits the antibody mediated response. In addition, exposure to transition metals results in increased secretion of reactive intermediates of oxygen ($O_2^{\cdot-}$, $OH^{\cdot}$ and H_2O_2) and nitrogen ($NO^{\cdot}$ and $ONOO^-$), producing a state of tissue inflammation. It is possible that other cytokines, such as some of the interleukins, are affected, as well (Schlesinger *et al.* 1995, Wilson *et al.* 1996,Martin *et al.* 1997, Ghio *et al.* 1999).

However, environmental pollutants likely also effect somatic cells directly. Exposure to $(NH_4)_2SO_4$ and NH_4NO_3 has been shown to increase lung tissue permeability, leading to saturation of the intercellular spaces with interstitial fluid. This could lead to pulmonary edema or a chronic inflammatory state, decreasing gas exchange in the lungs and resulting in a hypoxic state (Kleinman *et al.* 1995, Schlesinger *et al.* 1995).

Thus far, we have mentioned only diseases which develop favoured by exposure to air pollution. Other symptoms are exacerbated as well by exposure to certain pollutants such as ozone and PM, which are associated with increased asthmatic attacks, coughs without phlegm and wheezing (Pope *et al.* 1991, Roemer *et al.* 1993).

The mechanism by which these symptoms are increased could be related to effects on the immune system. Although the cause remains obscure, ozone, sulphates and PM can stimulate over induction of immunoglobulins, such as IgE, which initiates a series of signals resulting in the production of spasms of certain muscle groups (Wilson *et al.* 1996, Ghio *et al.* 1999).

2.4.2 Health effects due to chronic exposure to air pollutants

Pollution episodes, which have occurred in different cities around the world, have demonstrated the consequence of human exposure to high concentrations of air pollution. However, these episodes appear sporadically, and currently, exposure to low concentrations of pollutants over long periods of time is a daily phenomenon. Recent studies have focussed on establishing the effects of chronic exposure over prolonged periods.

A synthesis of all the available information concerning chronic exposure is an extremely complex task due to the enormous number of factors which could be associated with the same types of symptoms, such as active and passive smoking, nutritional level, etc. It is very difficult to establish a single causal agent which could be responsible for a cancer, for instance, since this type of disease develops over a long period of time and involves various interacting factors (Möller *et al.* 1994, Schlesinger *et al.* 1995).

Health effects due to chronic exposure are very similar to those reported for acute exposure. There are several reports of increased mortality, however, most cases involve mainly elderly individuals where respiratory and cardiovascular problems are already the principle cause of death (Anderson 1996, Borja 1997, Pope 1996).

Increased respiratory diseases (such as bronchitis) have also been reported associated to chronic exposure. The mechanisms causing these diseases should be very similar to those occurring for acute exposure.

The best documented chronic effect of exposure to air pollution is cancer. Approximately 70 to 80% of all cancer types have been reported as due to exposure to environmental pollutants. The mutagenic properties of different substances (e.g. diesel) have been demonstrated, and, as we well know, mutation is an essential step in the transformation of a normal cell to a cancerous cell. The mutagenic ability of a substance is not the only property that can stimulate cell transformation, however. Over-activation or inhibition of regulatory enzymes can also lead to cellular transformation.

A chronic inflammatory state can also lead to cancer development. Exposure to some environmental pollutants (transition metals) can result in a chronic inflammatory state due to altered secretion of reactive intermediaries of oxygen ($O_2^{\cdot-}$, $OH^{\cdot}$ and H_2O_2) and nitrogen ($NO^{\cdot}$ and $ONOO^{-}$), possibly induced by increased secretion of a cytokine that induces the production of these reactive intermediaries and the activation of macrophages long-term result of a continuous inflammatory state can result in tissue lesions and even cancer (Martin *et al.* 1997).

For both cases of chronic and acute exposure to air pollutants, populations are exposed to a complex mixture of compounds whose combined toxic effects could differ from that of each isolated compound. In a study performed on volunteers who were exposed to ozone with and without pre-exposure to H_2SO_4, the pre-exposed group suffered more severe toxic effects than the group that was not pre-exposed (Thurston and Ito 1999).

Other mixtures that have proven more toxic than the individual compounds include SO_2 - ozone, SO_2 - black smoke and PM_{10} - ozone (Katsouyanni 1995). It is therefore necessary to develop models and protocols to analyse the different interactions among environmental pollutants (Samet *et al.* 1993).

2.5 PM_{10} particles

In the field of environmental pollution toxicology, much interest has been recently shown in the study of PM_{10} and $PM_{2.5}$ particles. These particles are associated with diverse respiratory system pathologies and they contribute to indoor exposure, since their size allows them to penetrate interior spaces. PM_{10} and $PM_{2.5}$ particles are defined as a mixture of different compounds with 50% of the solid material able to pass through a 10 μm (PM_{10}) or 2.5 μm ($PM_{2.5}$) sieve (Koutrakis and Sioutas 1996).

Among the different PM_{10} and $PM_{2.5}$ components are organic compounds, such as benzene, 1-3 butadiene, polycyclic aromatic hydrocarbons, dioxins, etc., inorganic compounds, such as carbon, sulphates, nitrates, chlorides and even some metals (Wilson *et al.* 1996, Pooley *et al.* 1999).

The particles produce toxic effects according to their chemical and physical properties, as described above. However, they primarily affect susceptible individuals, where their effects are much more severe than those produced in normal individuals (Schlesinger *et al.* 1995, Toster 1999).

Due to the size of the PM_{10} and $PM_{2.5}$ particles, their half-life in the atmosphere is generally very high since they do not settle to the ground but remain suspended and can be transported very far from their origin. This property is very important to consider since a population far from the pollution emission site may be exposed to the same extent as one close by (Wilson *et al.* 1996).

2.6 Ozone

Ozone is poorly soluble but highly reactive gas, is mainly produced in the troposphere by series of sunlight-driven reactions involving nitric oxides and volatile organic compounds. It is partially depleted in the upper airways when inhaled but a major fraction does reach the lower airways. Ozone can react with uric acid, which is secreted by human airway's submucosal glands and is present in near mmol/l concentrations in nasal surface liquid. Pryor and his colleagues have proposed that some of the toxic products of the latter reaction (hydroxyhydroperoxides, hydroxyaldehides) are important mediators of ozone effects on underlying epithelium and some scientists have calculated that ozone per se does not even reach the epithelial cell apical membrane in conducting airways (Bromberg 1999).

The proportion of ozone uptake attributed to surface liquid decreases progressively as the surface liquid thins and/or its reactivity with ozone diminishes. Accordingly, the highest epithelial tissue dose is predicted for the terminal bronchiole-respiratory bronchiole region. This is indeed a site of damage in ozone-exposed animals. Bronchoscopic sampling along airways also indicates that a substantial fraction (35%) of orally inspired ozone is taken up in the upper airway and trachea and that ozone in exhaled air is limited to the initially expired volume representing airways dead space (Bromberg 1999).

That inhalation produces toxicity in large airways is supported by evidence of ciliated cell loss and increased epithelial mitotic index in small animals, netrophilic inflammation in humans, increased bronchial artery blood flow in sheep and by the symptoms of cough and of substernal pain exacerbated by deep inspiration in humans(Bromberg 1999).

2.7 Populations at risk

Every individual has a different susceptibility to air pollutants. The level of individual risk is defined by genetics and biology, age (especially vulnerable are those individuals at the life cycle extremes), nutritional state, presence and severity of respiratory and cardiac conditions and the use of medications (Wilson *et al.* 1996). A good example of varying individual risks is demonstrated by a study evaluating maximum expiratory flow in healthy children, children with minor respiratory disease and those with asthma, with and without pharmacological treatment, all exposed to various environmental pollutants. The results showed an association between exposure and disease only in children with asthma who were under pharmacological treatment, in other words, those children who were most seriously ill (Roemer *et al.* en 1999). Similar studies showed that adolescents suffering from asthma are extremely sensitive to exposure to SO_2 (Speker 1999).

Other susceptibility factors that could be associated with respiratory diseases are the presence of certain alleles (genetic susceptibility), enzymatic isotypes involved in the metabolism of environmental xenotoxins (such as members of the cytochrome P-450 family, glutathione s-transferase), and enzymes involved in the DNA repair process (Möller *et al.* 1994). Age is also an important factor, with preadolescents (< 13 years) and the elderly (> 65) at greatest risk (Wilson *et al.* 1996, Ghio *et al.* 1999).

2.8 Air pollution exposure factors

The major sources of human exposure to air pollution are, as mentioned above, those produced by human activity. Pollutants can enter the organism in various ways such as ingestion, absorption through the skin and inhalation (Möller *et al.* 1994, Wilson *et al.* 1996). Inhalation is the major route of entry for exposure to air pollution. An important aspect of inhalation that is often ignored is oral breathing. When individuals breath through the mouth, the physical and mechanical barriers of nasal breathing are absent, and oral breathing has been shown to decrease the ability to eliminate particles deposited in the respiratory tract, mainly in the upper air ways (Wilson *et al.* 1996).

Until recently, only outdoor areas (exterior) were considered as exposure sites since that was where an individual would contact the majority of air pollutants. We now know that this is true only for certain types of pollutants such as metals, which due to their particle size are found essentially only outdoors (this is true for any particulate pollutant with a particle diameter greater than 10 μm). Carbon monoxide (CO) and nitrogen dioxide (NO_2), on the other hand are found in greater quantity indoors (Möller *et al.* 1994, Maynard 1999).

A study in the United States showed that individuals spend an average of 87.2% of their time indoors, 5.6% of their time outdoors and 7.2% in transit (Wilson *et al.* 1996), and values for Mexico are 83.7%, 11.50% and 0.05% correspondingly (Rojas-Bracho 1994). These data demonstrate the importance of determining indoor, as well as outdoor, exposure when precisely defining an individual's true exposure.

Other factors must also be considered when determining exposure. The degree of dispersion or accumulation of contaminants depends on weather conditions. An increase in temperature, for instance, provides convection currents that help to disperse pollutants (Brauer *et al.* 1995), although some studies claim more respiratory problems reported on warmer days (Katsouyanni 1995). Mexico City is recognised world wide as a prime example of where geographical and weather characteristics play an important role in pollution accumulation. The conditions in Mexico City generally favour accumulation of pollutants (Programa para mejorar la calidad del aire en el valle de México 1995-2000).

All these factors must be taken into consideration when establishing exposure levels to environmental pollutants. This requires a fractionated evaluation where pollutants in the microenvironment, the time the individual spends in this environment as well as other factors which could confuse a precise evaluation of exposure are all considered (Möller *et al.* 1994, Wilson *et al.* 1996). Over all, establishing exposure to environmental pollutants for an urban dwelling individual is extremely complex (Möller *et al.* 1994, Wilson *et al.* 1996).

3. Meta-analysis of human health effects of particulate matter and ozone

In order to evaluate the health risks and costs due to air pollution (specifically ozone and PM_{10}) in the Mexico City Metropolitan Area (MCMA), we required estimates of the changes in incidence of adverse health effects associated with projected changes in air quality. Estimates of the changes in air quality and the population exposed are presented in another section of this report. This section presents the method used to derive the concentration-response functions.

The number of published studies of the health effects of air pollution has grown during the last decade; however, specific studies in the MCMA are still limited. Therefore, we decided to summarise international and national published relevant reports via a meta-analysis. The methodology of this analysis focuses on combining the results from the various studies to identify consistent patterns. Due to the rapid growth of the field of epidemiology since the 1960's, the number of publications is overwhelming and the classical narrative review is no longer appropriate for summarising findings in this field. Meta-analysis of published papers has several limitations. Heterogeneity (including confounding) and publication bias are among the most important. Pooled estimates should be taken with caution if heterogeneity between studies is high, sensitivity analysis would be preferable (Blettner,1999). Conventional statistical analysis with fixed effects, that is to assume only sampling error in studies, do not take into heterogeneity resulted from sampling sites differences. When heterogeneity is present, random models incorporate variation between the studies, assuming that each study has its own true exposure effects and that there is a random distribution of the true exposure effects around a central effect. However, if we presume heterogeneity, the use of random effects is limited too, since it is not sufficient to explain the heterogeneity between studies, since the random effect merely quantifies unexplained statistical variation. Heterogeneity between studies should yield careful investigation of the sources of the differences, i.e. population characteristics, household conditions, particles composition, statistical models used, control of confounders etc. Since information on relevant characteristics like particulate composition was not available for Mexico City, and due to time constraints we decided to reduce heterogeneity with the inclusion criteria and use the between-study variance to weight the studies with random effects models.

3.1 Methods

3.1.1 Identification of publications

The first step in this analysis was an exhaustive search of published studies on human health effects due to exposure to ozone and PM_{10} via Medline, Pubmed, Biomed-net and Aries databases. Manual library searches were also performed examining particularly Mexican publications. Besides providing a general theoretical structure for the analysis, these search results served to compile a summary of the major toxicology aspects of environmental pollution.

No results of laboratory animal studies were included in the analysis because of the difficulty to extrapolate results to environmentally exposed humans. Human populations exposure occurs with a variety of diseases and different severity levels, unlike most laboratory animal studies, which are performed using healthy animals. Humans are usually exposed to several pollutants simultaneously while most animal studies deal with exposure to a single compound. In addition, humans are normally exposed to chronic doses of pollutants while animals are subjected to acute or sub-acute exposure, and obviously the biological responses to the same chemical varies for different species (Kodanvanti 1999).

Selection and Classification of Material

Not all the bibliographic material collected was used in the statistical analysis. Criteria of inclusion was: a) peer-reviewed published papers evaluating the association between exposure to ozone or particles and clinically identifiable human health effect (biochemical and molecular effects were not included), b) quantification of any type of particles, Total suspended particles (TSP), black smoke (BS), Coefficient of haze (CoH) or any PM. Criteria for exclusion was: a) papers not presenting information for the variance, standard error or confidence intervals for the association estimate (percent change, RR or OR), b) reports based on small populations, c) absence of control for temperature and seasonal variation over the study time period. In order to separate the effects of particles and ozone, specially mortality, we classified the studies that used multivate models to take into account spatial and time correlation of these pollutants.

3.1.2 Air pollutants

Reports were classified according to location and time period as well as average and range of PM_{10} and ozone levels. For studies covering a period of several years, annual averages were used, and for shorter studies of one year or non-continuous time periods, pollutant averages given by the authors recorded. For ozone studies, if possible the average maximum for one hour was used. If this value was not available, the author's reported value recorded.

Not all articles provided PM_{10} data since for each case this depended on the method used for particle quantification. Usually the particles were reported as total suspended particles (TSP) including black smoke (BS), PM_{15}, PM_{13}, PM_{10}, PM_{7}, $PM_{2.5}$ or the Haze coefficient (CoH). In order to produce homogeneous results in terms of PM_{10}, the following table of approximate equivalencies was used.

Table 3. **Approximate Equivalencies PM_{10}**

$PM_{10} \cong PM_{15}$
$PM_{10} \cong PM_{13}$
$PM_{10} \cong TSP * 0.55$
$PM_{10} \cong PM_{2.5} / 0.6$
$PM_{10} \cong CoH / 0.55$
$PM_{10} \cong BS$

Source: Dockery *et al.* 1994.

3.1.3 Information on health effects

The analysis included all health effects reported for human populations. These included total mortality, mortality due to respiratory causes, mortality due to cardiovascular causes, mortality in individuals above 65 years of age, child mortality, total hospitalisations, hospitalisations due to respiratory causes, hospitalisations due to cardiovascular causes, emergency room attendance, emergency room attendance for respiratory causes, emergency room attendance for cardiovascular causes, all effects reported for asthmatic individuals, all effects reported for asthmatic individuals using bronchial dilators, effects on functional respiratory parameters (FVC, FEV-1, etc) and all respiratory effects reported for the general population. However, for the purpose of the final analysis only non-overlapping health effects are to be used in order to avoid double counting of benefits from overlapping endpoints. For example, the literature reports relationships for hospital admissions for single respiratory ailments, as well as for all respiratory ailments combined.

3.1.4 Concentration response functions

Most studies express the health effect (y) a function of an amount of change air pollutant level (ΔAP). The calculation of the corresponding (Δy) depends on a C-R function from epidemiological studies. The C-R estimated in these studies may differ from each other in several ways, standard definitions of health endpoints, baseline populations and the shape of the relationship. Some studies assume linear relationships, while others log-linear functions. The linear relationship is of the form $y = \alpha + \beta P$. The log linear relationship is of the form: $y = \beta e^{\beta P}$ or, equivalently $\ln(y) = \alpha + \beta P$. Despite some statistical limitations, results from different studies were transformed to represent percent changes in the heath effect for each 10 units of variation in the pollutant concentration. Since authors reported values in different C-R functional forms as odds risk (OR), relative risk (RR), percent increase, and regression results or coefficients of regressions, we used the following transformations:

- For RR or OR: RR or OR value was subtracted 1 and from the result multiplied by 100. This operation converted the units to percentages of the health effect. Each quantity was then divided by the value of change according to the concentration used by the author in the article. These values could be some percentile rank, maximum value, average, 100 units of concentration, 50 units of concentration, etc. When the author used continuous variables, the RR or surrogate was multiplied by 10 to provide a percent change for 10 units of concentration.

- For percent change. In this case, the percent change was divided by the value of concentration used by the author in the article When the author used continuous variables, the RR or surrogate was multiplied by 10 to provide a percent change for 10 units of concentration.

- For coefficients (Poisson or logarithmic). First we determined whether this coefficient had been multiplied by some unifying factor (usually done to simplify notation). If so, the original value was recovered through the appropriate operations, as indicated for each table in the methods or results. The original value was then multiplied by 1000 to convert β into a percentage for 10 units of concentration (100 x 10 = 1000).

To calculate the confidence interval, one of the following two procedures was used:

- If confidence intervals were reported in the article (these are commonly included for RR and OR), the same adjustment was made as for RR or OR, accordingly.

- If the results were given in terms of a regression coefficient or when no confidence interval was reported, the author usually provided a value for standard error. In this case the adjustment was made as if for a regression coefficient and then added and subtracted to the main value to provide intervals.

To simplify all this information graphical presentation was prepared for each health effect.

3.1.5 Pooled estimate

To obtain a single pooled estimate of the health effects reported from the selected studies a weighted average was used. C-R functions were weighted according to the statistical precision of the studies and the between-studies variance, using random effects models. Since the proposed mother project will be carried out in Mexico City, articles based on Mexico City population were given double the weight of international cases, because they are though to reflect more the Mexican reality in terms of susceptibility and sociodemographic characteristics. For pooled estimate are presented with confidence intervals at 95%.

4. Results

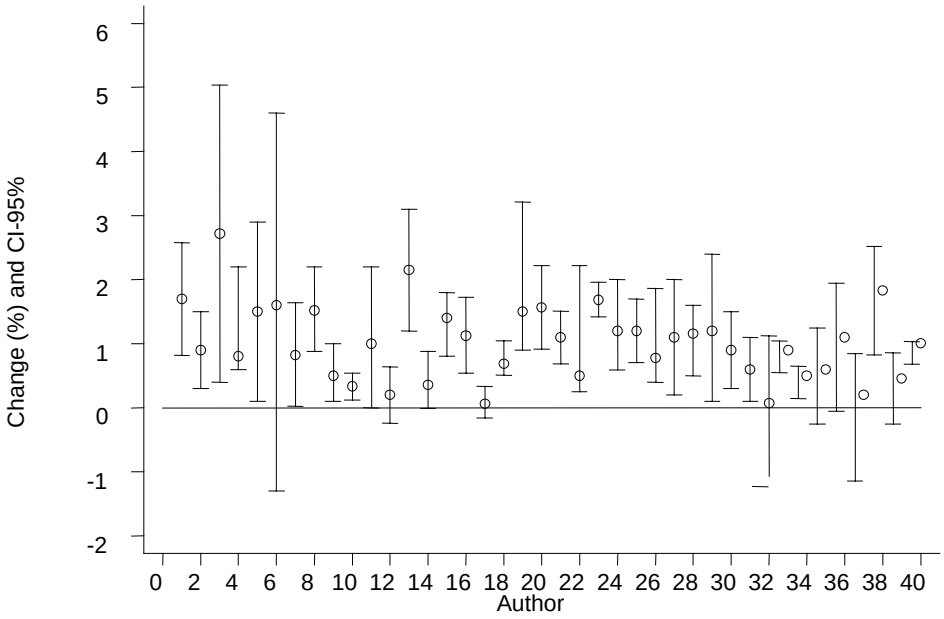
We performed an extensive meta-analysis with the most current national and international literature describing the effects of air pollution (specifically ozone and PM_{10}) on human health, with aim to characterise in a ecosystemic point of view, the contamination health risk, the magnitude of the damage and the cost on the human health. The report below summarises this review with the latest available information on this topic.

4.1 Meta-analysis of health effects caused by exposure to PM_{10}

a) Percent change in mortality due to exposure to PM_{10}

Of all the toxic effects attributed to PM_{10}, death has been the most thoroughly documented. Death due to effects of air pollution occurs generally between 1 and 5 days after the hazardous exposure. Since the 1950's, many studies have recorded increased mortality associated with high levels of pollution. In this analysis, we have included the major studies carried out in the Americas, Europe, Australian and Asia since 1970.

Figure 1. **Percent change in general, non-accidental mortality for each 10 μg/m^3 increase in PM_{10}**



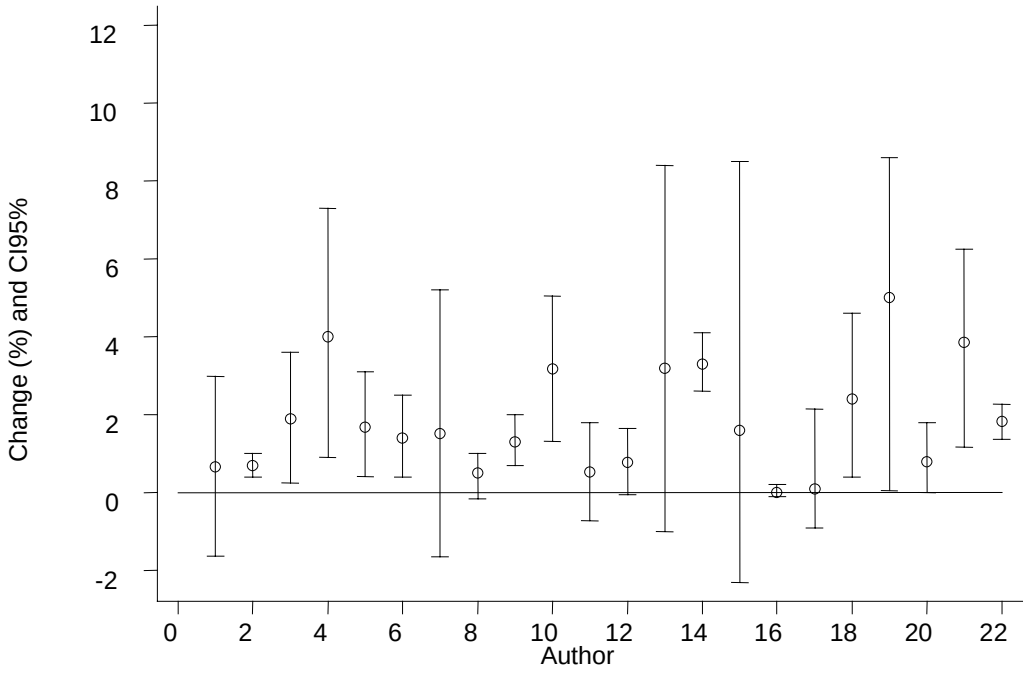
Note: The numbers represent the following studies: 1. Anderson 1996 (London), 2. Ballester 1996 (Valencia), 3. Borja-Aburto 1997 (Mexico), 4. Brenner 1999 (London), 5. Dockery 1992 (St. Louis), 6. Dockery 1992 (Tennessee), 7. Gamble 1996 (Chicago), 8. Gamble 1996 (Utah), 9. Ito 1996 (Chicago), 10. Kelsall 1997 (Philadelphia), 11. Kinney 1995 (Los Angeles), 12. Lee 1999 (Seoul), 13. Mazundar 1983 (Pittsburgh), 14. Moolgavkar 1996[b] (Ohio), 15. Moolgavkar 1996[a] (Philadelphia), 16. Neas 1999 (Philadelphia), 17. Ostro[b] 1995 (California), 18. Ostro 1996 (Santiago), 19. Pope III 1996 (Utah), 20. Pope III 1999 (Ogdem), 21. Pope III 1999 (Provo), 22. Pope III 1999 (Utah), 23. Samet 1998 (Philadelphia), 24. Schwartz 1994[c] (Cincinnati), 25. Schwartz 1992[a] (Philadelphia), 26. Schwartz 1992[b] (Steubenvile), 27. Schwartz 1993[a] (Birmingham), 28. Schwartz 1991 (Detroit), 29. Schwartz 1996[b] (Ohio), 30. Simpson 1997 (Brisbane), 31. Spix 1993 (Erfurt), 32. Sunyer 1996 (Barcelona), 33. Touloumi 1993 (Athens), 34. Touloumi 1996 (Athens), 35 Verhoeff 1996 (Amsterdam), 36. Wordley 1997 (Birmingham), 37. Zmirou 1996 (Lyon), 38. Castillejos 2000 (México), 39. Cropper 2000 (Delhi), 40. Pooled estimate.

Figure 1 shows the percent change in general mortality associated with an increase in air pollution. The percent change, considering all the cases, establishes an increase in mortality of between 0.06 and 2.82% with a weighted estimate of 1.01 (CI 95% 0.83-1.18). These data are for total, non-accidental deaths.

Despite the consistency of this association with excess mortality there are aspects of this association that are still uncertain. There is always concern that some confounder, another variable correlated with the exposure and causally related to the effect, might actually be responsible for an association found by an epidemiological study. However, many studies have separated the effects of particles including other pollutants in the statistical models. The coherence of associations with other effects makes this association plausible. Additionally, clinical studies have demonstrated decreased lung function, increased frequencies of respiratory symptoms, heightened airway hyper-responsiveness, and cellular and biochemical evidence of lung inflammation in exercising adults exposed to ozone concentrations at low exposures.

The pooled estimate we obtained is larger than that obtained by Levy (2000) because of the inclusion of more worldwide recent reports. Although the above results are significant, death could be more certainly attributed to air pollution exposure if the cause of death were determined as due to some ailment which is caused or aggravated by air pollution, such as death due to respiratory or cardiac diseases (Figures 2 and 3).

Figure 2. **Percent change in mortality due to respiratory causes for each 10 μg/m^3 increase in PM_{10}**

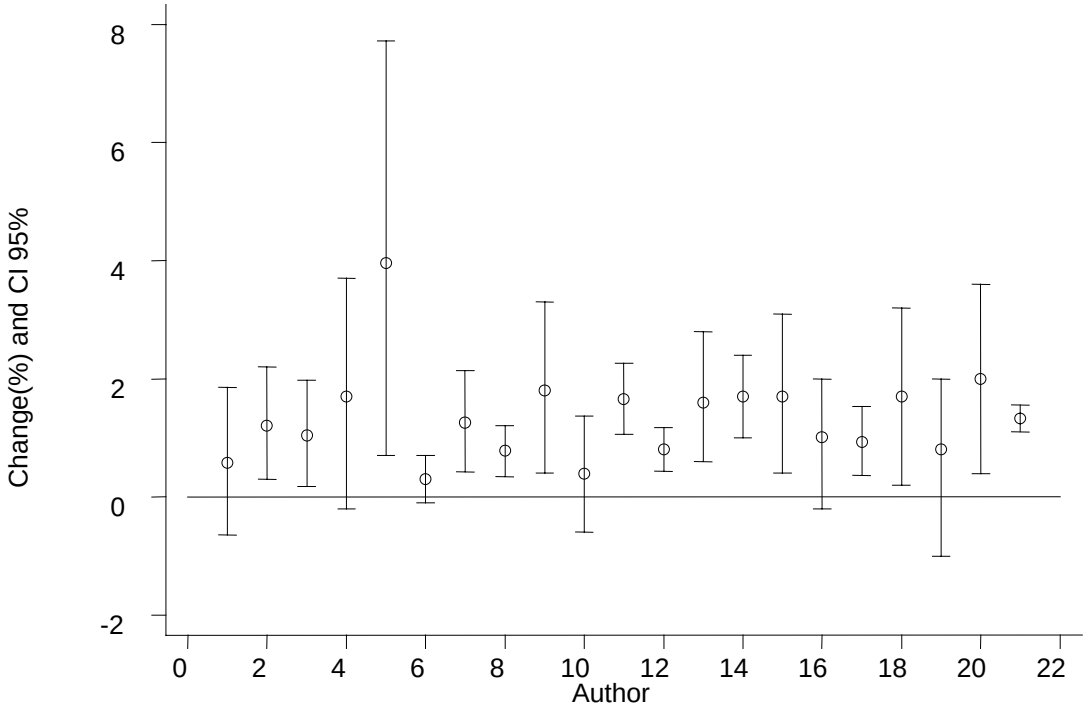


Note: The numbers represent the following studies: 1. Anderson 1996 (London), 2. Ballester 1996, (Valencia), 3. Borja-Aburto 1997 (Mexico), 4. Brenner 1999 (London), 5. Dab 1996 (París), 6. Ito 1996 (Chicago), 7. Neas 1999 (Philadelphia), 8. Ostro 1995[b] (California), 9. Ostro 1996 (Santiago), 10. Pope III 1999 (Ogdem), 11. Pope III 1999 (Provo), 12. Pope III 1999 (Utah), 13. Schwartz 1994[c] (Cincinnati), 14. Schwartz 1992[b] (Philadelphia), 15. Schwartz 1993[a] (Birmingham), 16. Simpson 1997 (Brisbane), 17. Sunyer 1996 (Barcelona), 18. Vigotti 1996 (Milan), 19. Wordley 1997 (Birmingham), 20. Zmirou 1996 (Lyon), 21. Castillejos 2000 (Mexico), 22. Pooled estimated.

Figure 2 shows the studies where an increase in death due to respiratory causes was evaluated with high levels of PM_{10} pollution. The increases are greater than those describing total death, with a range of percent increase from 0.4 to 5.0%. Only the two studies by Simpson *et al.* in 1997 (0.01%) and Sunyer *et al.* in 1996 (0.09%) reported low increases. For these studies the pooled estimated is greater than that reported for total, non-accidental death, 1.82 (CI 95% 1.37-2.22).

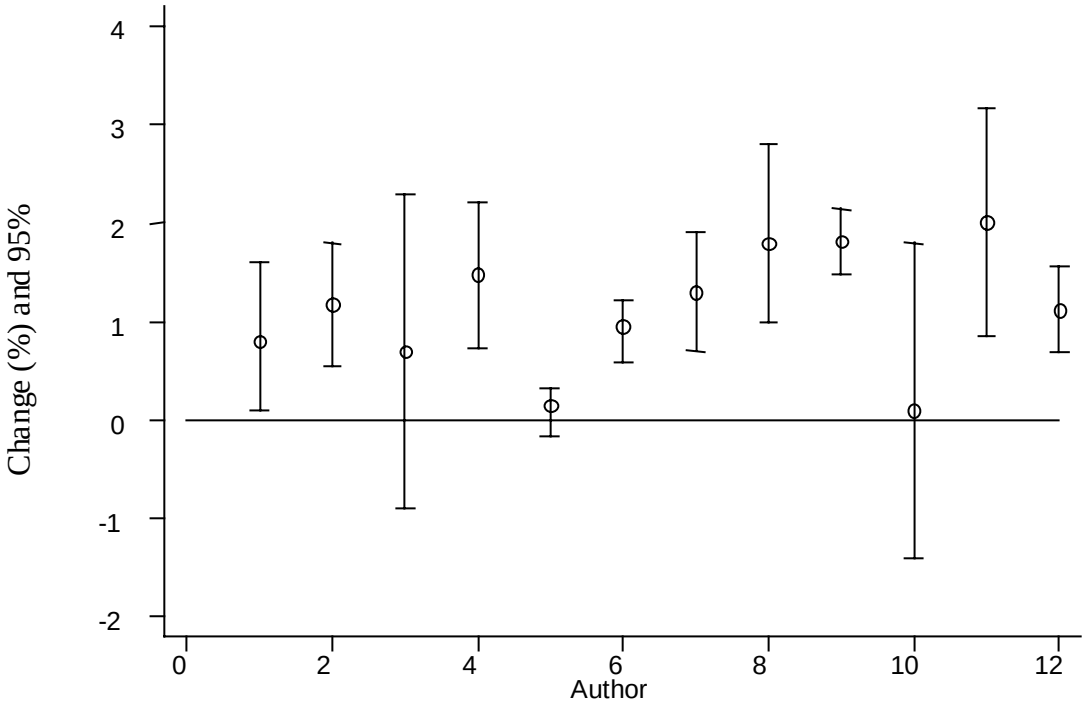
Studies that have determined an increase in death due to cardiovascular system damage associated with exposure to PM_{10} are summarised in Figure 3. In this case the range of percent change is lower than for deaths due to respiratory ailments (0.30 to 1.80%). Only the 1996 Gamble *et al.* study reported percentages above 3% (3.96%). The weighted average is 1.32 (CI 95% 1.10-1.55).

Figure 3. **Percent change in mortality due to cardiovascular causes for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Anderson 1996 (London), 2. Ballester 1996 (Valencia), 3. Borja-Aburto 1997 (Mexico), 4. Bremner 1999 (London), 5. Gamble 1996 (Utah), 6. Ito 1996 (Chicago), 7. Neas 1999 (Philadelphia), 8. Ostro 1996 (Santiago), 9. Pope III 1996 (Utah), 10. Pope III 1999 (Ogdem), 11. Pope III 1999 (Provo), 12. Pope III 1999 (Utah), 13. Schwartz 1994[c] (Cincinnati), 14. Schwartz 1992[a] (Philadelphia), 15. Schwartz 1993[a] (Birmingham), 16. Simpson 1997 (Brisbane), 17. Sunyer 1996 (Barcelona), 18. Wordley 1997 (Birmingham), 19. Zmirou 1996 (Lyon), 20. Castillejos 2000 (Mexico),21. Pooled estimate.

Figure 4. **Percent change in mortality for individuals older than 65 years for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Ballester 1996 (Valencia), 2. Borja-Aburto 1997 (Mexico), 3. Brenner 1999 (London), 4. Neas 1999 (Philadelphia), 5. Ostro 1995[b] (California), 6. Ostro 1996 (Santiago), 7. Saldiva 1994 (Sao Paulo), 8. Schwartz 1994[c] (Cincinnati), 9. Schwartz 1992[a] (Philadelphia), 10. Simpson 1997 (Brisbane), 11. Castillejos 2000 (Mexico), 12. Pooled estimate.

Once again, the elderly, those individuals 65 years of age and older, must be dealt with in an independent analysis from the rest of the population, because their physiology renders them at high risk of suffering toxic effects from exposure to air pollution. Figure 4 summarises the major studies where increases in total mortality (non-accidental) have been reported associated with exposure to PM_{10}. Percent change for these studies varies from 0.1 to 1.82%. The pooled estimate is 1.18 (CI 95% 0.66-1.57).

b) Infant mortality associated with exposure to PM_{10}

Only a few studies document the association of infant mortality associated with PM_{10} is very important. To date only three publications report an increase in post neonatal mortality (Table 4). Two of these studies were performed in the U.S. and the other in the Czech Republic. The U.S. studies reported a percent change from 1.05 to 1.20%, while the Czech study showed an increase between 3.65 and 7.08%.

The results shown in Table 4, however, demonstrate differences in the magnitude of the changes in increased mortality. In the Czech study, the increase in mortality for respiratory disease associated deaths is almost twice the increase in general, non-accidental deaths. The Woodrouff *et al.* study, on the other hand, reports very slight differences. Despite the differences, both studies indicate increased death. Another interesting result from these studies is that low birth weight babies (1.05%) had a lesser increase in mortality than normal birth weight babies (1.20%). The studies also reported that deaths from sudden infant death syndrome increased more (1.12%) than deaths from other causes (1.04%).

Two studies have reported on neonate and infant death associate with exposure to PM_{10}. One study was carried out in the Czech Republic (cross-sectional) and the other in Mexico (time-series)

General, non-accidental mortality was reported as more than twice as high for infants as for neonates. Such a difference could be due to greater exposure for infants than neonates.

The relationship between parental exposure to high concentrations of PM_{10} and low birth weight is another relevant toxicological parameter. To date only one study by Wang *et al.*, 1998, has dealt with this topic. Wang reported on infants born between 1988 and 1991 with a significant 1% decrease in new-born weight associated with mothers exposures to PM_{10} concentrations between 9 and 308 $\mu g/m^3$ (CI 95% 0.5-1.4).

Table 4. **Percent change in mortality post neonatal, neonate and infant for each 10 $\mu g/m^3$ increase in PM_{10}**

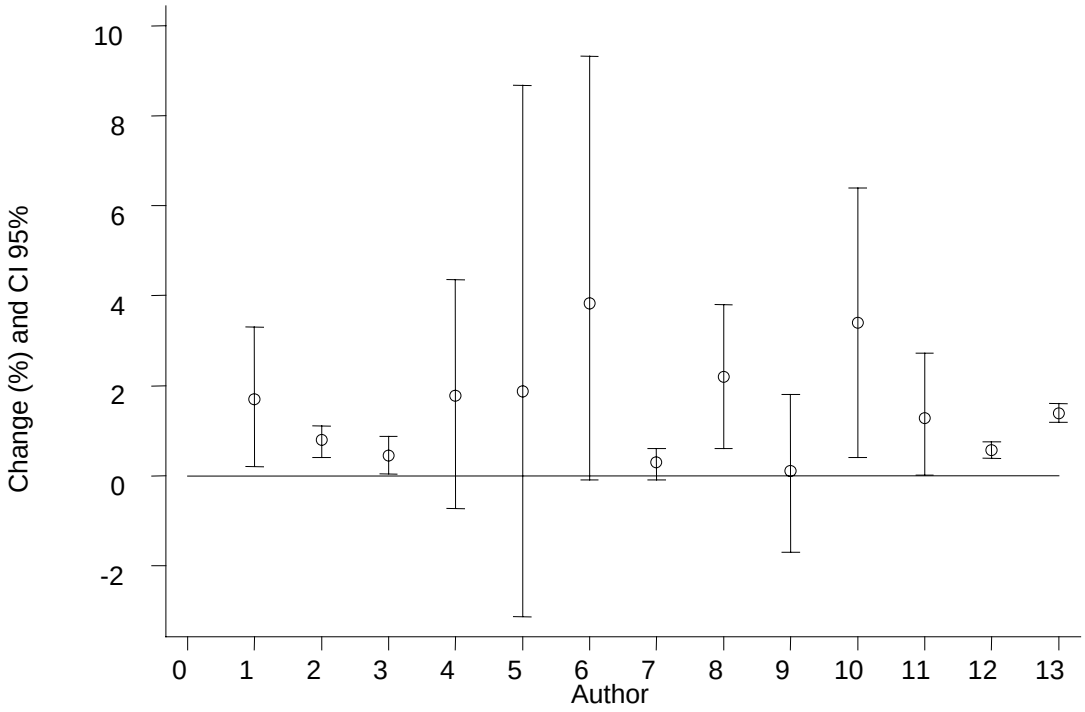
Author	Year	• Effects	Study	Country	Period	% change	95% CI LL	95% CI UL
Bobak	1992	• Post neonatal mortality	Cross-sectional study	Czech Rep.	1986 to 1988	3.65	0.59	7.43
Bobak	1992	• Death associated with respiratory system	Cross-sectional study	Czech Rep.	1986 to 1988	7.08	4.25	47.93
Woodroff	1997	• Post neonatal mortality	Cross-sectional study	U.S.A.	1989 to 1991	1.04	1.02	1.07
Woodroff	1997	• Death associated with respiratory system • Sudden infant death syndrome • Normal birth weight	Cross-sectional study	U.S.A.	1989 to 1991	1.12	1.07	1.17
Woodroff	1997	• Death associated with respiratory system • Normal birth weight	Cross-sectional study	U.S.A.	1989 to 1991	1.20	1.06	1.36
Woodroff	1997	• Death associated with respiratory system • Low birth weight	Cross-sectional study	U.S.A.	1989 to 1991	1.05	0.91	1.22
Bobak	1992	• Infant and neonate mortality	Cross-sectional study	Czech Rep.	1986 to 1988	1.65	-0.23	3.77
Loomis	1999	• Infant and neonate mortality	Time-series study	Mexico DF	1993 to 1995	3.52	0..72	6.31

c) Percent change in hospitalisations due to respiratory diseases

The number of individuals hospitalised due to respiratory ailments for a given period is another useful indicator often employed to determine the effects of exposure to low concentrations of air pollution (specifically PM_{10}) on the population.

Figure 5 shows some of the studies where an association has been assessed between pollution levels and increased hospitalisations due to respiratory causes. The reported increases adjusted to a change of 10 units of pollutant concentration were between 0.30 and 3.83%. All of these studies were carried out exclusively in developed countries, which points out the need for the same type of research in developing nations, where exposure to environmental pollutants tends to be greater. In this case the pooled estimate increase was 1.39 (CI 95% 1.18-1.60).

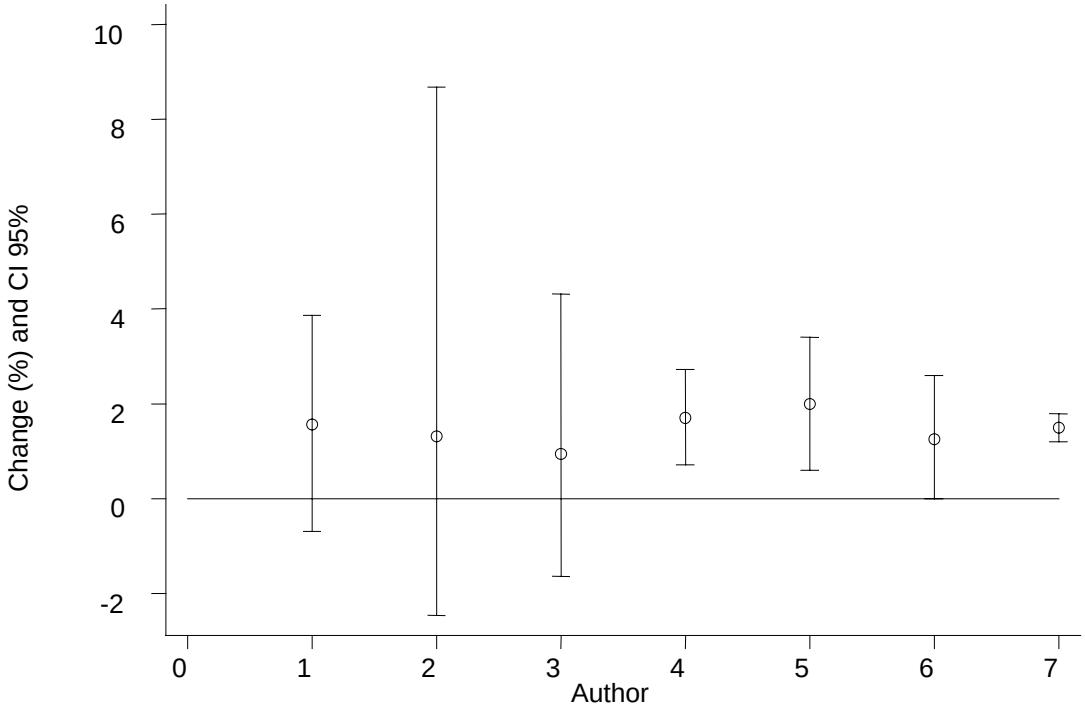
Figure 5. **Percent change in hospitalisations due to respiratory ailments for 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Abbey 1995 (California), 2. Burnett 1995 (Ontario), 3. Dab 1996 (Paris), 4. Ponce de León 1996 (London), 5. Schouten 1996 (Amsterdam), 6. Schouten 1996 (Rotterdam), 7. Schwartz 1996[a] (Cleveland), 8. Thurston 1992 (Buffalo), 9. Thurston 1992 (New York), 10. Thurston 1994 (Ontario), 11. Vigotti 1996 (Milan), 12. Linn 2000 (Los Angeles). 13. Pooled estimate.

Figure 6 summarises the studies where an association was established between hospitalisations due to respiratory ailments and exposure in individuals older than 65 years of age. The trend of the changes was the same with an average increase raging between 0.94 and 1.70% . The weighted average is 1.49 (CI 95% 1.20 – 1.78).

Figure 6. **Percent change in hospitalisations due to respiratory diseases in individuals older than 65 years for each 10 μg/m^3 increase in PM_{10}**

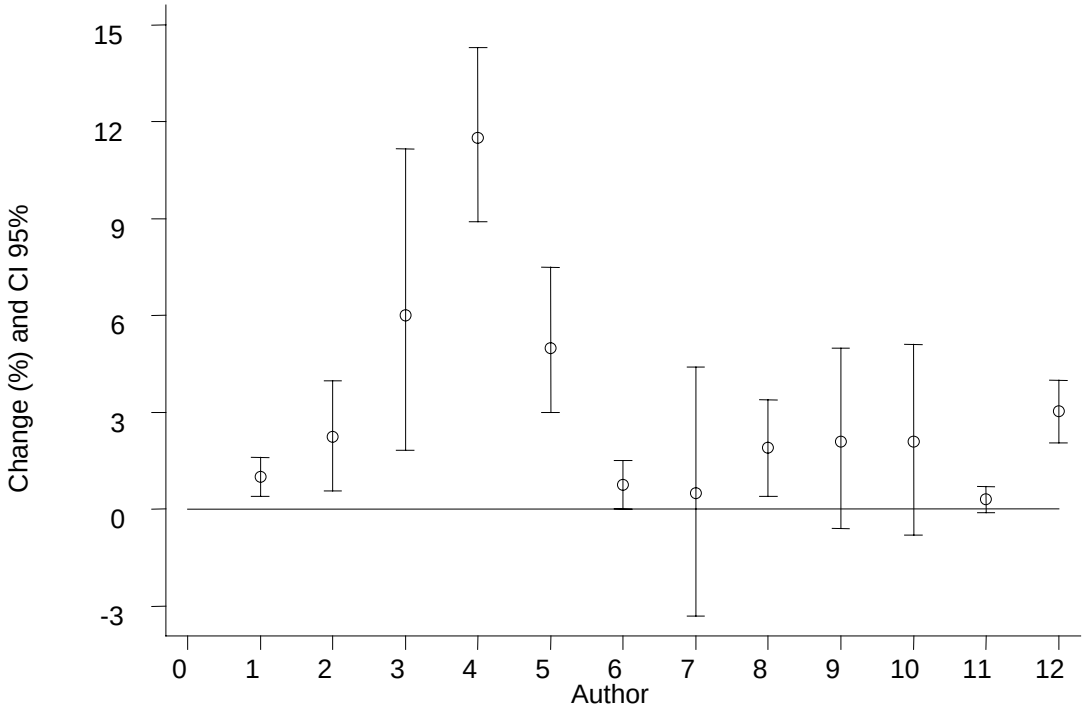


Note: The numbers represent the following studies: 1. Ponce de León 1996 (London), 2. Schouten 1996 (Amsterdam), 3. Schouten 1996 (Rotterdam), 4. Schwartz 1999 (Spokane), 5. Schwartz 1999 (New Heaven), 6. Schwartz 1995[a] (Tacoma), 7. Pooled estimate.

Besides establishing the increase in hospitalisations due to PM_{10}, the types of diseases for which patients were hospitalised and are most associated with exposure should also be determined in order to recognise which individuals will be more at risk during an episode of elevated environmental pollution. Figures 7-9 show the association between PM_{10} exposure and hospitalisation for asthma, COPD (chronic obstructive pulmonary disease) and pneumonia, respectively.

Figure 7 summarises studies where an association was found between PM_{10} levels and hospitalisation for asthma attacks. The results from the different studies show a general increase in the percent change from 0.5 to 11.5%. The pooled estimate increase was 3.02% (CI 95% 2.05 - 4.00).

Figure 7. **Percent change in hospitalisations for asthma for each 10 μg/m^3 increase in PM_{10}**

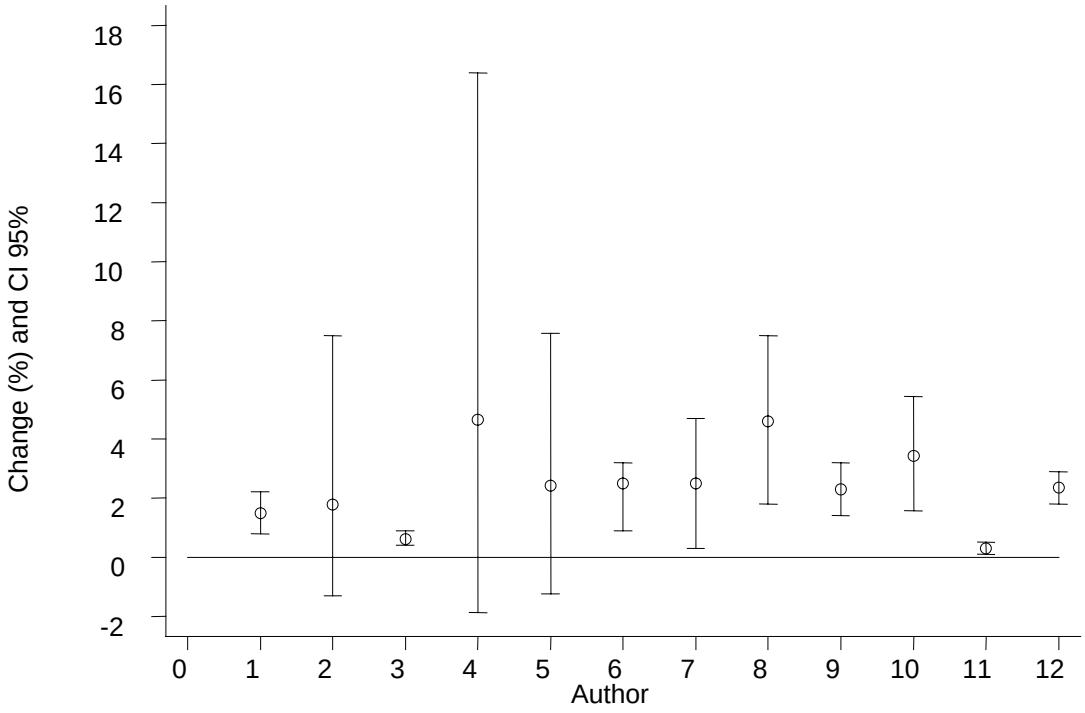


Note: The numbers represent the following studies: 1. Burnett 1995 (Ontario), 2. Delfino 1994 (Montreal), 3. Lipsset 1997 (Santa Clara), 4. Ostro 1991 (Denver), 5. Romieu 1996 (Mexico), 6. Sheppard 1999 (Seattle), 7. Schwartz 1995[a] (Tacoma), 8. Thurston 1992 (Buffalo), 9. Thurston 1992 (New York), 10. Thurston 1994 (Ontario), 11. Linn 2000 (Los Angeles), 12. Pooled estimate.

Figure 8 summarises the studies where a significant association was established between increased hospitalisation for COPD and PM_{10} levels in the general population. The percent change ranged from 0.6 to 4.66%. The pooled estimated increase was 2.34% (CI 95% 1.80 - 2.89).

In this same category, the percent increase for individuals older than 65 years of age was clearly higher than for the rest of the population (Schwartz, 1999) (not shown in the figure).

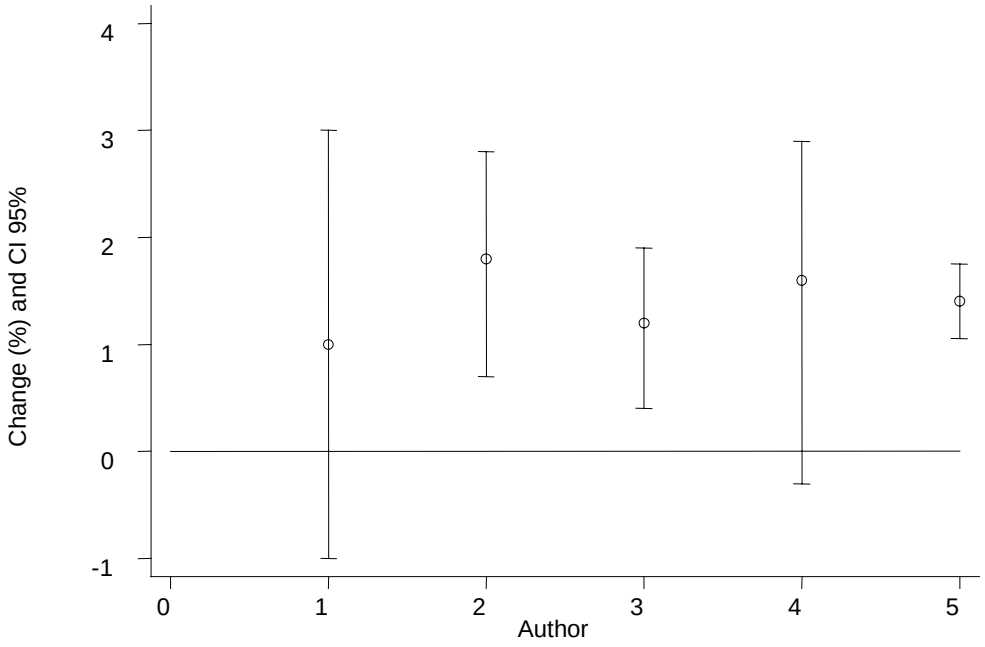
Figure 8. **Percent change in hospitalisations due to COPD for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Burnett 1995 (Ontario), 2. Moolgavcar 1997 (Birmingham), 3. Ostro 1995 (Santiago), 4. Schouten 1996 (Amsterdam), 5. Schouten 1996 (Rotterdam), 6. Schwartz 1993[a] (Birmingham), 7. Schwartz 1995[a] (Tacoma), 8. Schwartz 1994[d] (Minneapolis), 9. Sunyer 1995 (Barcelona), 10. Schwartz 1999 (Spokane), 11. Linn 2000 (Los Angeles) 12. Pooled estimate.

Pneumonia is another disease of the pulmonary system for which increased incidence has been reported associated to exposure to PM_{10}. Figure 9 shows the major studies realised to date on this topic. All the studies were carried out in the U.S. and published by Schwartz *et al.* and Moolgavcar *et al.* For pneumonia, the increases reported ranged from 1.2 to 1.8%. The pooled estimated increase 1.40% CI 95% 1.05 - 1.75) was greater than for COPD.

Figure 9. **Percent change in hospitalisations due to pneumonia for each 10 μg/m^3 increase in PM_{10}**

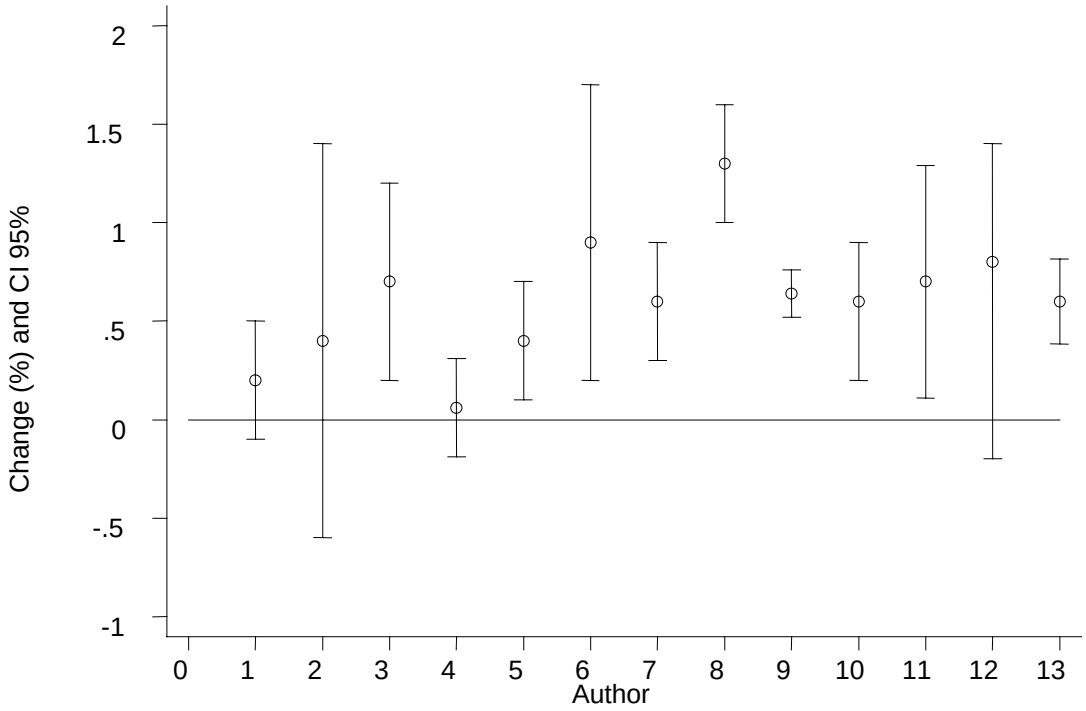


Note: The numbers represent the following studies: 1. Moolgavkar 1997 (Minneapolis), 2. Schwartz 1993[a] (Birmingham), 3. Schwartz 1995[a] (Tacoma), 4. Schwartz 1994[d] (Minneapolis), 5. Pooled estimate.

It is logical that respiratory diseases should be used as a first choice parameter in determining adverse effects associated with air pollution. Hospitalisation for cardiac ailments is also an important parameter for determining harmful exposure to PM_{10}. Figures 10 and 11 summarise these studies.

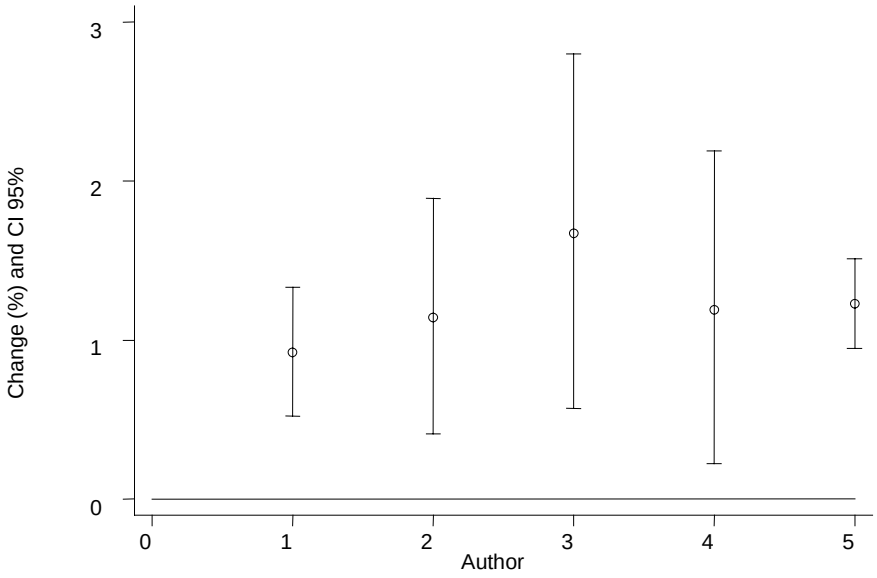
Figure 10 shows the percent change in hospitalisations due to cardiac diseases in all ages with increases ranging from 0.40 to 0.90%. Weighted average 0.60% (CI 95% 0.42 - 0.79). Figure 11 shows the effect for individuals older than 65 years of age with all increases above 1.22% (95% CI 0.94 - 1.50). All percent changes and the pooled estimated increase (1.22 vs. 0.60) are greater than those in Figure 10. This reiterates the importance of considering this age group specifically.

Figure 10. **Percent change in hospitalisations due to cardiovascular diseases for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Linn 2000 (Los Angeles) arrhythmia), 2. Burnett 1995 (Ontario) (arrhythmia), 3. Burnett 1995 (Ontario) (coronary artery), 4. Linn 2000 (Los Angeles) (cerebrovascular), 5. Linn 2000 (Los Angeles) (congestive hearth failure), 6. Burnett 1995 (Ontario) (congestive hearth failure), 7. Linn 2000 (Los Angeles) (myocardial infarction), 8. Linn 2000 (Los Angeles) (occlusive stroke), 9. Linn 2000 (Los Angeles) (total), 10. Schwartz 1995[b] (Detroit) (total), 11. Schwartz 1997 (Michigan) (total), 12. Morris 1998 (Chicago) (total), 13. Pooled estimate.

Figure 11. **Percent change in hospitalisations for cardiac disease in individuals more than 65 years old for each 10 μg/m^3 increase in PM_{10}**



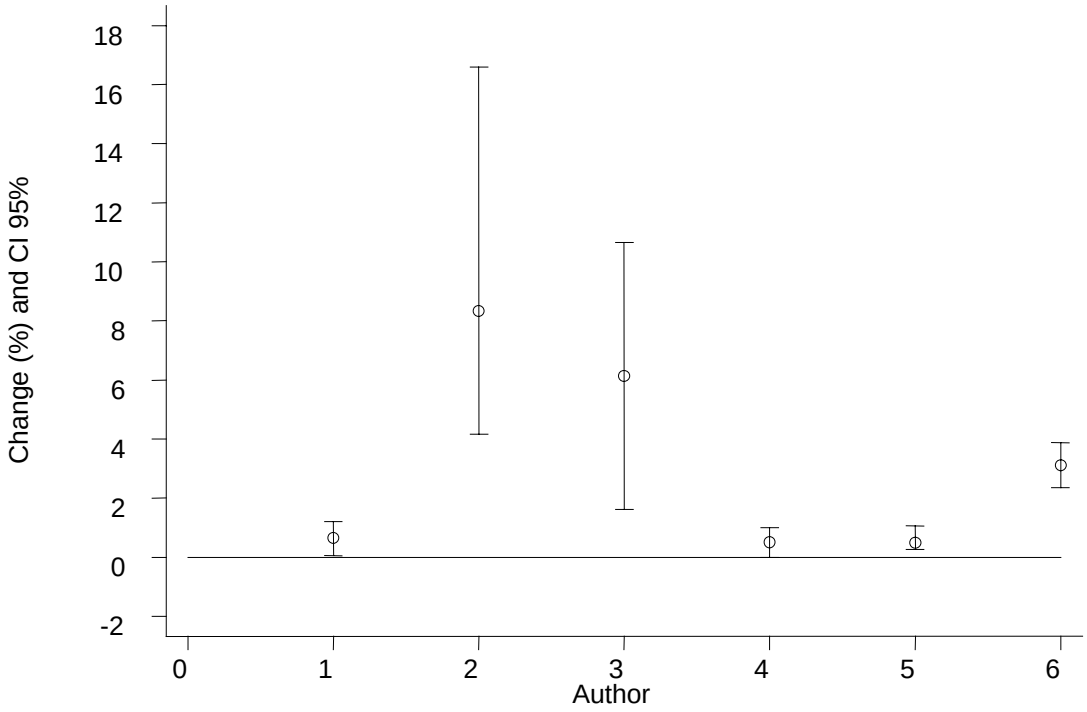
Note: The numbers represent the following studies: 1. Schwartz 1999 (Chicago), 2. Schwartz 1999 (New Heaven), 3. Schwartz 1999 (St Paul), 4. Schwartz 1997 (Tucson), 5. Pooled estimate.

d) Percent change in hospital emergency room admissions

Hospitalisations are not the only parameter useful for chronic exposure studies of PM_{10}. Hospital emergency room admissions for respiratory ailments are also considered as an indicator. The number of studies analysing this factor is much lower than for hospitalisation studies, probably due to the lack of complete and accurate records for these patients.

Figure 12 summarises some of the studies that report an association between increased emergency room admissions due to respiratory ailments and increased pollutant concentration. The increases determined vary widely up to 8.34% with a pooled estimated increase of 3.11% (CI 95% 2.35 - 3.88).

Figure 12. **Percent change in hospital emergency room admissions due to respiratory causes for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Atkinson 1999 (London), 2.Damakosh 2000 (Mexico) (low respiratory symptoms), 3. Delfino 1997 (Quebec),4. Samet 1995 (Steubenville), 5. Atkinson 1999 (London), 6. Pooled estimate.

The increased emergency room admissions for children´s asthma attack associated with exposure to particles was 4.50% (CI 95% 2.16 - 7.0) in a study by Lipset (for a childhood study).

Increased emergency room admissions associated with increased pollutant levels have been evaluated for other conditions as well with the reported results for croup (2.48%), tracheitis (12.5%), pneumonia (20.8%) and total admission (3.40%). Pneumonia shows an especially high increase in emergency room treatment (Table 5).

Table 5. **Percent change in hospital emergency room admission for different respiratory ailments for each 10 μg/m^3 increase in PM_{10}**

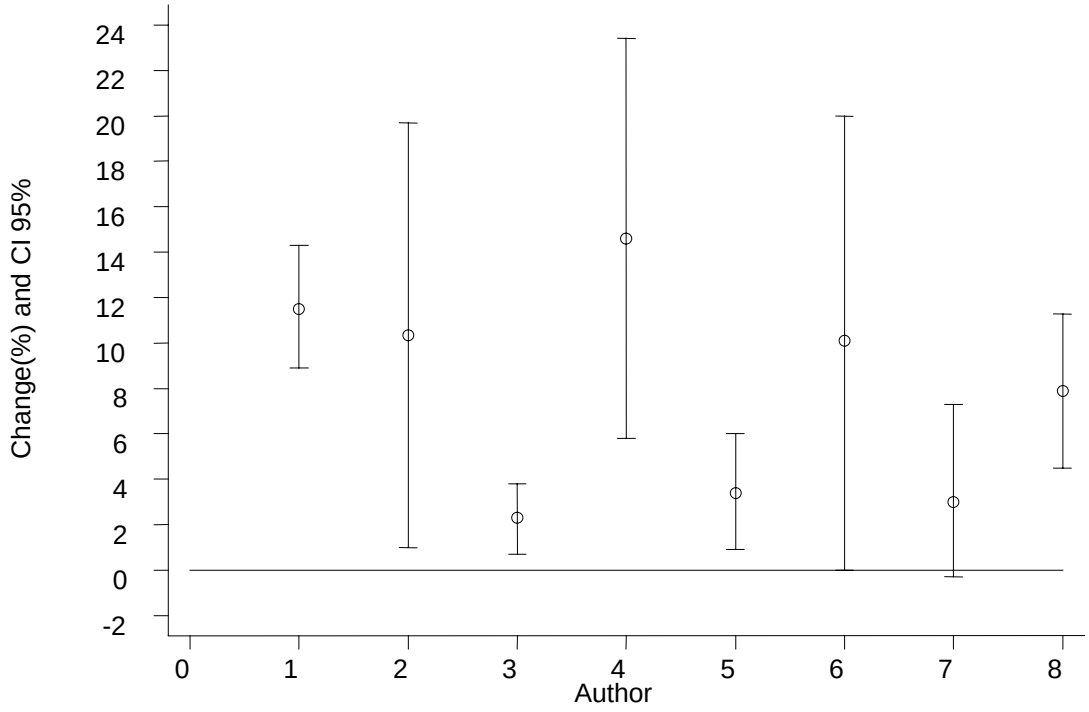
Author	Year	City	Period	PM_{10} levels	% change	95% CI	
				Mean (range)		LL	UL
Schwartz[1]	1993[c]	Seattle	1989 – 1990	26.9 (6.00 - 103.0)	3.40	0.90 to 6.00	
Damakosh [2]	2000	Mexico	1993 – 1994	45.0 (48.0 - 121.0)	12.5	0.00 to 29.2	
Damakosh [3]	2000	Mexico	1993 – 1994	45.0 (48.0 - 121.0)	20.8	4.16 to 45.8	
Schwartz	1991	Germany	1983 - 1985	32.40 (16.8 – 70.20)	2.48	3.10 to 4.34	

[1] Total visits, [2] Visits for tracheitis, [3] Visits for pneumonia, [4]Cruop.

e) Percent change in different respiratory symptoms in asthmatic individuals

Because individuals who suffer from asthma are especially susceptible to the effects of pollution, it is important to evaluate this population in detail. Figure 13 shows the results of several studies where an association was assessed between exposure and increased occurrence of asthmatic attacks. The reported increases range from 2.23% to 14.6%. Weighted average 7.87% (CI 95% 4.48 - 11.27).

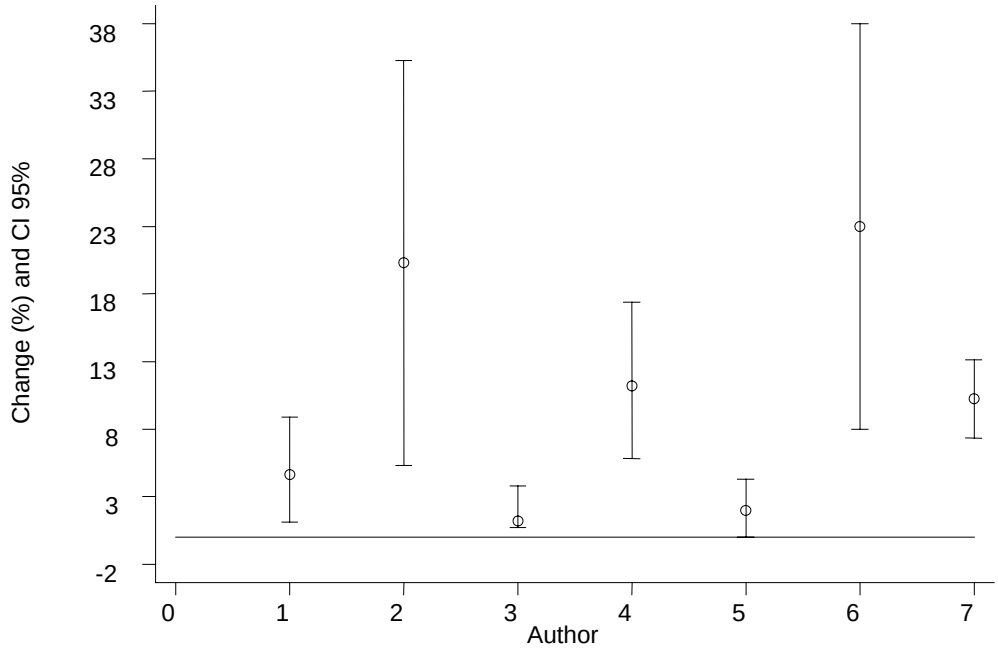
Figure 13. **Percent change in the occurrence of asthma attacks for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Ostro 1991 (Denver), 2. Ostro 1995[a] (Los Angeles), 3. Roemer 1993 (Holland), 4. Neukrich 1998 (Paris) (adult), 5. Schwartz 1993[c] (Seattle), 6. Roemer 1993 (Holland) 7. Abbey 1995 (California) 8. Pooled estimate.

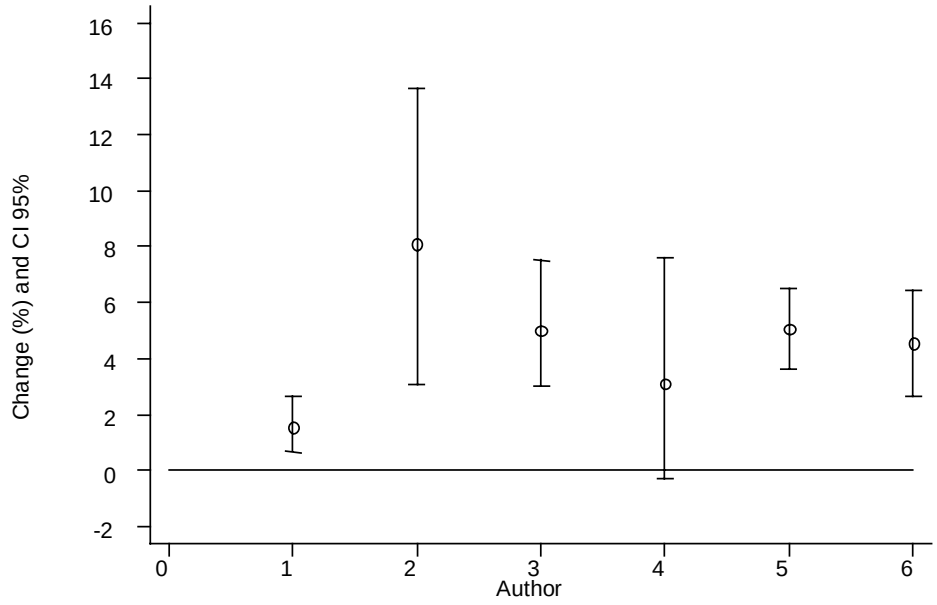
A closer look at this population, however, reveals that more severe effects are found for individuals who are undergoing medical treatment for their condition. It is possible that asthmatic symptoms are more severe in this group making them even more sensitive than others to the presence of pollutants. Percent changes for this type of study ranged from 4.48% (only one report showed an increase below 10%) to 20%, again with the greatest percent change appearing in a survey of adults. The pooled estimated for this group were similar than pooled estimates for the previous table.

Figure 14. **Percent change in the occurrence of asthma attacks and the use of bronchial dilators for each 10 μg/m^3 increase in PM_{10} in children**



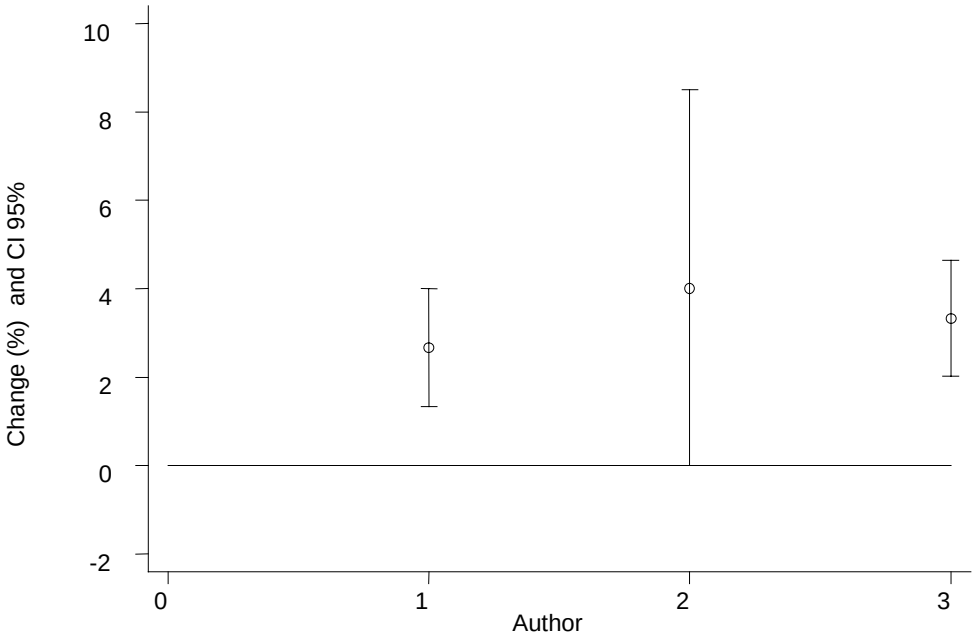
Note: The numbers represent the following studies: 1. Gielen 1997 (Amsterdam), 2. Peters 1997[a] (Sokolov), 3. Pope 1991[a] (Utah) (school population) ,4. Pope 1991[a] (Utah), 5. Dusseldorp 1995 (Holland), 6. Romer 1993 (Holland), 7. Pooled estimate.

Figure 15. **Percent change in the presence of cough without phlegm in asthmatic children for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Peters 1997[a] (Sokolov.), 2. Peters 1997[b] (Sokolov), 3. Romieu 1996 (Mexico), 4. Dusseldorp 1995 (Holland), 5. Pope 1992 (Utah), 6. Pooled estimate.

Figure 16. **Percent change in the presence of cough with phlegm in asthmatic children for 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Peters 1997[a] (Sokolov.), 2. Romieu 1996 (Mexico), 3. Pooled estimate.

Besides counting asthmatic attacks, the presence of a cough for asthmatics has also provided valuable results as a parameter for determining pollutant effects on the asthmatic population. The results of this type of study are summarised in Figures 15 and 16. In all cases, the results varied even for a single cough type. Increases reported for cough without phlegm ranged from 2.65% to 6.44 and for cough with phlegm, from 2.01 to 4.64%. These data again reaffirm the importance of this factor for susceptibility to environmental pollutants.

Table 6. **Percent change in the presence of different respiratory symptoms in asthmatic for each 10 μg/m^3 PM_{10}**

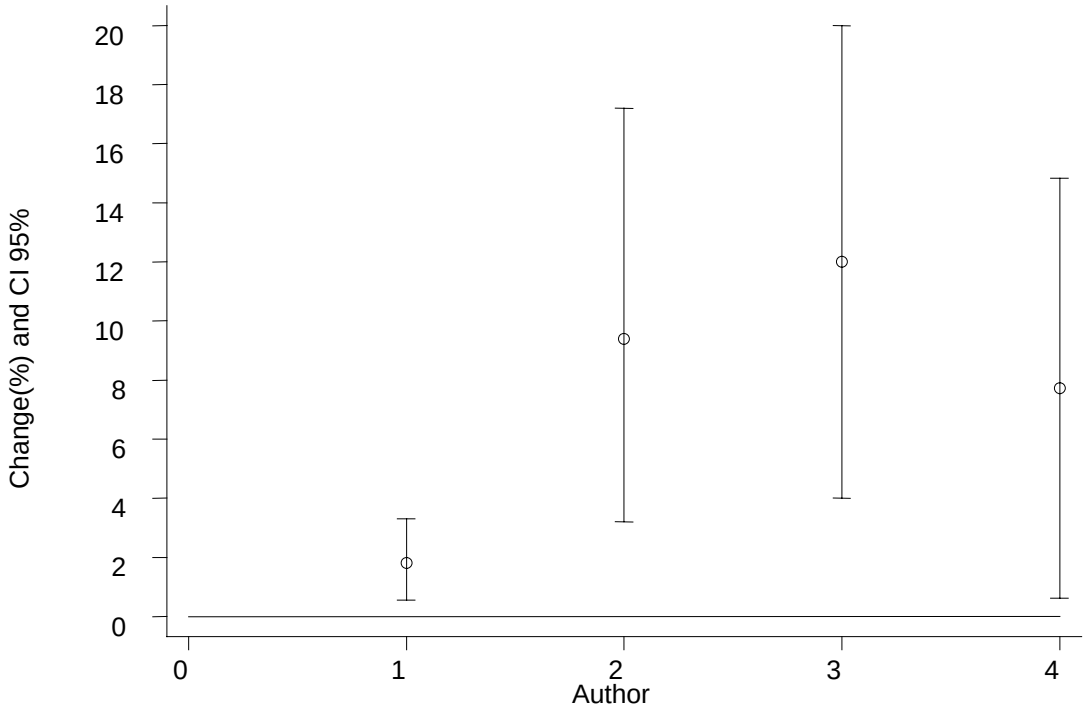
Author	Year	City	Period	PM_{10} Levels	% change	95% CI
				Mean (range)		LL UL
Peters[1]	1997[a]	Sokolov	1991 – 1992	N.R.	24.60	1.62 to 59.23
Peters[2]	1997[b]	Sokolov	1991 – 1992	47.0 (3.00 - 47.00)	1.33	0.44 to 2.22
Roemer[2]	1993	Holland	1990-1991	NR (2.00 – 120.0)	10.64	1.44 to 19.84
Dusseldorp[2]	1995	Holland	1993	NR	2.5	-2.10 to 9.70

[1] Fever. [2]. Wheezing, NR= Not Reported. Peters´s study was done on children.

f) *Percent change in different respiratory symptoms in the general population*

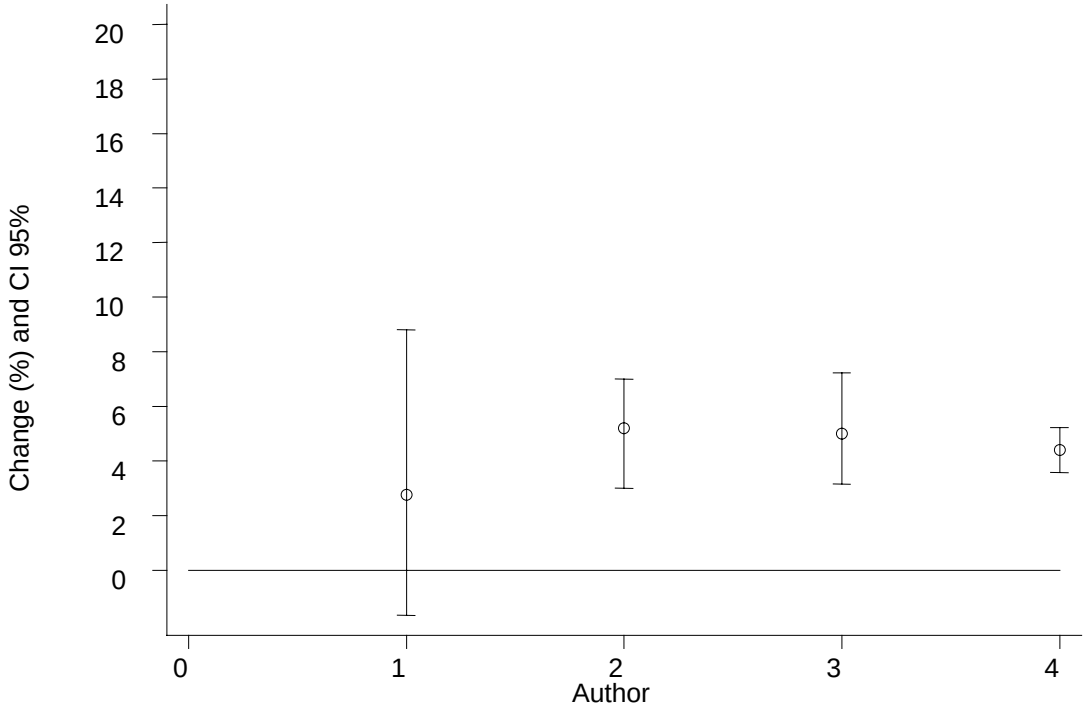
Although evaluating increased symptoms within populations whose age or health make them more susceptible than others to the toxic properties of pollutants is important, it is also crucial to study the effects on the rest of the population. Figure 17 of this section summarised the results obtained by associating the presence of respiratory symptoms with pollution levels within the general population. The reported increases vary from 1.8% to 12.0, with a weighted average of 7.72 (CI 95% 0.61 - 14.84).

Figure 17. **Percent change in the presence of respiratory symptoms in the general population for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Abbey 1993 (U.S.A.), 2. Peters 1997[c] (Erkfurt), 3.Schwartz 1993[b] (U.S.A.), 4.Pooled estimated.

Figure 18. **Percent change in the presence of respiratory symptoms in the upper respiratory tract for each 10 μg/m^3 increase in PM_{10}**

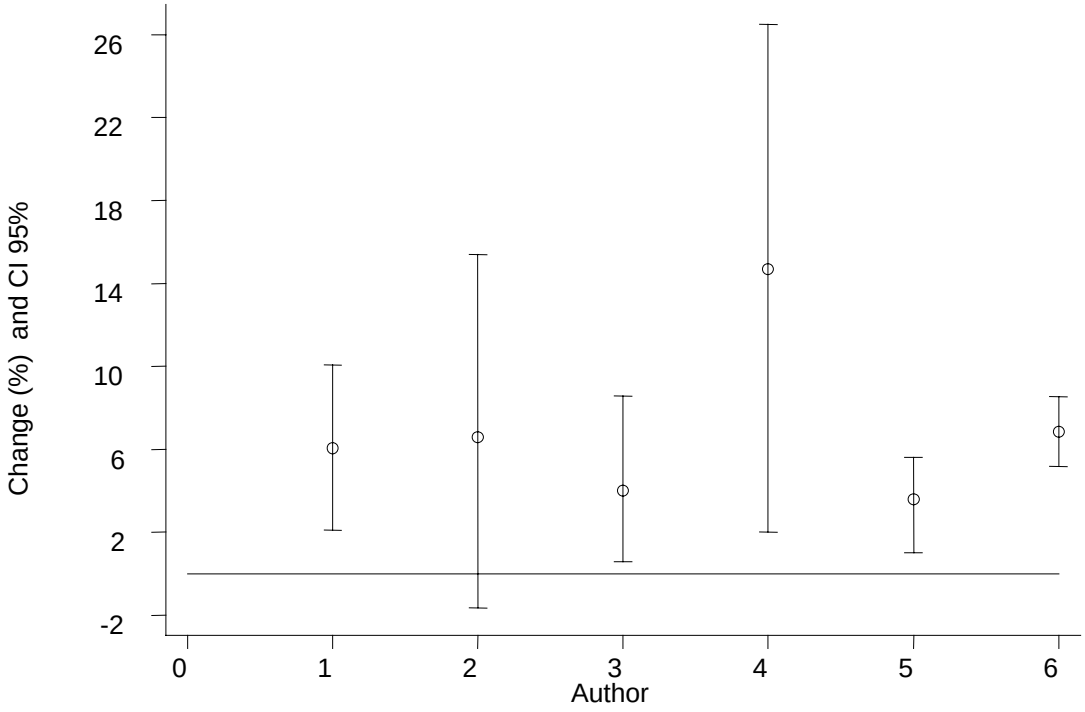


Note: The numbers represent the following studies 1. Ostro 1993 (California), 2. Pope 1991[b] (Utah), 3. Pope 1992 (Utah), 4. Pooled estimate.

Figure 18 summarises increases in symptoms specific to the upper respiratory tract. In the two studies which were carried out between 1989 and 1991, very similar increases (5.00 and 5.19%) were reported, while the lowest increase was reported for a study performed at the end of the 1970's (2.75%). The pooled estimate is 4.39 (CI 95% 3.56 - 5.12).

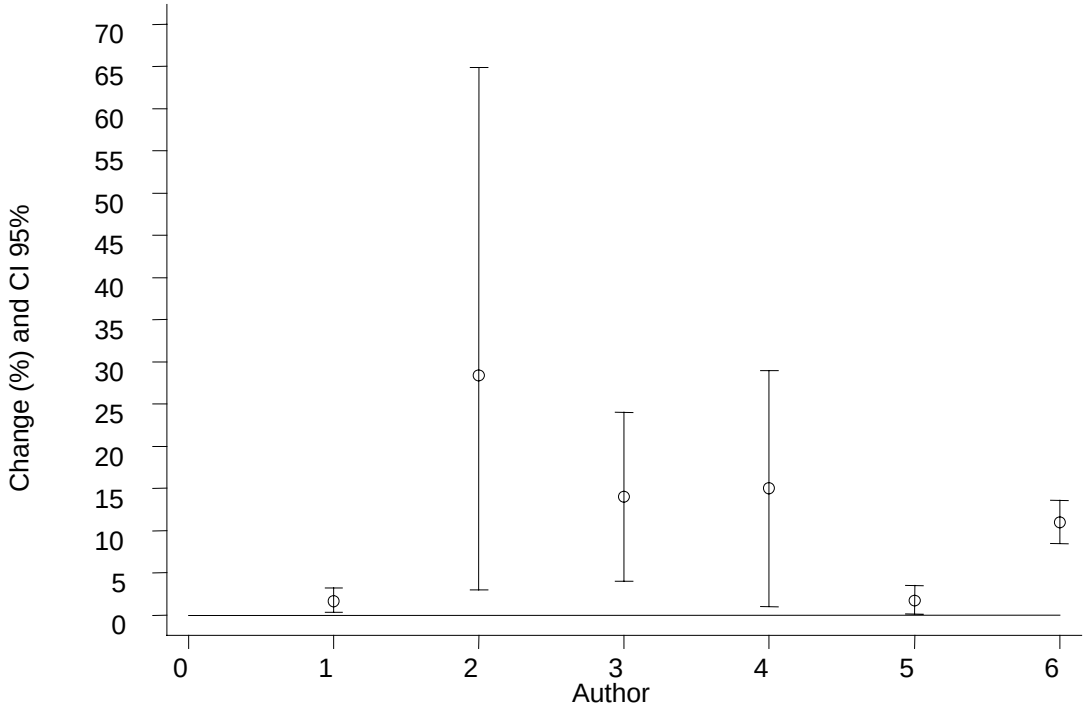
Changes in the presence of lower respiratory symptoms varied only slightly between 5% and 8.55% and are quite similar to those found in the previous figure. The largest increase of 14.7% considered corresponds to a study carried out on children. The pooled estimated 6.85%, (CI 95% 5.16 - 8.54) is greater than that for the previous figure (4.39%).

Figure 19. **Percent change in the presence of lower respiratory symptoms for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Ostro 1993 (California), 2. Pope 1991[b] (Utah), 3. Pope 1992 (Utah), 4. Romieu 1996 (Mexico), 5. Gielen 1997 (Amsterdam), 6. Pooled estimate.

Figure 20. **Percent change in the presence of chronic bronchitis for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Abbey 1993 (U.S.A.), 2. Aunan 1996 (U.S.A.), 3. Dockery 1989 (U.S.A.), 4. Schwartz 1993[b](U.S.A.), 5. Abbey 1995 (California), 6. Pooled estimate.

Chronic bronchitis can be another useful parameter in determining the effects of exposure to PM_{10}. However, relatively few studies are available assessing the role of PM_{10} related to this ailment. Figure 20 shows four studies, all performed in the U.S. which found an increase in the presence of bronchitis associated with PM_{10} levels. Only one study by Abbey *et al.* reported a low increase of 1.65%.

Other respiratory symptoms have also been associated with exposure to pollutants as discussed above. Among these are the presence of a cough, shortness of breath and difficulty breathing upon awakening. In Table 7, the most significant increases from 6% to 27% were observed for the presence of a cough, followed by breathing difficulties upon awakening (4.8%) and shortness of breath (3.4%).

Table 7. **Percent change in the presence of different respiratory symptoms for each 10 μg/m^3 increase in PM_{10}**

Author	Year	City	Period	PM_{10} levels Mean (range)	% change	95% CI LL	95% CI UL
Dockery [1]	1989	U.S.A.	1980 - 1981	20.1 (NR)	27.0	0.0 to 54.0	
Peters [1]	1997[c]	Erfurt	1991 - 1992	60.0 (20.0 – 155.0)	6.00	1.8 to 11.0	
Zemp [1]	1999	Switzerland	1991	21.2 (10.1 – 33.40)	27.0	8.0 to 50.0	
Hiltermann [2]	1998	Leiden	1994 – 1995	NR	3.40	0.6 to 6.8	
Hiltermann [3]	1998	Leiden	1994 - 1995	NR	4.80	0.2 to 6.8	

[1] Cough. [2] Shortness of breath. [3] Difficulty breathing upon awakening. NR= Not reported.

A final parameter, which has been associated directly with high levels of PM_{10} pollution and indirectly with the toxic effects resulting from exposure, is child absenteeism from school. Of the very few reports that have been published on this parameter, Table 8 presents two which show increases in absenteeism associated with PM_{10} pollution levels. The large disparity between the reported increases is immediately apparent. One study registered an increase of only 1% while the second reported an increase of greater than 50%. As information on exposure levels is unavailable for the Peters *et al.* study, it is impossible to determine whether this factor would explain the large difference in reports. However, the study was performed for asthmatic children under medical treatment, while the Ransom *et al.* study considered apparently healthy children. As discussed above, there tend to be significant differences in percent change for the observed variables between healthy individuals and asthmatics under medical treatment.

Table 8. **Percent change in child school absenteeism for each 10 μg/m^3 increase in PM_{10}**

Author	Year	Location	Period	PM_{10} levels Mean (range)	% change	95% CI LL	95% CI U L
Peters [1]	1997[c]	Sokolov	1991 – 1992	N.R.	52.30	15.38 to 76.15	
Ransom	1992	Utah	1985 – 1990	50.0 (NR - 365.0)	0.21	0.25 to 0.67	

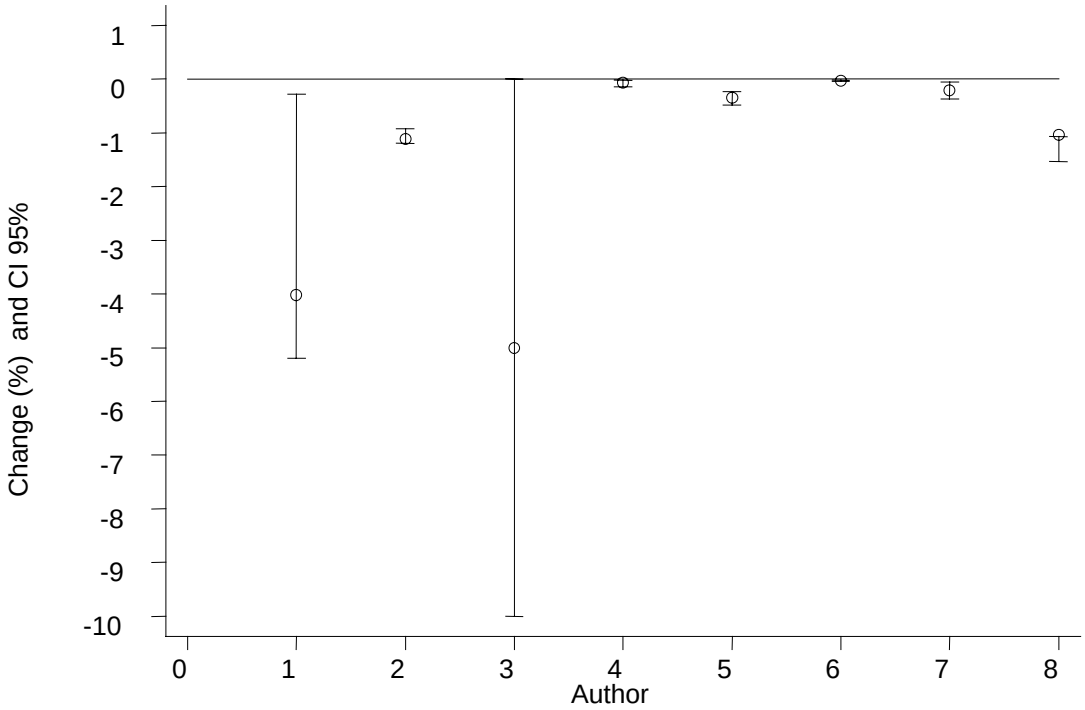
[1]Use of medications, NR = Not reported.

g) Percent change in FEV-1, FVC, PEF y MMEF

The presence of symptoms or occurrence of certain diseases is not the only parameter used to determine air pollution toxicity. It is often advisable to define some diagnostic technique that can detect toxic effects prior to the appearance of clinically recognized symptoms. Spirometric parameters represent just such a tool and have been used by associating pollution levels to forced expiratory volume at first second, (FEV-1), forced vital capacity (FVC), maximal mid-expiratory flow (MMEF) and peak expiratory flow (PEF).

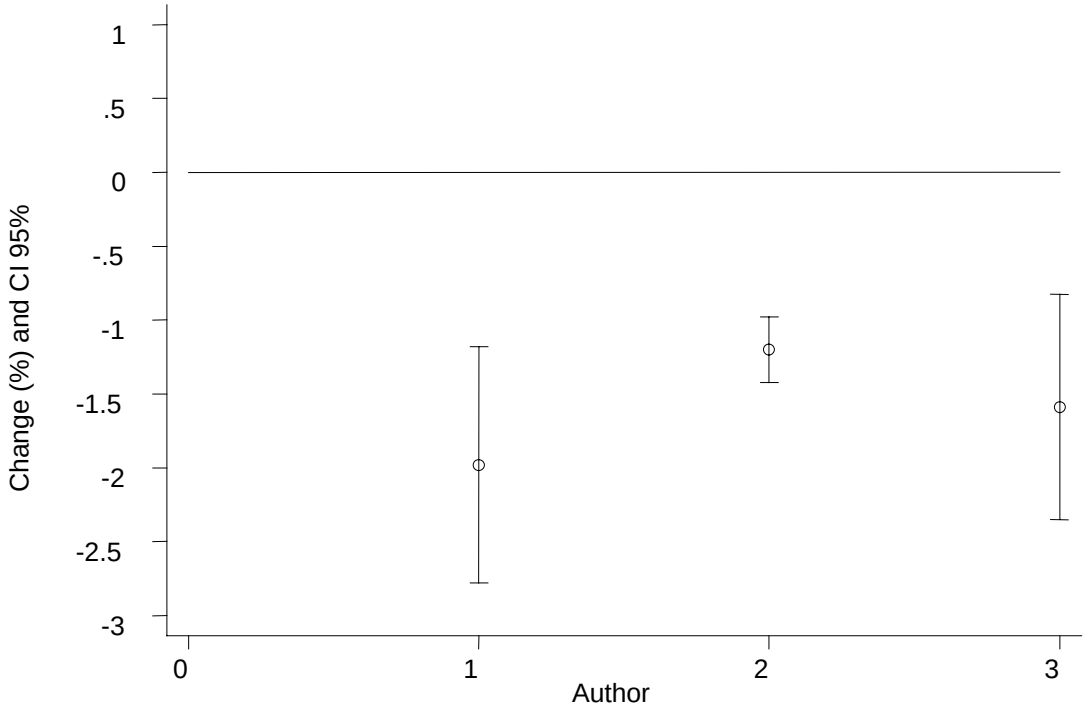
Figure 21 shows the percent change in FEV-1. In general, except for the studies by Brunekreef (4.02%), Dockery (5.00%) and Chesnut (1.12%), the reported values show percent decreases of between 0.06 and 0.98%. However, the first two values mentioned above were performed measuring FEV-0.75, which could explain the different results. Evaluation of these studies provided a very small pooled estimated decrease and a very broad confidence interval.

Figure 21. **Percent absolute change in FEV with 95% CI for each 10 μg/m^3 increase in PM_{10}**



Note: The numbers represent the following studies: 1. Brunekreef 1991 (Steubenville), 2. Chestnut 1991 (U.S.A.), 3. Dockery 1982 (Steubenville), 4. Hoek 1993 (Holland), 5. Hoek 1993 (Wageningen), 6. Koenig 1993 (Seattle), 7. Pope 1993 (Salt Lake City), 8. Pooled estimate.

Figure 22. **Absolute percent change in FVC for each 10 μg/m^3 increase in PM_{10} with 95% CI**

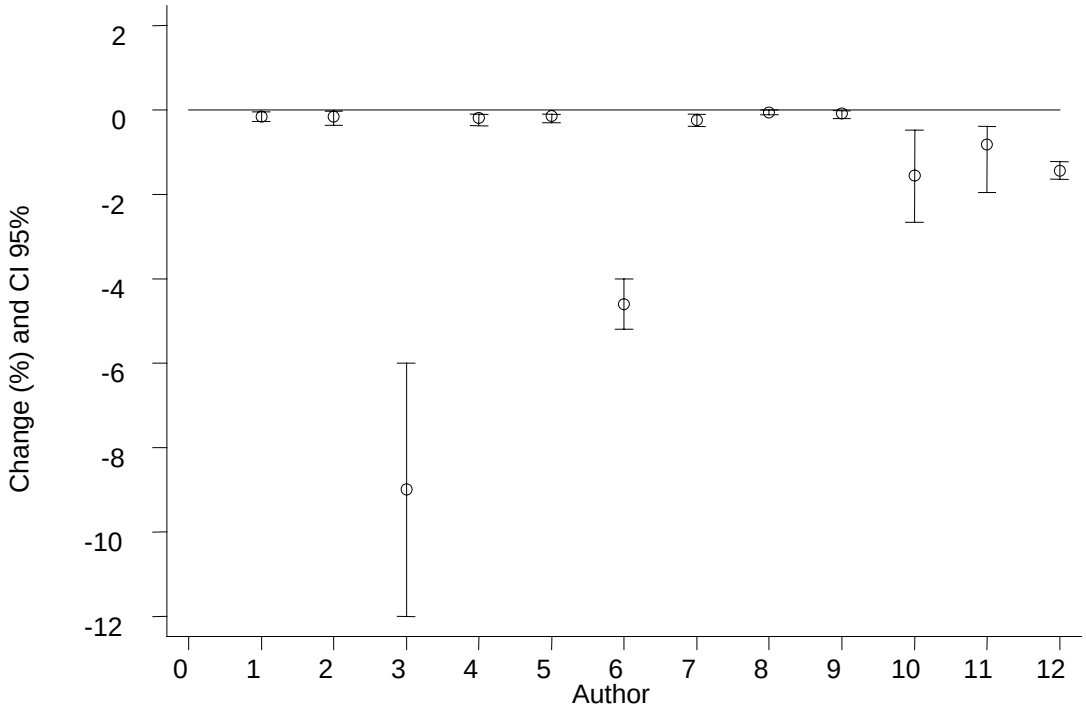


Note: The numbers represent the following studies: 1. Brunekreef 1991 (Steubenville), 2. Chestnut 1991 (U.S.A.), 3. Pooled estimated.

Fewer studies are available documenting the toxic effects of PM_{10} associated with FVC than for the previous parameter. Figure 22 shows the two major studies determining the effects of this pollutant on this spirometric diagnosis. Both studies were carried out in the U.S., and the absolute percent change in pulmonary function is very similar between the two (-1.30 and -1.58%). The pooled estimated was –1.30%, (CI 95% -1.53 to –1.07).

The association between pollutant levels and the PEF parameter has been widely documented recently and Figure 23 summarizes these studies. The results show that except for the studies by Hoek, 1994 (9.0%), Peters, 1997 (4.6%), Gold, 1999 (1.56%) and Romieu, 1996 (1.2%), the changes reported are not greater than 0.39%.

Figure 23. **Absolute percent change in PEF for each 10 μg/m^3 increase in PM_{10} with 95% CI**



Note: The numbers represent the following studies: 1. Hoek 1993 (Holland), 2. Hoek 1993 (Wageningen), 3. Hoek 1994 (Holland), 4. Neas 1992 (Uniontown), 5. Neas 1996 (Pennsylvania), 6. Peters 1997[c] (Erfurt), 7. Pope 1991[a] (Utah), 8. Pope 1992 (Utah), 9. Roemer 1993 (Wageningen), 10. Gold 1999 (Mexico), 11. Romieu 1996 (Mexico), 12. Pooled estimate.

MMEF is the least documented of the pulmonary function diagnoses for association with pollution levels. Only one report was found to evaluate this spirometric parameter. The study, performed in Holland is summarized in Table 9.

Table 9. **Percent change in MMEF[1] for each 10 μg/m^3 increase in PM_{10} estimated in time series studies**

Author	Year	Location	Period	PM_{10} levels	% decrease	IC 95%	
				Mean (range)		LL	UL
Hoek	1994	Holland	1987 – 1990	44.9 (14.1 - 126.1)	-8.00	-11.00 to –5.0	

[1] Maximal mid-expiratory flow.

h) Percent change in chronic effects

The effects of long term exposure to air pollutants on human health are extremely important since the majority of people living in urban environments are permanently exposed to low concentrations of these pollutants. Quantitative determination of such exposure is difficult given the characteristics of cities, themselves, the long term temporal-spatial pollutant distribution and varying individual patterns of activity, transit and occupations inherent in the urban environment. For all of these reasons, few studies have achieved evaluations of this type of exposure.

For studies of chronic respiratory effects associated with pollutant levels, Abbey *et al.* 1993 describes percents of change in occurrence of respiratory symptoms according to variations in PM_{10} levels to 3.6% (CI 95% 6.6 – 1.1).

There are a few reports that find significant effects on mortality due to chronic effects; Dockery in 1993 in Ohio, found a 5.70% (95% CI, 10.44-1.7%) and Pope in 1995 in USA found 3.84% (95% CI, 2.93 – 6.75), the pooled estimated for these studies was 4.97 (95% CI 3.19 - 6.75).

i) Percent change in restricted activity days and minor restricted activity days

From an economical point of view the days that a worker stops his labour also called restricted activity days (RAD), or his productivity going down, denominated minor restricted activity days (MRAD), because of a sickness, represent an important factor, since this time as traduce like lost of monetary ingress. That is why it is important to quantify RAD or MRAD and the economical weight that these factors represent. In this case the Table 10 shown the percent change on RAD and MRAD.

Table 10. **Percent change for RAD and MRAD for each 10 μg/m^3 increase in PM^{10}**

Author	Locality	Year	Period	Parameter	Best estimate
Ostro	USA	1990	1979-1981	DAR	7.74%
Ostro	USA	1980	1976 – 1986	DAR	9.48%
Ostro	USA	1989	1976 – 1986	DARM	4.92%

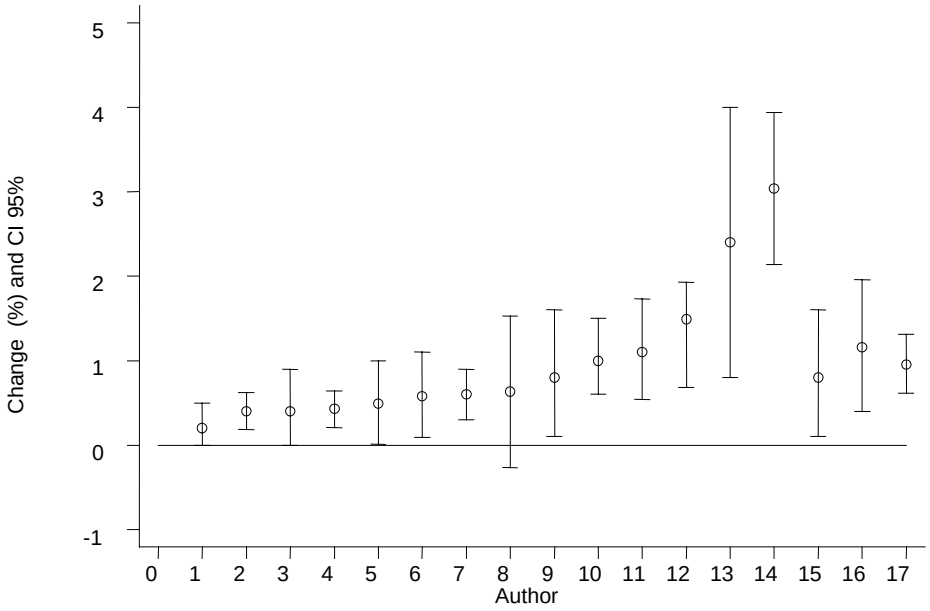
4.2 Meta-analysis of health effects due to Ozone exposure

a) Percent change in mortality due to ozone exposure

The increase in mortality is one of the most significant parameters in determining the impact of a pollutant on the health of a population. However, in the case of ozone, in contrast to particulate exposure these endpoints have been debated, mainly because most of the time the pollutants are present at the same time. Trying to establish the weight of the particulate matter in the associations between ozone and total mortality we performed an evaluation considering models adjusted and not adjusted for particulate matter. Figure 25 shows studies, not adjusted by particulate matter, where an increase in total mortality (excluding accidental death) was evaluated.

Figure 24 shows studies where an increase in total mortality (excluding accidental death) was evaluated. The increases reported in these studies is low (0.2 to 1.49%), although two other studies published in the 1970's report increases as high as 2.4% and 3.04%, and pooled estimate was 0.995% per 10ppb (CI 95% 0.62 - 1.31).

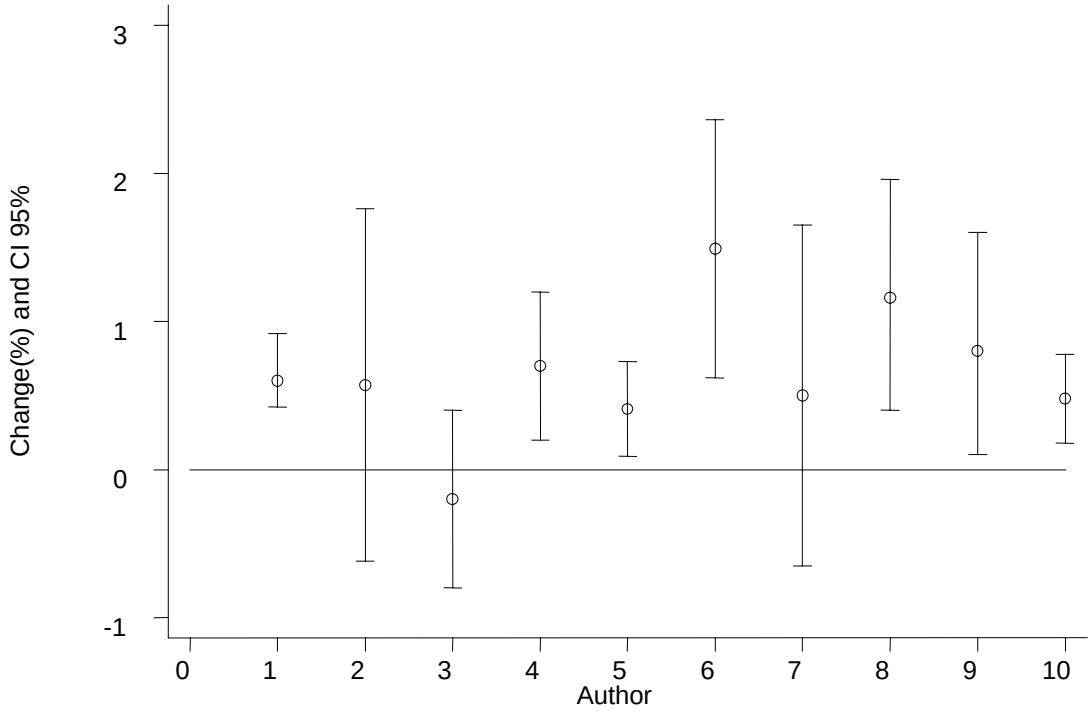
Figure 24. **Percent change in total (non-accidental) death with 95% CI for each 10 ppb increase in ozone (not adjusted for particulate matter)**



Note: The numbers correspond to the following studies: 1. Kinney 1995 (Los Angeles), 2. Loomis 1996 (Mexico), 3. Ostro 1996 (Santiago), 4. Borja 1997 (Mexico), 5 Verhoeff 1996 (Amsterdam), 6. Sunyer 1996 (Barcelona), 7. Anderson 1996 (London), 8. Borja 1998 (Mexico), 9. Hoek 1997 (Rotterdam), 10. Ito 1996 (Chicago), 11. Kelsall 1997 (Philadelphia), 12. Moolgavkar 1996a (Philadelphia), 13. Simpson1997 (Brisbane), 14. Kinney 1991 (Los Angeles), 15. Hoek 1997 (Rotterdam), 16. Toloumi 1997 (APHEA cities), 17. Pooled estimate.

Particulate matter and ozone are often correlated spatially and over time, making it difficult to separate the effects of the individual pollutants. Thus, it could be unclear how much each pollutant may individually influence elevated mortality and mobidity rates. As a result, some cost-benefit studies have chosen one index air pollutant, rather than estimating effects for multiple air pollutants individually and then adding their effects to get a total air pollution effect. The focus on a single pollutant provides a conservative approach to estimating air pollution effects. In fact, recent analyses (e.g., Thurston and Ito, 1999) suggest that ozone and PM air pollution effects are relatively independent, since controlling for one pollutant has only modest effects on the concentration-response of the other. Thus, the use of a single index pollutant underestimates the overall public health effects and monetary valuations of air pollution changes. Recognizing that the effect of ozone on mortality independent of particulates is still on debate, we re-evaluated the effect of ozone restricting the analysis to those studies that controlled for particles in the statistical analysis

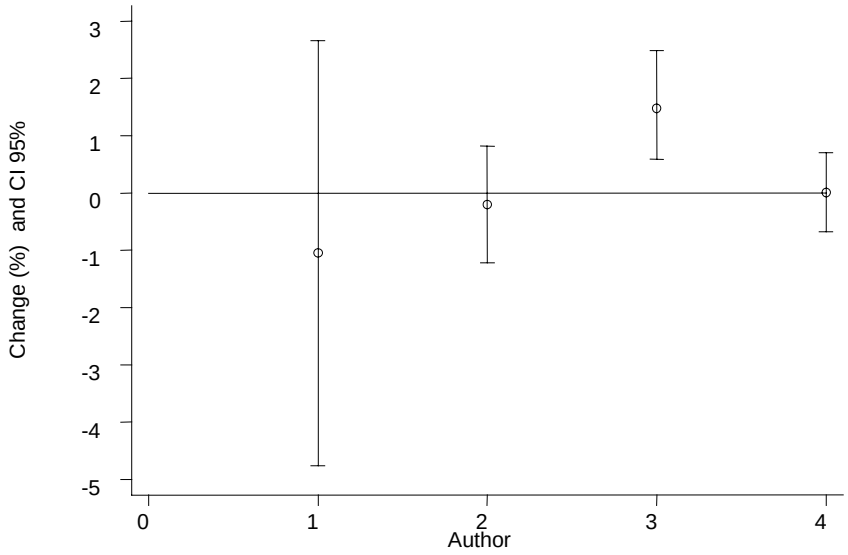
Figure 25. **Percent change in total (non-accidental) death with 95% CI for each 10 ppb increase in ozone**



Note: The numbers correspond to the following studies: 1. Anderson 1996 (London), 2. Borja 1998 (Mexico), 3. Borja 1997 (Mexico), 4. Ito 1996 (Chicago), 5. Kelsall 1997 (Philadelphia), 6. Moolgavkar 1996a (Philadelphia), 7 Verhoeff 1996 (Amsterdam),8. Toloumi 1997 (APHEA cities), 9. Hoek 1997 (Rotterdam), 10. Pooled estimate.

Figure 25 shows the studies where an association between ozone and total mortality (non accidental) adjusting for particulate matter .In this case the increases reported in these studies are lower than the ones presented in the figure 25 (-0.2 to 1.49%). Also the pooled estimated is lower than (0.59% per 10ppb for this studies, CI 95% 0.30 - 0.86).

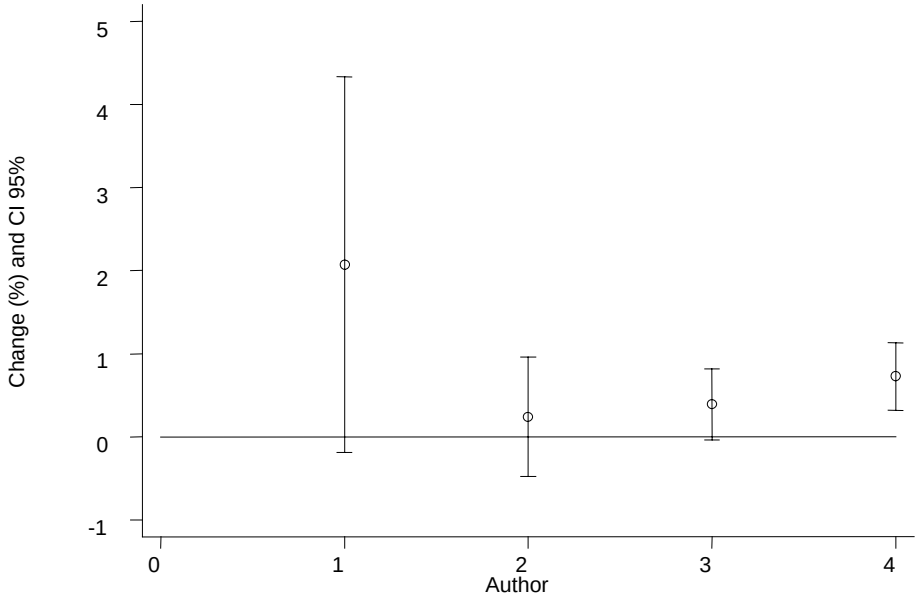
Figure 26. **Percent change in mortality due to respiratory disease with 95% CI for each 10 ppb increase in ozone**



Note: Numbers correspond to the following studies: 1. Anderson 1996 (London), 2. Borja 1997 (México), 3. Borja 1998 (México) 4. Pooled estimate.

However, determining total mortality (not accidental) can be considered a non-specific parameter. Deaths that could be related to the route of exposure, such as those due to respiratory or cardiac ailments, must also be considered. Considering respiratory ailments, only a few articles have established an association between ozone exposure and mortality (Figure 26). These studies were performed in Europe and Mexico. For these studies the pooled showed insignificant effects.

Figure 27. **Percent change in mortality due to cardiovascular disease with 95% CI for each 10 ppb increase in ozone**



Note: Numbers correspond to the following studies: 1. Anderson 1996 (London), 2. Borja 1997 (México), 3. Borja 1998 (México) 4. Pooled estimate.

Mortality due to cardiac ailments the highest percent change of 1.76% is found in the Borja *et al.* 1998 study, determined an elevated increase of risk. Here the pooled estimated shown in Figure 27 was 0.73 (CI 95% 0.31 - 1.13).

Individuals older than 65 years of age should be studied independently from the rest of the population since this group could be at increased risk because of reduced systemic defences against pollution's toxic effects. Table 11 summarises studies that evaluated mortality for this population. Both studies were non-significant.

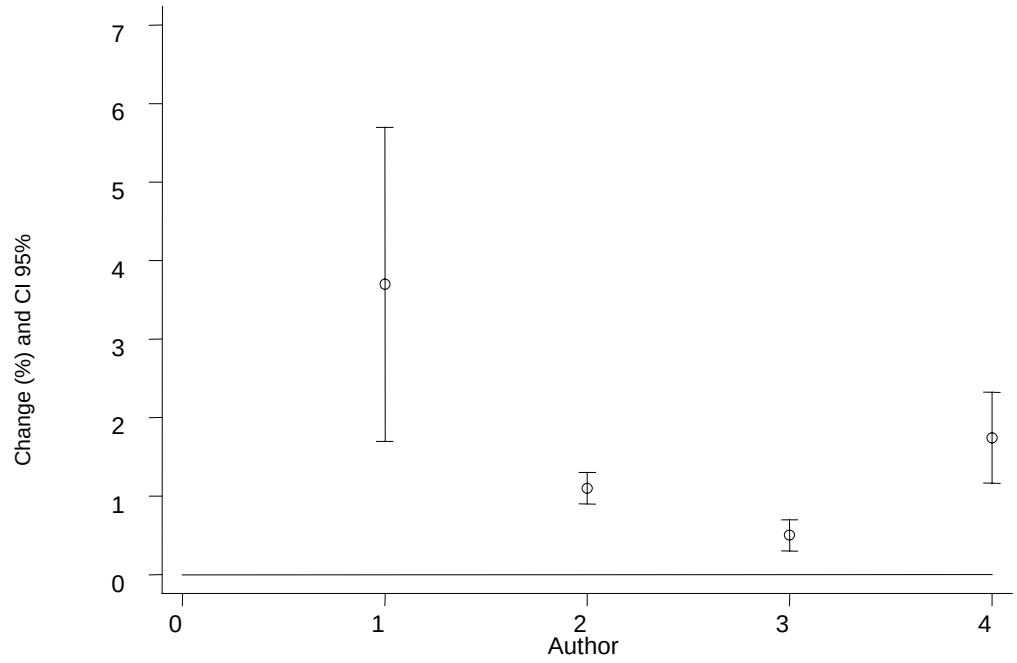
Table 11. **Effects of O_3 on mortality in individuals 65 years or older for each 10 ppb increase in ozone**

Author	Year	Locality	Period	Mean	IC 95%
Borja	México	1998	1993 - 1995	0.07	-2.15 – 2.29
Borja	México	1997	1990 - 1992	-0.10	-0.56 – 0.36

b) Percent change in total hospitalisations

Total hospital admissions (non-accidental) represents another parameter for which measuring pollution impact. Studies evaluating change in total admissions are summarised in Figure 28 of this section. The studies were performed in the United States and Canada, with the largest percent change registered in Buffalo, New York (3.70%). The pooled estimated change was 1.74% (CI 95% 1.16 - 2.32).

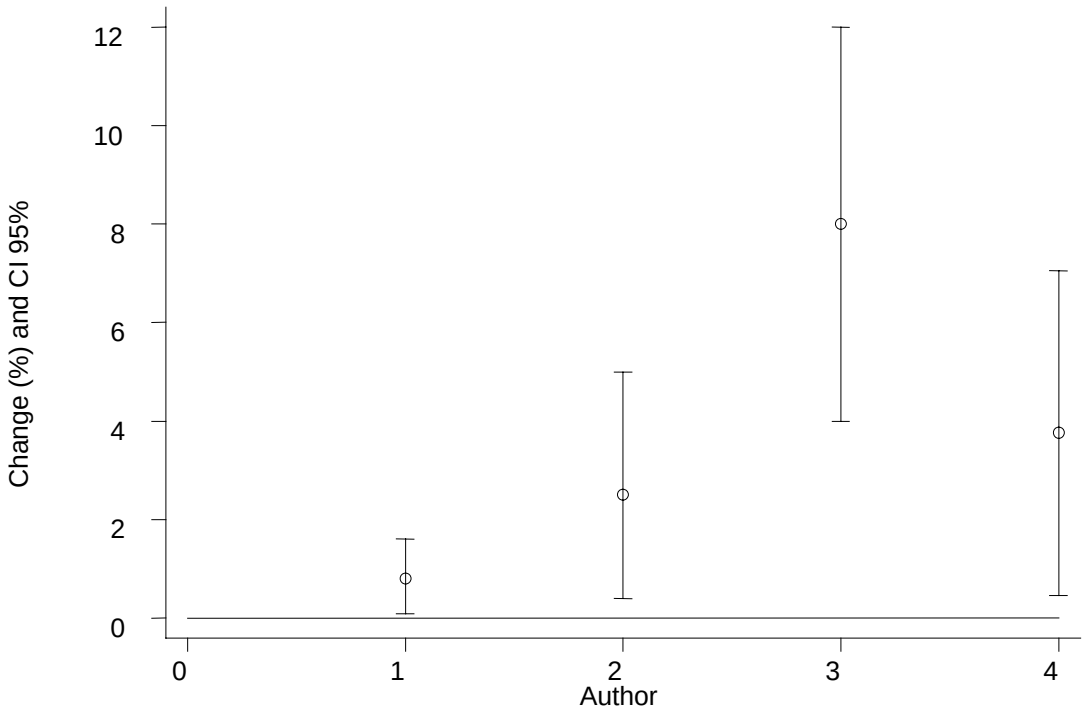
Figure 28. **Percent change in total hospitalisations with 95% CI for each 10ppb increase in ozone**



Note: The numbers represent the following studies: 1. Thurston 1992 (Buffalo), 2. Thurston 1992 (New York), 3. Thurston 1994 (Ontario), 4. Pooled estimate.

Total hospitalisation is a fairly non-specific parameter for determining toxic effects due to ozone contamination. It is therefore necessary to deal with specific causes of hospitalisation, again, concentrating on those causes which could be related to exposure route (hospitalisations for respiratory and cardiac ailments).

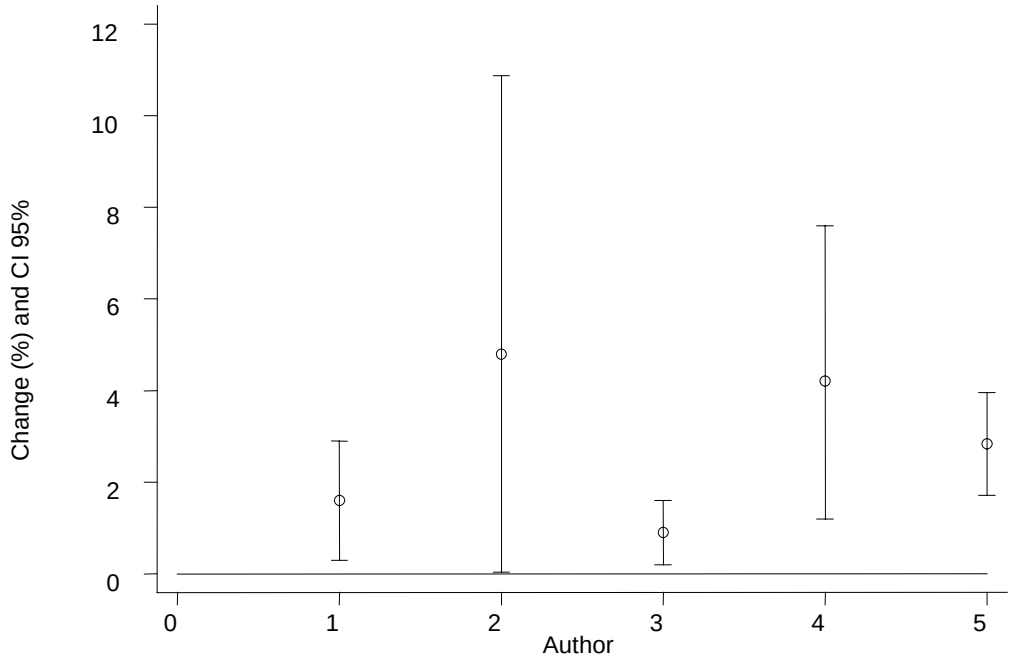
Figure 29. **Percent change in hospitalisations due to respiratory diseases with 95% CI for each 10 ppb increase in ozone**



Note: The numbers represent the following studies 1. Ponce de León 1996 (London), 2. Schouten 1996 (Rotterdam), 3. Linn 2000 (Los Angeles) 4. Pooled estimate.

Figure 29 presents the results from two studies where a significant increase in hospitalisation was reported for respiratory diseases. The studies were carried out in developed American and European countries. Percent increases between 0.8 and 8 % were reported. The weighted average increase in specific hospitalisations for respiratory diseases 3.76% (CI 95% 0.45 - 7.05).

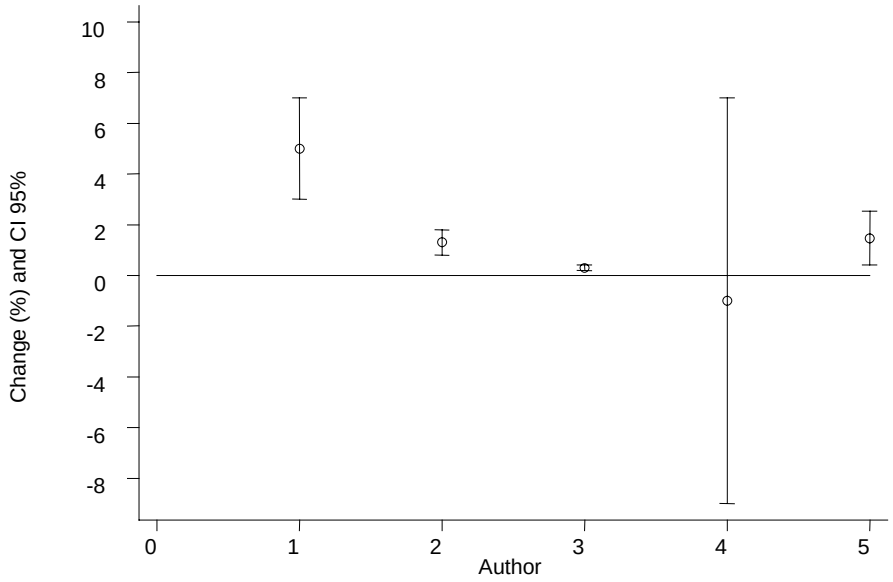
Figure 30. **Percent change in hospitalisations for individuals older than 65 years due to respiratory disease CI-95% for each 10 ppb increase in ozone**



Note: Asthma is one of the respiratory ailments for which an increase in hospitalisations has been observed.

Figure 30 shows the results of hospital admissions for respiratory diseases for individuals older than 65 years. The highest pooled estimated was 2.83 (CI 95% 1.71 – 3.95).

Figure 31. **Percent change in hospitalisations due to asthma with 95% CI for each 10 ppb increase in ozone**



Note: The numbers represent the following studies: 1. Thurston 1992 (Buffalo), 2. Thurston 1992 (NY), 3. Thurston 1994 (Ontario), 4.Linn 2000 (Los Angeles), 5. Pooled estimate.

Figure 31 presents the results of some of the most important studies where an increase in hospitalisation has been reported for this illness. Again, the city of Buffalo, New York, registers the highest increase of 5.0%. The pooled estimated increase was 1.47% (CI 95% 0.41 - 2.53).

Hospitalisations for chronic obstructive pulmonary disease (COPD) and pneumonia are two other factors that increase with exposure to ozone. Only two reports were found in Detroit, Illinois, and Minneapolis, Minnesota, where both diseases were studied. The percent change for COPD was similar to the pneumonia, between 4.2 and 5.5% increase in COPD, and 5.2 and 5.7% increase in pneumonia.

Table 12. **Percent change in hospitalisations for COPD for each 10 ppb increase in ozone**

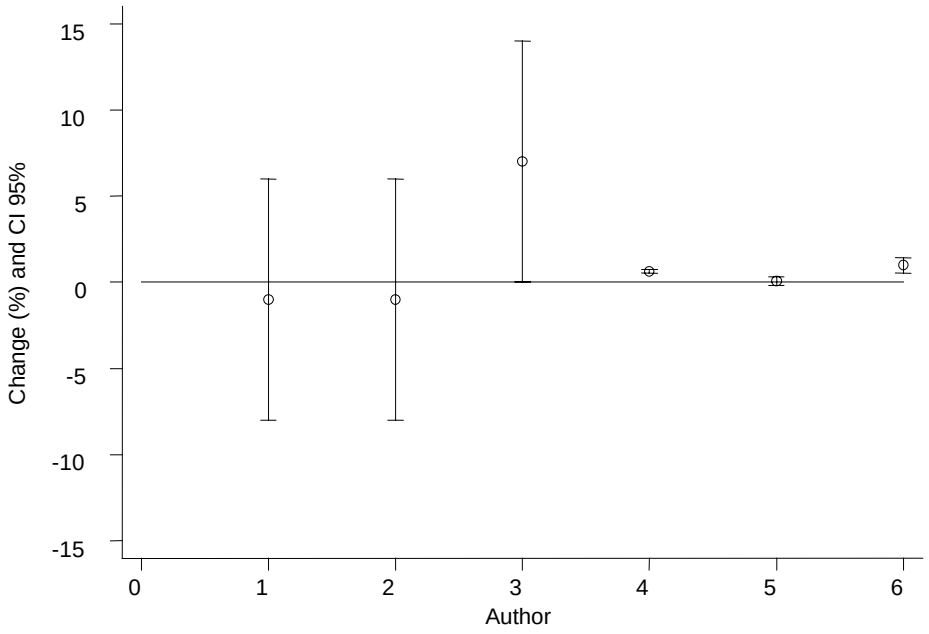
Author	Locality	Year	Period	Mean	IC 95%
Schwartz	Detroit	1994	1986 - 1989	5.5	-3.4 – 7.5
Moolgavcar	Minneapolis	1997	1986 - 1991	4.2	-1 – 9.4

Table 13. **Percent change in hospitalisations for individuals older than 65 years due to pneumonia for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	IC 95%
Schwartz	Detroit	1994	1986 - 1989	5.2	2.6 – 8.0
Moolgavcar	Minneapolis	1997	1986 - 1991	4.7	-5.2 – 9.0

Finally, changes in hospitalisations due to cardiovascular disease is an important end point, some of the most important studies are presented in the Figure 32 where occlusive stroke has the biggest change with a positive percent (7.00%). The pooled estimate was 0.98% (CI 0.53 - 1.43).

Figure 32. **Percent change in hospitalisations due to cardiovascular disease with 95% CI for each 10 ppb increase in ozone**



Note: All the plots belong to Linn 2000 (Los Angeles) study with the following diagnostics: 1. Congestive Heart failure, 2. Cardiac arrhythmia, 3. Occlusive stroke,4. Total cardiovascular 5. Cerebrovascular,6. Pooled estimate.

c) Percent change in hospital emergency room admissions

Increase in hospital emergency room admissions for respiratory ailments and asthma represents another useful parameter for studying the toxic effects of ozone exposure. Results of studies evaluating this parameter are summarised in Tables 14 and 15. It is immediately obvious that the values differ widely between populations. For respiratory diseases, the pooled estimate for general population increase was 3.172% (CI 95% 1.672 - 4.671) and for asthma from 3.5 to 15.0%. A study in Mexico City reported an increase of 20% in emergency room admission for diagnosed tracheitis (Table 16).

Table 14. **Percent change in emergency room admissions for respiratory diseases for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	IC 95%
Delfino	Montreal	1997	1992 - 1993	7.22	2.9 – 11.5
Tellez-Rojo	México	1997	1993	1.98	1.40- 2.58
Burnett	Ontario	1998	1994	0.42	-0.38- 1.22

Table 15. **Percent change in emergency room admissions for asthma for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	IC 95%
Damakosh	México	2000	1993 - 1994	15	0 – 40.0
Stieb	New Brunswick	1996	1984 - 1992	3.5	1.7 – 5.3

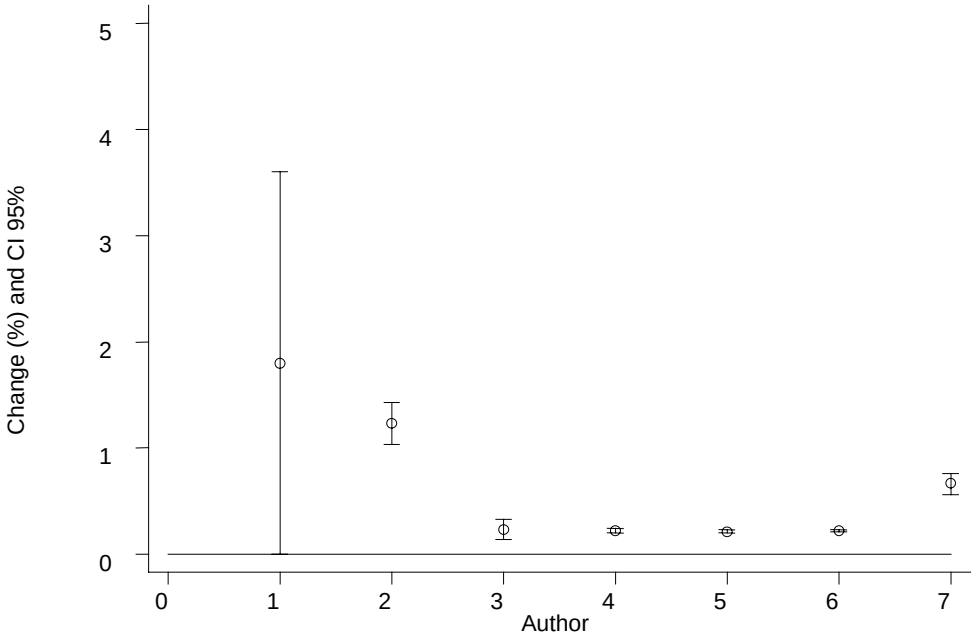
Table 16. **Percent change in emergency room admissions for tracheitis for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	CI 95%
Damakosh	Mexico City	2000	1993 – 1994	20.0	0.00 - 40.0

d) Percent change in different respiratory symptoms in asthmatic children

Asthmatic children are can be more sensitive to the effects of contamination and thus must be considered as another group worthy of special attention. Figure 33 of this section presents the association between increased asthmatic attacks and average ozone concentrations. The results show an increase in the presence of respiratory diseases of 0.66% (CI 95% 0.55 - 0.76) was also reported for this group. These figures reaffirm what we already know about this population which suffers the effects of pollution to a much greater extent than others.

Figure 33. **Percent change with 95% CI in different respiratory symptoms in asthmatic children for each 10 ppb increase in ozone**



Note: The numbers represent the following studies: 1. Hiltermann 1998 (Leiden) (Difficulty breathes), 2. Gielen 1997 (Amsterdam) (upper respiratory symptoms),3. Peters 1999 (Califirnia) (Cough), 4. Romieu 1996 (Mexico) (upper respiratory symptoms), 5. Romieu 1996 (Mexico) (lower respiratory symptoms), 6. Romieu 1996 (Mexico) (Difficulty breathes), 7 Pooled estimate.

Table 17 shows other studies with increase of 2.45% to 5% in asthmatic attacks reported by Ostro *et al.* 1995[a] and Dockery 1989 followed by a 1.80% increase in asthmatic attacks (where a bronchial-dilator was used) in the Hiltermann report and the presence of lower respiratory tract symptoms 0.23%.

Table 17. **Percent change in different respiratory symptoms in asthmatics for each 10 ppb increase in ozone for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	95 % CI
Peters [1]	California	1999	1986 - 1990	0.23	0.14 - 0.33
Ostro [2]	Los Angeles	1995	1992	5.00	1.75 - 9.00
Dockery [2]	U.S.A.	1989	1980 - 1981	2.45	0.0 –5.9
Hilterman [3]	Leiden	1998	1995	1.80	0.20 - 3.60

[1] Lower respiratory tract symptoms, [2] Asthmatic attacks, [3] Asthmatic attacks and use of bronchial-dilator.

e) Percent change in different respiratory symptoms for the general population

Besides increased hospitalisations and emergency admissions, an association has been observed between ozone exposure and the increase of certain diseases. Although few publications document this association, existing data report an increase in lower (Table 18) and upper (Table 19) respiratory tract diseases and wheezing episodes in children (Table 20). A possible reason for the scant literature reporting these types of associations is that more emphasis has been placed on studying the special, high-risk populations.

Table 18. **Percent change in lower respiratory tract symptoms for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	95 % CI
Ostro	California	1993	1978 - 1979	2.2	1.1 – 3.4
Olaiz	México	2000	1996 - 1997	1.1	-0.3 – 2.4

Table 19. **Percent change in wheezing for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Mean	95 % CI
Buchdahl	Londres	1996	1992 - 1993	1.32	0.47 –2.4
Hiltermann	Leiden	1998	1995	4.4	1.0 – 8.8

Table 20. **Percent change in upper respiratory tract symptoms for each 10 ppb increase in ozone**

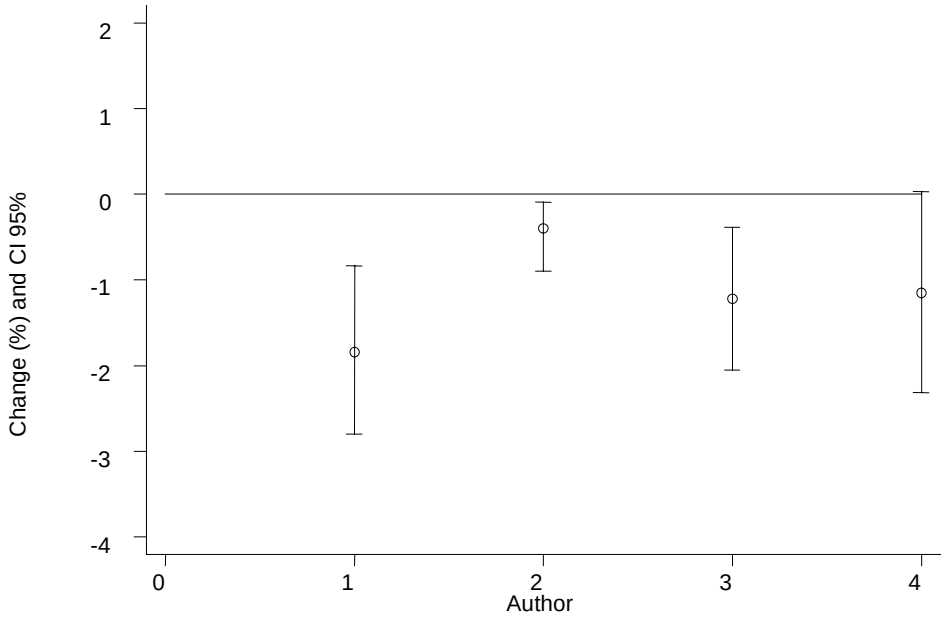
Author	Locality	Year	Period	Mean	95 % CI
Olaíz	Mexico	2000	1996 – 1997	1.5	1.1 – 2.2

f) Percent change in PEF, FEV-1 and FVC

A commonly employed strategy to establish the toxic effects of ozone at low concentration is the measurement of spirometric parameters such as peak expiratory flow (PEF), forced expiratory volume per second (FEV-1) and the forced vital capacity (FVC).

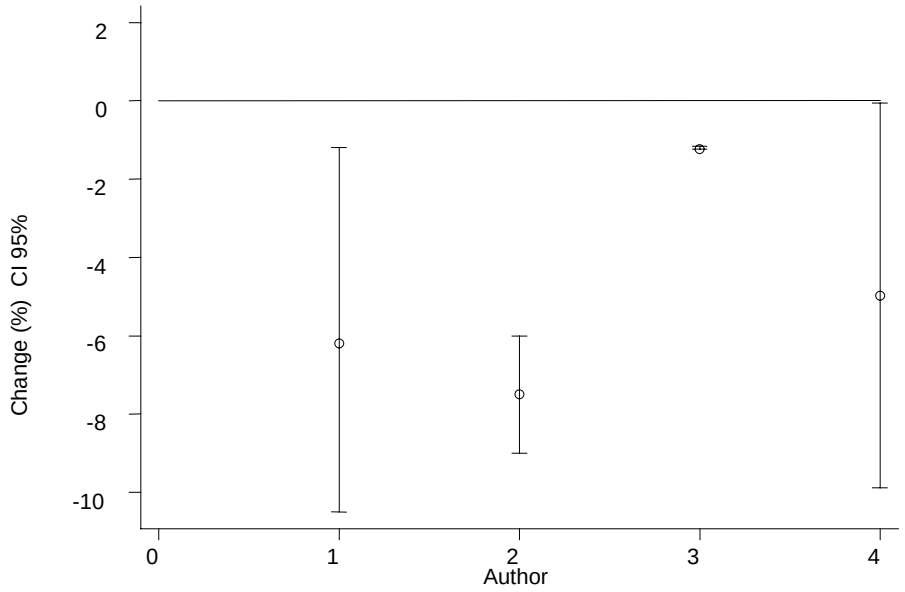
Figures 34, 35 and 36 in this section summarise the reports relating changes in PEF, FEV-1 and FVC. Among the three parameters, the PEF was noticeably less with an range of values between -0.4 and -1.84%. The decreases found for FEV-1 were between -6.2 and -7.5%. The range of values for FVC between -6.0 and -7.2.

Figure 34. **Percent change with 95% CI of PEF with each 10 ppb increase in ozone**



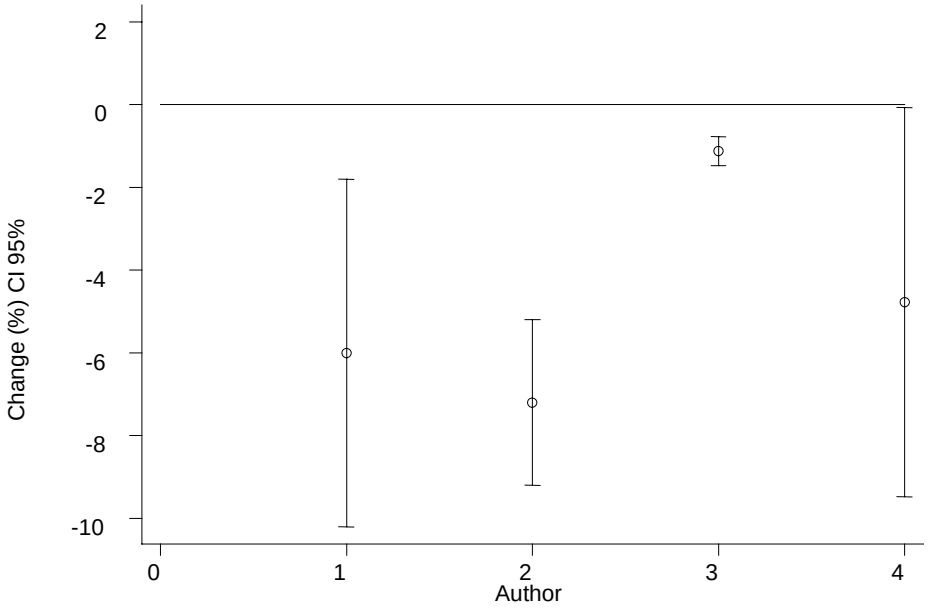
Note: The numbers represent the following studies: 1. Gold 1999 (Mexico), 2.Romieu 1996 (Mexico), 3. Castillejos 1992 (México), 4. Pooled estimated.

Figure 35. **Percent change with 95% CI for FEV-1 for each 10 ppb increase in ozone**



Note: The numbers represent the following studies: 1. Brunnekreef 1991 (Kingston), 2. Brunnekreef 1991 (New Jersey), 3. Castillejos 1992(México), 4. Pooled estimate.

Figure 36. **Percent change with 95% CI for FVC for each 10 ppb increase in ozone**



Note: The numbers represent the following studies: 1. Brunnekreef 1991 (Kingston), 2. Brunnekreef 1991 (New Jersey), 3. Castillejos 1992 (México), 4. Pooled estimate.

g) Percent change in restricted activity days and minor restricted activity days

Table 21 present the percent change on RAD and MRAD where just for the first one, there are significative results.

Table 21. **Percent change for RAD and MRAD for each 10 ppb increase in ozone**

Author	Locality	Year	Period	Parameter	Best estimate
Ostro	USA	1980	1976 – 1986	RAD	18.5%
Ostro	USA	1989	1976 – 1986	MRAD	0

5. Summary Tables

Pooled estimated of the Health Effects of PM_{10} and O_3	Ozone		PM_{10}	
	Mean[1]	IC 95%	Mean[2]	IC 95%
1.1 Acute Mortality (adjusted by particles)				
Total mortality	0.59 (9)	0.30 0.86	1.01 (39)	0.83 - 1.18
Respiratory mortality	0.01 (3)	-0.68 - 0.70	1.82(21)	1.37 - 2.22
Cardiovascular mortality	0.73 (3)	0.32 - 1.13	1.32(20)	1.10 - 1.55
> 65 mortality	0.07 (1)	-2.15 - 2.29	1.18 (11)	0.66 - 1.57
Infant mortality	-	-	3.52 (1)	0.72 – 6.31
1.2 Hospital admissions				
Total	1.74 (3)	1.16 - 2.32		
Respiratory hospital admissions	3.76 (3)	0.45 - 7.05	1.39 (11)	1.18 - 1.60
Respiratory hospital admissions (>65)	2.83 (4)	1.71 - 3.95	1.49 (6)	1.20 - 1.78
Asthma hospital admissions	1.47 (4)	0.41 - 2.53	3.02 (11)	2.05 - 4.00
ECOP hospital admissions	5.50 (1)	-3.40 - 7.50	2.34 (11)	1.80 - 2.89
Neumonia hospital admissions	5.20 (1)	2.60 - 8.00	1.40 (4)	1.05 - 1.75
Cardio & Cerebro- vascular hospital admissions	0.98 (5)	0.53 - 1.43	0.60 (12)	0.42 - 0.79
Cardio & Cerebro vascular hospital admissions (>65)	-	-	1.22 (4)	0.94 - 1.50
1.3. Emergency room visits (ERVs)				
Total				
Respiratory causes	3.172 (3)	1.67 - 4.67	3.11 (5)	2.35 – 3.88
Asthma causes	3.50 (1)	1.70 – 5.30	4.50 (1)	2.16 – 7.00
Tracheitis	12.5 (1)	0.0 - 29.16	-	-

[1] Percent change per 10 ppb. [2] Percent change per 10 $\mu g/m^3$

The number in parenthesis are the studies included in the calculation of the pooled estimated.

	Ozone		PM_{10}	
	Mean[1]	IC 95%	Mean[2]	IC 95%
1.4 Effects in asthmatics				
Asthma attacks	2.45 (1)	0.00 –5.90	7.87 (7)	4.48 – 11.27
Asthma attacks & Bronchodilator usage	1.80 (1)	0.20 - 3.60	10.22 (6)	7.30 – 13.14
Cough without phlegm (Children)	-	.	4.54 (5)	2.65 – 6.44
Cough with phlegm (Children)			3.32 (2)	2.01 – 4.64
Some respiratory symptoms (Children)	0.66 (6)	0.55 - 0.76		
Lower respiratory symptoms	0.23 (1)	0.14 - 0.33		
1.5 Respiratory symptoms in the General Population				
Respiratory symptoms			7.72 (3)	0.61 – 14.84
Upper respiratory symptoms	1.50 (1)	1.10 – 2.20	4.39 (3)	3.56 – 5.12
Lower respiratory symptoms	2.20 (1)	1.10 – 3.40	6.85 (5)	5.16 – 8.54
Bronchitis			11.00 (5)	8.96 – 13.58
Wheeze	1.32 (1)	0.47 –2.40		
1.6 Lung functions indices				
PEF	-1.15 (3)	-2.32 - 0.02	-0.39 (11)	-0.48 to – 0.31
FEV	-4.97 (3)	-9.89 to –0.06	-1.30 (7)	-1.53 to –1.07
FVC	-4.77 (3)	-9.47 to –0.07	-1.58 (2)	-2.35 to –0.82
MMEF			-8.00 (1)	-5.00 to -11.00
1.7 Restricted activity days and minor restricted activity days				
RAD	18.50 (1)		7.74 (1)	
MRAD			4.92 (1)	
2. Evaluation of Chronic Effects by Endpoint and Pollutant				
2.1. Chronic Total Mortality			5.700 (1)	1.77 – 10.4
2.2 Chronic morbidity (respiratory symptoms)			3.6 00 (1)	1.10 – 6.60

Note: The number in parenthesis are the studies included in the calculation of the pooled estimated
[1] Percent change per 10 ppb. [2] Percent change per 10 $\mu g/m^3$.

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