Human Health Effects of Criteria Pollutants

Appendix D

Introduction

In response to the mandate of section 812 of the Clean Air Act Amendments of 1990 (CAAA), EPA identified and estimated the quantifiable health benefits Americans should enjoy in 2000 and 2010 due to improved air quality resulting from the CAAA. The results suggest that the CAAA will result in significant reductions in mortality, respiratory illness, heart disease, and other adverse health effects, in addition to those reported in EPA's (1997) retrospective analysis of the Clean Air Act. In that analysis, the Agency found that significant health benefits accrued between 1970 and 1990, especially as a consequence of the reductions in ambient particulate matter (PM).

This appendix presents an overview of EPA's approach for modeling the human health effects of the CAAA. It outlines the principles used to guide the human health benefits analysis, describes methods used to quantify criteria air pollutant exposure nationwide, and discusses issues that arise in using health effect information. Following this overview, the appendix presents the modeling results, reported as estimates of avoided incidences of adverse health effects.

Health Effects Modeling Approach

In the section 812 retrospective analysis, EPA (1997) developed an approach for quantifying the effects of reduced pollutant exposure in the 48 continental states and the District of Columbia, with particular focus on those effect categories for which monetary benefits could be estimated. The study design adopted for this analysis follows a similar approach, using a sequence of linked analytical models to estimate benefits. The first step is an analysis of the likely implementation activities undertaken in response to the CAAA. These forecasted activities provided a basis for modeling criteria pollutant emissions under the two scenarios considered (the Pre-CAAA scenario and the Post-CAAA scenario), as documented in Appendix A. The emissions estimates were input into the air quality models (Appendix C), and ambient pollutant concentrations estimated by the air quality models were input into the health benefits model, the focus of this appendix.

The health benefits model relies on two inputs: (1) forecasted changes in pollutant exposures across the study period, and (2) concentration-response (C-R) functions that quantify the relationship between the forecasted changes in exposure and expected changes in specific health effects.We discuss the inputs used for the 48 continental states and the District of Columbia below.[1]

Quantifying Changes in Pollutant Exposures

Quantifying changes in pollutant exposures in this analysis relies on two inputs: (1) forecasts of ambient pollution levels at the available air quality monitors in the 48 contiguous states, and (2) extrapolations from the available air quality monitors (which are not uniformly distributed across the U.S.) to a population grid system of eight km by eight km cells that covers the 48 contiguous states and the District of Columbia.

[1] These inputs could also be used to estimate exposure in the border regions of Mexico and Canada that might have improved air quality in the Post-CAAA scenario.

Forecasting 2000 and 2010 Pollution Levels at Ambient Air Quality Monitors

When quantifying adverse human health effects, the section 812 prospective analysis estimated 2000 and 2010 ambient concentrations for both the Pre-CAAA and Post-CAAA scenarios for the following pollutants and air quality parameters:

- Particulate matter, less than 10 microns in diameter (PM_{10})
- Particulate matter, less than 2.5 microns in diameter ($PM_{2.5}$)
- Ozone (O_3)
- Nitrogen dioxide (NO_2)
- Sulfur dioxide (SO_2)
- Carbon monoxide (CO)

The sixth criteria pollutant, lead (Pb), is not included in this analysis since airborne emissions of lead were virtually eliminated by pre-1990 CAA programs. The methods used to estimate the concentrations of these pollutants at monitors are described in Appendix C.

Extrapolating Forecasts at Air Quality Monitors to Population Grid Cells

The next step is to extend forecasts for a limited number of air quality monitors to estimate population exposure at all locations in the continental United States, using the Criteria Air Pollutant Modeling System (CAPMS). CAPMS divides the United States into eight kilometer by eight kilometer grid cells and estimates the changes in incidence of adverse health effects associated with given changes in air quality in each grid cell. The national incidence change (or the changes within individual states or counties) is then calculated as the sum of grid-cell-specific changes. To calculate changes in population exposure in a grid cell, CAPMS requires data on the population in the grid-cell and the change in air quality.

First, grid-cell-specific population counts for 1990 are derived from U.S. Census Bureau block level population data (Wessex, 1994). Future year grid-cell population estimates are then extrapolated from 1990 grid-cell population levels using the ratio of future-year and 1990 state-level population estimates provided by the U.S. Bureau of Economic Analysis (1995). CAPMS assumes that all grid cell populations in a state grow at the same rate as the state population as a whole (where a grid cell is defined as being in a state if the grid cell centroid is in the state).

Second, CAPMS requires estimates of two air quality regimes at CAPMS grid cell centers: baseline (in this case, 1990) air quality levels and regulatory alternative air quality levels in future years (in this case, 2000 and 2010). Air quality inputs to CAPMS for pre- and Post-CAAA scenarios must use the averaging time required by the C-R functions being used.[2] For example, a C-R function relating mortality to annual median $PM_{2.5}$ concentrations requires that annual median $PM_{2.5}$ concentrations be available at CAPMS grid cell centers. Although the input $PM_{2.5}$ data must be in the form of daily averages, the monitors need not be at CAPMS grid cell centers. Given any set of location-specific air quality data, CAPMS interpolates the corresponding air quality values at each CAPMS grid cell center.

To reduce computational time when estimating the change in health effects associated with daily pollution levels, CAPMS approximates a year's (or season's) worth of daily pollutant concentrations at each monitor by 20 "bins" of pollutant concentrations. Each bin represents five percent of the daily pollutant concentrations in the period of interest, and is set at the midpoint of the percentile range it represents. For n = 20 and a year's worth of observations, the first bin represents the first (lowest) five percent of the distribution of 365 pollutant concentrations at the given location, and is set at the 2.5th percentile value; the second bin represents the next five percent of the distribution of daily values,

[2]The development of C-R functions is discussed later in this appendix.

and is set at the 7.5th percentile value, and so on. Each of the twenty bins therefore represents 18.25 (=365/20) days. Interpolation of air quality levels at CAPMS grid cell centers is based on these input location-specific bins, so that the annual incidence changes in each grid cell are calculated for twenty pollutant concentrations (the 20 bins of air quality) rather than for 365 pollutant concentrations. The resulting incidence change is then multiplied by 18.25 to reconstruct an entire years' worth of incidence change in the CAPMS grid cell.

As shown in Figure 1, actual ambient pollution data is only available from limited monitor sites. Data must be extrapolated to unmonitored locations, in order to estimate the impact of air pollution on the health and welfare effects considered in this analysis. The available air monitoring data were extrapolated from all available monitor locations to a grid of eight km by eight km population grid-cells throughout the contiguous 48 states, using a Voronoi neighbor averaging (VNA) spatial interpolation procedure.[3]

The VNA procedure interpolates air quality estimates from the set of surrounding air quality monitors to the center of each population grid-cell. The VNA procedure is a generalization of planar interpolation. Rather than arbitrarily limiting the selection of monitors, VNA identifies the set of monitors that best "surrounds" the center of each grid-cell by identifying which monitor is closest (considering both angular direction and horizontal distance) in each direction from the grid-cell center. Each selected monitor will likely be the closest monitor for multiple directions. The set of monitors found using this approach forms a polygon around the grid-cell center.

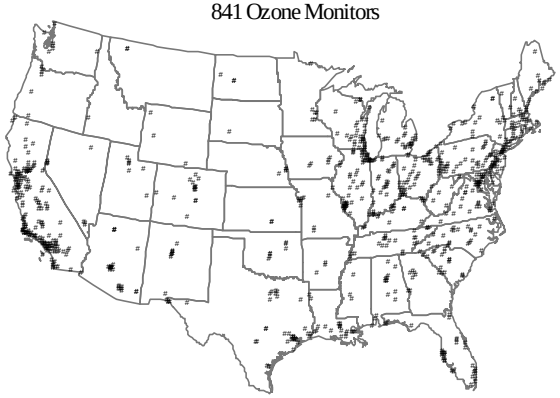
For each grid cell, CAPMS calculates the distance to each member of a set of monitors surrounding that grid cell. Monitors close to the grid cell are assumed to yield a more accurate air quality description of that grid cell, and are given a larger weight when calculating the average air quality for that grid cell. Conversely, monitors that are further away receive less weight. After determining the final set of surrounding monitors, the grid cell's air quality level is calculated as an inverse, distance-weighted average of the air quality levels at the selected monitors.

Air quality estimates generated using this VNA method are likely to be most uncertain at population grid cell locations far removed from the nearest monitor. For example, if a grid cell encompasses a relatively unpolluted rural area, but the nearest (albeit distant) monitors are measuring air quality in industrialized urban areas, the VNA method described above will overestimate the pollution level for that grid cell. As a result, this monitor-based VNA extrapolation method is used only at grid cells located within 50 kilometers of an air pollution monitor.

At distances greater than 50 kilometers from a monitor, additional information is needed to improve the estimates of air quality in unmonitored areas. A modified VNA method incorporating both monitor data and air quality modeling predictions is employed at these grid cell locations. In addition to the distance-weighted averaging of monitor concentrations, this modified extrapolation method incorporates a spatial adjustment factor that reflects the ratio of model-derived air quality predictions at the target and source locations. The addition of the modeling results helps account for differences in geography, meteorology, land use and other factors affecting air pollution levels between the target and source areas. Additional details on both VNA extrapolation methods can be found in Abt Associates (1999).

[3]For locations within 50 kilometers of a monitor, the interpolation method is the same as that used by Abt Associates (1998) for the NO_x SIP call analysis; previously termed the "convex polygon" method, it is more accurately described as Voronoi neighbor averaging (VNA) spatial interpolation, which will be used throughout this document.

841 Ozone Monitors

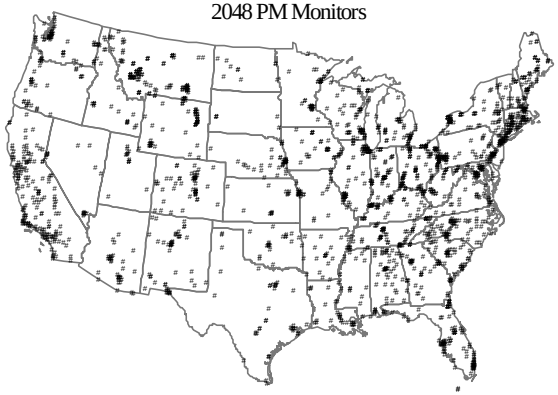


761 SO2 Monitors

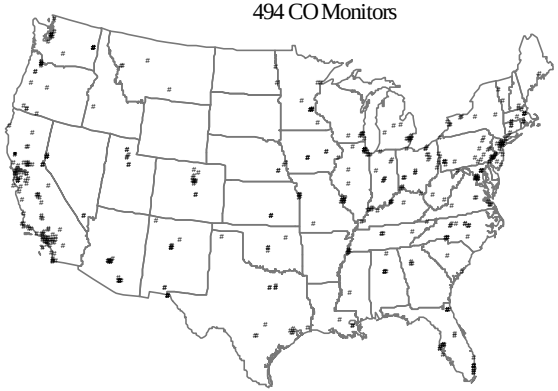
348 NO2 Monitors

Figure D-1
Location of Air Quality Monitors
Section 812 Analysis

2048 PM Monitors



494 CO Monitors



Quantifying Human Health Effects of Exposure

To calculate point estimates of the changes in incidence of a given selection of adverse health and welfare effects associated with a given set of air quality changes, CAPMS performs the following steps for each grid cell: (1) Interpolation of the air quality in the baseline scenario and in the control scenario at each CAPMS grid cell center for each pollutant. (2) Calculation of the changes in air quality from baseline to control scenario in the CAPMS grid cell. The changes in air quality are calculated as the differences between the baseline bins and the corresponding control scenario bins. (3) Identification of the selected C-R functions being used, and the required baseline incidence rates and the relevant grid cell population. (4) Calculation of the change in incidence of each adverse health effect for which a C-R function has been identified. The resulting annual incidence change for each grid cell is then summed with those of the other grid cells, to calculate the estimated change in incidence nationwide.

Types of Health Studies

Research on the health effects of air pollution strongly suggests that reductions in the incidence of adverse health effects are a significant benefit of air pollution control. The available human health studies that could serve as the basis of the section 812 prospective assessment can be categorized into chamber studies and epidemiology studies. Chamber studies involve examination of human responses to controlled conditions in a laboratory setting, while epidemiological studies investigate the association between exposure to ambient air pollution and observed health effects in a study population. The relative advantages of reliance on each type of research are described below.

Chamber Studies

Chamber studies of air pollution involve exposing human subjects to various levels of air pollution in a carefully controlled and monitored laboratory situation. The physical condition of the subjects is measured before, during and after the exposure. These measurements can include general biomedical information (e.g., pulse rate and blood pressure), physiological effects specifically induced by the pollutant (e.g., altered lung function), the onset of symptoms (e.g., wheezing or chest pain), or the ability of the individual to perform specific physical or cognitive tasks (e.g., maximum sustainable speed on a treadmill). These studies often involve exposing the individuals to pollutants while exercising, which increases respiration and the amount of pollution introduced into the lungs.

One advantage of chamber studies is that they can potentially establish cause-effect relationships between pollutants and certain human health effects. In addition, repeated experiments altering the pollutant level, exercise regime, and type of participants can potentially identify effect thresholds, the impact of recovery (rest) periods, and the differences in response among population groups. While cost considerations tend to limit the number of participants and experimental variants examined in a single study, chamber studies can follow rigorous laboratory scientific protocols, such as the use of placebos (clean air) to establish a baseline level of effects and precise measurement of certain health effects of concern.

There are drawbacks to using chamber studies as the basis for a comprehensive benefits analysis. Chamber studies are most appropriate for examining acute symptoms caused by exposure to a pollutant for a few hours. While this permits examination of some important health effects from air pollution, such as broncho-constriction in asthmatic individuals caused by sulfur dioxide, it precludes studying effects caused by long term exposure. Another drawback is that health effects measured in some well-designed chamber studies are selected on the basis of the ability to measure precisely an effect, for example forced expiratory volume, rather than a larger symptom. Some of these measurable but relatively minor health effects, such as reduced lung function, have an unclear impact on future medical condition and lifestyle, although some research discussed later has addressed this question.

Ethical considerations in experiments involving humans also impose important limits on the potential scope of chamber research. Chronic effects cannot be

investigated because people cannot be kept in controlled conditions for an extended period of time, and because chronic effects are generally irreversible. Participation is generally restricted to healthy subjects, or at least excludes people with existing health conditions that compromise their safe inclusion in the study. This can result in a lack of direct evidence about populations of most concern, such as people who already have serious respiratory diseases. Ethical considerations also limit experimental pollutant concentrations to relatively modest exposure levels, and confine studies to examining only mild health effects that are believed to do no permanent damage. Obviously, for ethical reasons, evidence from chamber studies cannot be obtained on the possible relationship between pollution and mortality, heart attack, strokes, or cancer.

The information derived from chamber research raises some questions as to how well it applies to the general population and their activity patterns and pollution exposures. (1) The dose-response functions developed from chamber research are specific to the population participating in the study. Chamber studies typically study a small population -- certainly much smaller than those typically evaluated in epidemiological studies (discussed below) -- so there are concerns that the results may not apply to the much larger and likely more diverse general population. (2) Chamber studies evaluate only a certain number of activity patterns (e.g., exercise), and cannot replicate the diverse pattern of activity seen in the course of a day. (3) Chamber studies cannot easily replicate the varied pollution levels to which people are exposed during the course of their day at work, on the freeway, at home, and other places.

As discussed below in the section on health effects study selection, the generalizability of results is an important factor in this analysis. Studies that use a large, diverse group of subjects are easier to apply to the general population than studies using smaller, narrowly defined group of subjects. This does not, however, rule out studies that focus on asthmatics, children, or the elderly, since these groups may be particularly sensitive to air pollution. Similarly, studies that use exposure regimes and exercise levels similar to what large groups of the population experience are easier to apply in a benefits model than are less representative studies.

Epidemiological Studies

Epidemiological studies present the results of a statistical analysis of the relationship between ambient pollution exposure and adverse health effects. The data for these studies includes ambient air quality monitoring data and adverse health effects data such as mortality incidence (e.g., National Center for Health Statistics, 1994), hospital admissions (e.g., Graves and Gillum, 1997), questionnaires (e.g., Adams and Marano, 1995), and diaries that are kept by study participants over a period of time (e.g., Ostro et al., 1991).

At least to some extent, these estimated relationships implicitly take into account complex real-world human activity patterns (including actions to avoid air pollution), spatial and temporal differences in air pollution distributions, and possible synergistic effects of multiple pollutants. Epidemiological studies typically involve a large number of people and may not suffer as much from the extrapolation problems common to chamber studies, which often have a limited number of subjects. In addition, observable health endpoints are measured, unlike chamber studies, which often monitor endpoints that do not result in observable health effects (e.g. forced expiratory volume).

Two types of epidemiological studies are considered for inclusion in this analysis: individual-level cohort studies and population-level ecological studies. Cohort-based studies track individuals over a certain period of time, with periodic evaluation of the individuals' exposure and health status. Cohort studies can either follow a group of initially disease-free individuals forward in time (a prospective cohort) or gather historical data on exposure and disease for a given group (a retrospective cohort). Studies about relatively rare events such as cancer incidence or mortality can require tracking the individuals over a long period of time, while more common events (e.g., respiratory symptoms) occur with sufficient frequency to evaluate the relationship over a shorter time period. An important feature of cohort studies is that information is collected about each individual that may include other variables that could be correlated with both the exposure and the disease outcome, such as smoking or income. If investigators do not identify and control for these variables, called confounders, in

a study, they may produce a spurious association between air pollution and adverse health effects.

A second type of study used in this analysis is a population-level ecological study. These studies assess the relationship between population-wide health information (such as counts for daily mortality, hospital admissions, or emergency room visits) and ambient levels of air pollution. There are two types of such studies: cross-sectional and time-series studies. Using data at a point in time from a variety of locations, cross-sectional studies examine the relationship between pollution exposure and adverse health effects, while trying to control confounding variables. Cross-sectional studies are not as desirable as prospective cohort studies, in part, because of their failure to control for important covariates such as smoking.[4] Rather than look at variety of locations at one point in time, a time series analysis studies a single location and typically examines the relationship between daily changes in ambient pollution level and daily changes in adverse health effects. An important advantage of the time-series design is that it allows the population to serve as its own control with regard to certain factors such as race and gender, and is thus similar to a cohort study (Schwartz, 1997, p. 372). Other factors that change over time can also affect health (tobacco, alcohol and illicit drug use, access to health care, employment, and nutrition). However, since such potential confounding factors are unlikely to vary from day to day in the same manner as air pollution levels, these factors are unlikely to affect the magnitude of the association between air pollution and daily variations in human health responses.

Drawbacks to epidemiological studies include difficulties associated with adequately characterizing exposure to individuals (that tends to lead to a downward bias in the estimated pollution-health effect relationship), and uncontrolled confounding variables, that can potentially lead to spurious conclusions. In particular, air pollutants are often highly correlated, so it is difficult to determine which may be associated with an adverse effect. In addition, epidemiological studies, by design, are unable to definitively prove a causal relationship between an exposure and a given health effect; they can only identify associations or correlations between exposure and the health outcome. However, given the major advantage of epidemiological studies -- relatively severe health effects may be observed in a large, more heterogeneous population -- epidemiological studies are used as the basis for determining the majority of health effects and C-R functions in this analysis. Chamber studies are used if there are health effects observed in chamber studies not observed in epidemiological studies, such as shortness of breath in young asthmatics induced by SO_2 (e.g., Linn et al., 1987).

Selection of C-R Functions

This section describes the methods used to derive the C-R functions used in this analysis to quantify the effect of CO, NO_2, SO_2, O_3, and PM on people's health. It discusses the general issues that arise with the choice and use of C-R functions, and the issues specific to C-R functions for mortality and morbidity.

C-R Function General Issues

Derivation of C-R Functions

For expository simplicity, the following discussion focuses on PM C-R functions, although it applies to all of the health effects and pollutants considered in the 812 prospective analysis. In what follows, the health effect estimated is simply denoted as y, and is estimated at a single location (population cell), where a change in PM air quality (ΔPM) corresponds to a change in the health endpoint (Δy). The calculation of Δy depends on a C-R function, derived typically from an epidemiological study.

There are a variety of epidemiological studies in the science literature, making it important to understand the nuances of each study before developing a C-R function. Different epidemiological studies may have estimated the relationship between PM and a particular health endpoint in different locations. The C-R functions estimated by these studies may differ from each other in several ways. They may have different functional forms; they may have measured PM concentrations in different ways;

[4]Criticisms of cross-sectional studies are considered in Evans et al. (1984), Lipfert and Wyzga (1995), and others.

they may have characterized the health endpoint, y, in slightly different ways; or they may have considered different types of populations. Some studies have assumed that the relationship between y and PM is best described by a linear form, where the relationship between y and PM is estimated by a linear regression in which y is the dependent variable and PM is one of several independent variables, while other studies have assumed that the relationship is best described by a log-linear form (i.e., the relationship between the natural logarithm of y and PM is estimated by a linear regression).[5] Some studies of the relationship between ambient PM concentrations and mortality have excluded accidental deaths from their mortality counts; others have included all deaths. One study may have measured daily (24-hour) average PM concentrations, while another study may have used two-day averages. Finally, one study may have considered changes in the health endpoint only among members of a particular subgroup of the population (e.g., individuals 65 and older), while other studies may have considered the entire population in the study location.

Estimating the relationship between PM and a health endpoint, y, consists of two steps: (1) choosing a functional form of the relationship, and (2) estimating the values of the parameters in the function assumed. The two most common functional forms in the epidemiological literature on health effects are the log-linear and the linear relationship. The log-linear relationship is of the form:

$$y = Be^{\beta \cdot PM} \ , \qquad \textbf{(1)}$$

or, equivalently,

$$\ln(y) = \alpha + \beta \cdot PM \ , \qquad \textbf{(2)}$$

where the parameter B is the incidence of y when the concentration of PM is zero, the parameter β is the coefficient of PM, ln(y) is the natural logarithm of y, and $\alpha = \ln(B)$.[6] If the functional form of the C-R relationship is log-linear, the relationship between ΔPM (= $PM_{baseline}$ - $PM_{after\ change}$) and Δy is:

$$\Delta y = y - y_{after\ change} = -y \cdot \left[e^{-\beta \cdot \Delta PM} - 1\right], \qquad \textbf{(3)}$$

where y is the baseline incidence of the health effect (i.e., the incidence before the change in PM). For a log-linear C-R function, the relative risk (RR) associated with the change in PM is:

$$RR_{\Delta PM} = \frac{y_{after\ change}}{y} = e^{-\beta \cdot \Delta PM} \qquad \textbf{(4)}$$

Epidemiological studies often report a relative risk for a given ΔPM, rather than the C-R coefficient, β. The coefficient can be derived from the reported relative risk and ΔPM, however, by solving for β in equation (4):

$$\beta = -\frac{\ln(RR)}{\Delta PM}. \qquad \textbf{(5)}$$

The linear relationship is of the form:

$$y = \alpha + \beta \cdot PM \ , \qquad \textbf{(6)}$$

[5] The log-linear form used in the epidemiological literature on ozone- and PM-related health effects is often referred to as "Poisson regression" because the underlying dependent variable is a count (e.g., number of deaths), believed to be Poisson distributed. The model may be estimated by regression techniques but is often estimated by maximum likelihood techniques. The form of the model, however, is still log-linear.

[6] Other covariates besides pollution clearly affect mortality. The parameter B might be thought of as containing these other covariates, for example, evaluated at their means. That is, $B = B_o \exp\{\beta_1 x_1 + ... + \beta_n x_n\}$, where B_o is the incidence of y when all covariates in the model are zero, and x_1, ... , x_n are the other covariates evaluated at their mean values. The parameter B drops out of the model, however, when changes in y are calculated, and is therefore not important.

where α incorporates all the other independent variables in the regression (evaluated at their mean values, for example) times their respective coefficients. When the C-R function is linear, the relationship between a relative risk and the coefficient, β, is not quite as straightforward as it is when the function is log-linear. Studies using linear functions usually report the coefficient directly.

If the functional form of the C-R relationship is linear, the relationship between ΔPM and Δy is simply:

$$\Delta y = \beta \cdot \Delta PM \ . \qquad \textbf{(7)}$$

If the C-R function is linear, equation (7) may be used to estimate Δy associated with ΔPM, assuming the measurement of ΔPM is consistent with the PM measurement used in the health effects study from which the C-R function was derived. If the function is log-linear, the baseline incidence for y and an appropriate measure for ΔPM may be used in equation (3).

A few epidemiological studies, estimating the relationship between certain morbidity endpoints and air pollution, have used functional forms other than linear or log-linear forms. Of these, logistic regressions are the most common. The details of the models used in these studies are given in the papers reporting the methods and results of the studies.

Thresholds

When conducting chamber and epidemiological studies, C-R functions may be estimated with and without explicit thresholds. Air pollution levels below the threshold are assumed to have no associated adverse health effects. When a threshold is not assumed, as is often the case in epidemiological work, any exposure level is assumed to pose a non-zero risk of response to at least one segment of the population.

Thresholds may *also* be incorporated by a policy analyst using a C-R function derived from the original study, even if the original study did not assume a threshold. A threshold may be set at any point, although some points may be considered more obvious candidates than others. One possible assumption is that there is a threshold at the non-anthropogenic background level of the pollutant. Another possibility is there is a threshold at the lowest observed level in the study that estimated the C-R function. Another might be a relevant standard for the pollutant.

One method to conduct policy analysis assuming a threshold model is to simply truncate the C-R function at the threshold (i.e., to exclude any physical effect changes associated with, say, PM levels below the designated threshold). This method uses the original C-R function, but calculates the change in PM as [max(T, baseline PM) - max(T, regulatory alternative PM)], where T denotes the designated threshold. An alternative method is to replace the original C-R function with a "hockey stick" model that best approximates the original function that was estimated using actual data. A typical hockey stick C-R function is horizontal up to a designated threshold PM level, T, and is linear with a positive slope for PM concentrations greater than T. This is just the following variation on equation (2) above:

$$\ln(y) = \alpha \quad for\ PM \le T\ , \qquad \textbf{(8)}$$

$$= \alpha + \beta \cdot PM \quad for\ PM > T\ ,\ where\ \beta > 0\ . \qquad \textbf{(9)}$$

The specification of such a 'hockey stick' model, while theoretically preferable to a simple truncation model, requires re-analysis of the underlying data from the original health effect study. Such primary re-analysis is beyond the scope of the section 812 analysis. Alternatively, if a simple truncation model is used, application of the resulting C-R function would likely result in a significant underestimate of the health effects avoided by reductions in pollutant exposures above the assumed threshold.

The possible existence of an effect threshold is a very important scientific question and issue for policy analyses such as the section 812 analysis. However, there is currently no scientific basis for selecting a particular threshold for the effects considered in this

analysis, if a threshold is defined as a level characterized by an absence of observable effects. Therefore, this analysis assumes there are no thresholds for modeling health effects. However, the potential impact of alternative threshold assumptions for PM-related premature mortality is explored as a key sensitivity analysis.

Pooling Studies

When only a single study has estimated the C-R relationship between a pollutant and a given health endpoint, the estimation of a population cell-specific incidence change is straightforward. For some endpoints, however, C-R functions have been estimated by several studies, often in several locations. In this case, if the input components (e.g., functional forms, pollutant averaging times, study populations) are all the same (or very similar), a pooled, "central tendency" C-R function can be derived from the multiple study-specific C-R functions.

One potential method of pooled analysis is simply averaging the coefficients from all the studies. This has the advantage of simplicity, but the disadvantage of not taking into account the measured uncertainty of each of the estimates. Estimates with great uncertainty surrounding them are given the same weight as estimates with very little uncertainty.

An alternative approach to pooling the estimates from different studies is to give more weight to estimates from studies with little reported uncertainty than to estimates with a great deal of uncertainty. The exact way in which weights are assigned to estimates of PM coefficients from different studies in a pooled analysis depends on the underlying assumption about how the different estimates are related to each other. If, for example, there is actually a distribution of true effect coefficients, or β's, that differ by location (referred to as the random effects model), the different coefficients reported by different studies may be estimates of *different* underlying coefficients, rather than just different estimates of the same coefficient. In contrast to the fixed effects model (which assumes that there is only one β everywhere), the random-effects model allows the possibility that different studies are estimating different parameters.

A third approach to pooling studies is to apply subjective weights to the studies, rather than conducting a random effects pooling analysis. If the analyst is aware of specific strengths and weaknesses of the studies involved, this prior information may be used as input to the calculation of weights which reflect the relative reliability of the estimates from the studies.

In some cases, studies reported several estimates of the C-R coefficient, each corresponding to a particular year or particular study area. For example, Ostro and Rothschild (1989b) report six separate regression coefficients that correspond to regression models run for six separate years. This analysis combined the individual estimates using a meta-analysis on the six years of data.

Pollution Exposure Measure

The study on which an acute exposure C-R function is based may have used pollution concentrations averaged over several days. Those studies that use multi-day averages are in effect using a smoothed data set, comparing each day's adverse health effects to recent average exposure rather than simply exposure on the same day. This does not have much effect on the estimated adverse health effects, especially when the C-R function has a linear or nearly linear functional form. For example, if the functional form were linear and based on a five-day pollution average, then the estimated effects over the course of the year would be essentially the same between using daily pollution observations in the C-R function or a two-day average. This is analogous to summing up five numbers (6,4,8,4,8=30) or taking their average and multiplying by five (6*5=30); in each case the answer is 30. This analysis uses daily pollution levels in cases where there are multi-day averaging times.

Regional Variation

Whether the C-R relationship between a pollutant and a given health endpoint is estimated by a single function from a single study or by a pooled function of C-R functions from several studies, that same C-R relationship is applied everywhere in the current benefits analysis. Although the C-R relationship may in fact vary somewhat from one location to another (for example, due to differences in population susceptibilities or differences in the composition of PM), location-specific C-R functions are available only for those locations in which studies were conducted. A single function applied everywhere may result in overestimates of incidence changes in some locations and underestimates of incidence changes in other locations. It is not possible, however, to know the extent or direction of the overall bias in the total incidence change introduced by application of a single C-R function everywhere.

PM Size and Composition

Current research suggests that particle size, and perhaps particle composition, matters when estimating the health impacts of PM. Particulate matter is a heterogeneous mix that varies over time and space, and may include solid or liquid compounds, including organic aerosols, sulfates, nitrates, metals, elemental carbon, and other material. Fine PM is generally viewed as having a more harmful impact than coarse PM, although it is not clear to what extent this may differ by the type of health effect or the exposed population. While one cannot necessarily assume that coarse PM has no adverse impact on health, it seems reasonable to prefer the use of $PM_{2.5}$ as a proxy for the impact of PM. Due to the relative abundance of studies using PM_{10}, however, and the reasonably good correlation between $PM_{2.5}$ and PM_{10} in urban areas, in many cases this analysis also uses PM_{10} studies to estimate the impact of PM. Similarly, at this stage of knowledge, it is not clear what composition distinctions to make, if any, when estimating the impact of PM. The C-R functions used in this analysis relate adverse health effects to an undifferentiated mass of particles (e.g., PM_{10}); they do not relate effects to individual PM components.

Baseline Incidence Rate

Some C-R functions (those expressed as a change relative to baseline conditions) require baseline incidence data associated with ambient levels of pollutants. Baseline incidence data necessary for the calculation of risk and benefits were obtained from national sources whenever possible, because these data are most applicable to a national assessment of benefits. County-specific estimates of baseline mortality incidences used in this analysis were obtained from the National Center for Health Statistics (1994). The National Center for Health Statistics also provided much of the information on national incidence rates. However, for some studies, the only available baseline incidence information comes from the studies themselves; in these cases, the baseline incidence in the study population is assumed to represent the baseline incidence nationally.

Population

Many studies focus on a particular age cohort. The age group chosen is often a matter of convenience (e.g., extensive Medicare data may be available for the elderly population) and not because the effects are necessarily restricted to the specific age group, even though their incidence may vary considerably over an individual's life span. Nevertheless, to avoid overestimating the benefits of reduced pollution levels, this analysis applies the given C-R relationships only to those age groups corresponding to the cohorts studied. Likewise, some studies were performed on individuals with specific occupations, activity patterns, or medical conditions because these traits relate to the likelihood of effect, such as in the estimation of worker productivity. In these cases, application of dose-response functions has been restricted to populations of individuals with these same characteristics. As discussed in more detail below, however, by assuming that the C-R relationships should only be applied to those subpopulations matching the original study population, the present analysis may be significantly underestimating the whole population benefits of reductions in pollutant exposures.

C-R Function Selection Criteria

A number of considerations arose in selecting and applying concentration-response (C-R) functions for the section 812 prospective assessment. These considerations are summarized in Table D-1 below. Because concentration-response functions are the means of relating changes in pollutant levels to changes in health endpoints, they are a critical component of a benefits analysis. While a study may be superior with regard to one consideration (e.g., number of pollutants considered), it may be inferior with regard to another consideration (e.g., number of observations). The selection of C-R functions for the benefits analysis was guided by the goal of achieving a balance between comprehensiveness and scientific defensibility. The issues considered are discussed below in some detail.

Table D-1
Summary of Considerations Used in Selecting C-R Functions

Consideration	Comments
Peer reviewed research	Peer reviewed research is preferred to research that has not undergone the peer review process.
Study type	Among studies that consider chronic exposure (e.g., over a year or longer) prospective cohort studies are preferred over cross-sectional studies (a.k.a. "ecological studies") because they control for important confounding variables that cannot be controlled for in cross-sectional studies. If the chronic effects of a pollutant are considered more important than its acute effects, prospective cohort studies may also be preferable to longitudinal time series studies because the latter type of study is typically designed to detect the effects of short-term (e.g. daily) exposures, rather than chronic exposures.
Study period	Studies examining a relatively longer period of time (and therefore having more data) are preferred, because they have greater statistical power to detect effects. More recent studies are also preferred because of possible changes in pollution mixes, medical care, and life style over time.
Study population	Studies examining a relatively large sample are preferred. Studies of narrow population groups are generally disfavored, although this does not exclude the possibility of studying populations that are potentially more sensitive to pollutants (e.g., asthmatics, children, elderly). However, there are tradeoffs to comprehensiveness of study population. Selecting a C-R function from a study that considered all ages will avoid omitting the benefits associated with any population age category. However, if the age distribution of a study population from an “all population” study is different from the age distribution in the assessment population, and if pollutant effects vary by age, then bias can be introduced into the benefits analysis.
Study location	U.S. studies are more desirable than non-U.S. studies because of potential differences in pollution characteristics, exposure patterns, medical care system, and life style.
Pollutants included in model	Models with more pollutants are generally preferred to models with fewer pollutants, though careful attention must be paid to potential collinearity between pollutants. Because PM has been acknowledged to be an important and pervasive pollutant, models that include some measure of PM are highly preferred to those that do not.
Measure of PM	$PM_{2.5}$ and PM_{10} are preferred to other measures of particulate matter, such as total suspended particulate matter (TSP), coefficient of haze (COH), or black smoke (BS) based on evidence that $PM_{2.5}$ and PM_{10} are more directly correlated with adverse health effects than are these more general measures of PM.
Economically valuable health effects	Some health effects, such as forced expiratory volume and other technical measurements of lung functioning, are difficult to value in monetary terms. These health effects are not quantified in this analysis.
Non-overlapping endpoints	Although the benefits associated with each individual health endpoint may be analyzed separately, care must be exercised in selecting health endpoints to include in the overall benefits analysis because of the possibility of double counting of benefits. Including emergency room visits in a benefits analysis that already considers hospital admissions, for example, will result in double counting of some benefits if the category “hospital admissions” includes emergency room visits.

Peer-Review of Research

Whenever possible, peer-reviewed research rather than unpublished information has been used. Research that has been reviewed by the EPA's own peer review processes, such as review by the Clean Air Scientific Advisory Committee (CASAC) of the Science Advisory Board (SAB), has been used whenever possible. Research reviewed by other public scientific peer review processes, such as the National Academy of Science, the National Acidic Precipitation Assessment Program, and the Health Effects Institute is also included in this category.

Studies published (or accepted for publication) in peer reviewed journals but not reviewed by CASAC have also been considered for use in the section 812 prospective assessment, and have been used if they are determined to be the most appropriate available studies. Indications that EPA intends to submit research to the CASAC (such as inclusion in a draft Criteria Document or Staff Paper) are considered further evidence that specific journal-published research is acceptable for use in this analysis.

Air pollution health research is a very active field of scientific inquiry, and new results are being produced regularly. Many research findings are first released in university working papers, dissertations, government reports, non-reviewed journals and conference proceedings. Some research is often published in abstract form in journals, which does not require peer review. In order to use the most recent research findings and be as comprehensive as possible, unpublished research was examined for possible use.

Study Type and Quality

Epidemiological studies of the relationship between air pollutants and health endpoints can generally be categorized as (1) "ecological" cross-sectional, (2) prospective cohort, or (3) longitudinal time series studies. The first two types of study are concerned with longer exposure periods, such as a year or over several years, while the third type is concerned with short-term exposures over one or more days. Among studies that consider longer exposure periods, or chronic exposure, prospective cohort studies are preferable to "ecological" cross-sectional studies, because they control for important confounding variables which cannot be controlled for in "ecological" cross-sectional studies. If the effects of chronic exposures are considered more significant than acute effects, prospective cohort studies may also be preferable to longitudinal time series studies because the latter type of study is typically designed to detect the effects only of daily exposures, rather than chronic exposures.

Studies that control for a broad range of likely confounders can offer a more robust conclusion about an individual pollutant, even if the statistical confidence interval is larger due to the inclusion of more variables in the analysis. For example, a study that considers only air pollution, omitting other variables associated with a health outcome, could incorrectly conclude that a reduction in air pollution is exclusively responsible for a reduction in the health outcome. Potential confounders include weather-related variables (e.g., temperature) and ambient pollutants other than those being studied.

Study Population

Many of the studies relevant to quantifying the benefits of air pollution reductions have focused on subpopulations that may or may not be representative of the general population. Extrapolating results from studies on nonrepresentative subpopulations to the general population introduces uncertainties into the analysis, but the magnitude of the uncertainty and its direction are often unknown. Because of these uncertainties, benefit analyses often limit the application of the C-R functions only to those subpopulations with the characteristics of the study population. While this approach has merit in minimizing uncertainty, it can result in a severe underestimate of benefits if similar effects are likely to occur in the rest of the population. For these reasons, studies that examine broad, representative populations may be preferable to studies with narrower scope, because they allow application of the functions to larger numbers of persons. There are, however, tradeoffs to comprehensiveness of study population.

Selecting a C-R function from a study that considered all ages will avoid omitting the benefits associated with any population age category. However, if the age distribution of the study population from an "all population" study is different from the age distribution in the assessment population, and if pollutant effects vary by age, then bias can be introduced into the benefits analysis.

Study Period

Studies examining a relatively longer period of time are preferable because they have more data and therefore have greater statistical power to detect effects. In addition, more recent studies are preferable to older studies because of possible changes in pollution mixes, medical care, and life style over time. This latter issue is effectively a benefits transfer issue. Differences across time between the study period and the assessment period introduce uncertainties into the benefits analysis, because it is not known to what extent the C-R relationship estimated during the study period will be the same during the assessment period.

Study Location

Studies conducted in locations that are different from the assessment location are generally less desirable because of the introduction of possible benefits transfer problems. The characteristics of a population (e.g., the proportion of the population that is particularly susceptible to pollution, or the behavior patterns of the population) and/or the pollution mix to which it is exposed may differ notably between the study location and the assessment location. As with differences in time periods, these differences in location introduce uncertainties into the benefits analysis, because it is not known to what extent the C-R relationship estimated in the study location is the same in the assessment location. For that reason, studies conducted in the United States or Canada are preferable for this benefits analysis to studies conducted, for example, in Europe or in developing countries. In addition, studies that include a wide range of areas are preferred. Studies focusing on a single city are not as desirable as studies that focus on multiple cities.

The preference for studies that focus on a range of areas, in the U.S. and Canada, is driven by a concern that there may be significant regional variation in the estimated C-R functions. There has not, however, been enough research to establish regional specific values.

Pollutants Included in the Model

In many cases, several pollutants in a "pollutant mix" are correlated with each other -- that is, their concentrations tend to change together. Although there may be an association between an adverse health effect and this mix, it may not be clear which pollutant is causally related to the health effect -- or whether more than one pollutant is causally related. Using separate regressions (from single pollutant models) for each pollutant may overstate the effect of each pollutant alone. Models that consider pollutants simultaneously are therefore preferred, though careful attention must be paid to potential collinearity between pollutants. Because PM has been acknowledged to be an important pollutant, models that include some measure of PM are highly preferred to those that do not.

Measure of Particulate Matter

Different epidemiological studies examining the health effects associated with particulate matter (PM) have used different measures of PM. Some have used PM_{10} while others have used $PM_{2.5}$. The number of studies using $PM_{2.5}$ as the indicator of PM is substantially more limited than the number using PM_{10} because of the relative sparseness of $PM_{2.5}$ monitor data. A number of studies have used total suspended particulate matter (TSP), British Smoke, coefficient of haze (COH) and other measures of particulate matter. There is some evidence that the relationship between fine particulates ($PM_{2.5}$) and health effects may be stronger than that between other measures of PM and health effects. If this is true, then studies that use measures of PM that more closely approximate the fine fraction of PM (such as PM_{10}) are preferable to those that use other measures.

Economically Valuable Health Effects

A number of the health endpoints examined in the literature are difficult to value in monetary terms. These effects include forced expiratory volume and other technical measurements of lung functioning. It is not clear how to assign an economic value to such effects, as their impact on future medical condition and lifestyle are not well understood. One method to value these "clinical" measures is to estimate their association with adverse health effects that *are* valued.

Ostro et al. (1989a) reanalyzed data from four controlled ozone exposure studies, and found a statistically significant relationship between forced expiratory volume in one second (FEV_1) and the probability that an individual will report a mild, moderate or severe respiratory symptom. In this case, one could estimate ozone benefits by first calculating the change in FEV_1 associated with a given change in ozone concentration, converting this to a change in respiratory symptoms, and then valuing the respiratory symptom change. In a separate study, Neas and Schwartz (1998) found that certain measures of reduced pulmonary functioning are significant predictors of mortality. This result, however, would be difficult to use to calculate air pollution benefits, because they looked at the relationship between declines in lung function and mortality, and they did not estimate the impact of air pollution on this decline; separate work would be required to estimate the impact of air pollution on lung function.

The main concern when translating a clinical measure such as FEV_1 to an economically valuable one such as acute respiratory symptoms is that epidemiological work may already be available from which one can directly estimate a C-R function. To estimate acute respiratory symptoms directly (from an epidemiological study) and indirectly through the clinical measure, would double-count the effect. Another concern is that using the indirect method adds a layer of uncertainty because one must first translate the estimated clinical measure to the estimated economically valuable measure.

Non-Overlapping Health Effects

Several endpoints reported in the health effects literature overlap with each other. For example, the literature reports relationships for hospital admissions for single respiratory ailments (e.g. pneumonia or chronic obstructive pulmonary disease) as well as for all respiratory ailments combined. Similarly, several studies quantify the occurrence of respiratory symptoms where the definitions of symptoms are not unique (e.g., shortness of breath or upper respiratory symptoms). Measures of restricted activity provide a final example of overlapping health endpoints. Estimates are available for pollution-related restricted activity days, mild restricted activity days, and activity restriction resulting in work loss. While the benefits analysis estimates the benefits associated with individual endpoints, it takes care in deciding which endpoints to include in an estimate of total benefits, in order to avoid double-counting of benefits from overlapping endpoints.

Mortality

Health researchers have consistently linked air pollution with excess mortality. Prospective cohort and cross-sectional studies have found a relationship between mortality over the course of a year or more with pollution levels measured over the course of a year or several years. In addition, a number of so-called "short-term" mortality studies have linked daily variations in mortality with daily pollution levels.

The EPA Clean Air Council (U.S. EPA, 1999, p. 11) recommends using the prospective cohort study by Pope et al. (1995), rather than short-term mortality studies. Although short-term studies lend substantial support to the hypothesis that there is a relationship between PM and mortality, they focus only on the acute effects associated with daily peak exposures. In contrast, the Pope et al. study was designed to capture the effect of exposure over many years, however it may be less able to capture the short-term impact of peak exposures. This creates an overlap of unknown size between the mortality estimates based on short-term studies and Pope et al. Capturing the chronic impact, however, is judged more important than

missing the impact of an unknown number of deaths occurring shortly after short-term peak exposures. For this reason, the Pope et al. study is preferred. A second prospective cohort study by Dockery et al. (1993) is also used to estimate the impact of PM on mortality. However, the Dockery et al. study used a smaller sample of individuals from fewer cities than the study by Pope et al., and is therefore presented only as an illustrative calculation that is consistent with Pope et al. (1995); the Pope et al. estimate is used in the primary analysis.[7]

The total mortality effect estimated by the Pope et al. (1995) and the Dockery et al (1993) studies does not necessarily occur in the same year as the estimated exposure. However, the exact relationship between the time of exposure and mortality is not well known. In the primary analysis, we assume that mortality occurs over a five year period, with 25 percent of the deaths occurring in the first year, 25 percent in the second year, and 16.7 percent in each of the third, fourth, and fifth years. We also perform an analysis of the sensitivity of benefits valuation to the lag structure by considering a range of assumptions about the timing of mortality (see Appendix H). It is important to keep in mind that changes in the lag assumptions do not change the total number of estimated deaths, but rather the timing of those deaths.

At least some evidence has been found linking each of the criteria pollutants with mortality. This raises concerns that the mortality-related benefits of air pollution reduction may be overstated if separate pollutant-specific estimates, some of which may have been obtained from models excluding the other pollutants, are aggregated. In addition, there may be important interactions between pollutants and their effect on mortality.

The Pope et al. (1995) study included only PM, so it is unclear to what extent it may be including the impacts of ozone or other gaseous pollutants. Because of concern about overstating of benefits and because the evidence associating mortality with exposure to particulate matter is currently stronger than for other pollutants, only the benefits of PM-related mortality avoided are included in the total benefits estimate. The benefits associated with ozone reductions are estimated but are not included in the estimate of total benefits. The relationship between CO and mortality is briefly considered, but the evidence reviewed does not point to a clear link between the two.

Statistical Lives Saved Versus Statistical Life-Years Saved

Considerable attention has been paid to using life-years lost as an alternative to lives lost as a measure of pollution-related premature mortality. This analysis uses both approaches to estimating pollution-related premature mortality.

The actual number of years any particular individual is going to live cannot be known. Instead, one estimates the *expected*, or statistical average, number of "life-years lost". The number of life-years lost may be expressed as the average number of life-years lost for all of the people who are exposed (the *ex ante* measure), or as the average number of life-years lost for the people who died from exposure (the *ex post* measure).

The *ex ante* estimate of life-years lost depends on the individual having been exposed to a pollutant, *not* on the individual having died prematurely from that exposure. Suppose, for example, that a 25 year old has a life expectancy of 50 more years in the absence of PM exposure and only 48 more years in the presence of exposure. The exposed 25 year old would, on average, have her life expectancy shortened by two years. That is, two expected life-years would be lost by every *exposed* individual.

The *ex post* estimate of life-years lost depends on the individual actually having died from exposure to pollution. When an individual dies of exposure to

[7]The Pope et al., 1995 study estimated a C-R coefficient using median PM concentration data; however, mean pollutant concentration is the measure of central tendency commonly used in other health studies. We will explore the possibility of re-estimating the PM mortality C-R function using mean concentration data in future 812 prospective analyses.

PM, he is said to have lost the number of years he would have been expected to live; this can be calculated from age- and gender-specific life expectancy tables. Suppose that the life expectancy of 25 year olds is 75 -- a 25 year old can expect to live 50 more years. A 25 year old who dies from exposure to PM has therefore lost 50 expected years of life. This is the life-years lost that can be expected by every *affected* 25 year old (i.e., every 25 year old who actually dies from exposure to PM).

Estimates of the total life-years lost by a population exposed to PM depend on several factors, including the age distribution and the size of the exposed population, the magnitude of the PM change, the relative risk assumed to be associated with the change in PM, and the length of exposure. A population chronically exposed to a given increase in PM will lose more life-years than a population exposed to the same increase in PM for only a year or two.[8] A population that is generally older will lose fewer life-years, all else equal, than one that is generally younger, because older individuals have fewer (expected) years of life left to lose. And a population exposed to a greater increase in PM will lose more life-years than one exposed to a smaller increase in PM. Finally, the life-years lost by the population will increase as the relative risk associated with the increase in PM increases.

Life-years lost are usually reported as averages over a population of individuals. The population over which the average is calculated, however, can make a crucial difference in the reported average life-years lost. The average life-years lost *per exposed individual* (the *ex ante* estimate) is just the total life-years lost by the population of exposed individuals who died divided by the number of exposed individuals. Although those individuals who do die prematurely from exposure to PM may lose several expected years of life, most exposed individuals do not actually die from exposure to PM and therefore lose zero life-years. The average life-years lost per exposed individual in a population, alternatively referred to as the average decrease in life expectancy of the exposed population, is therefore heavily weighted towards zero.

The *ex ante* and *ex post* measures of life-years lost take the same total number of life-years lost by the exposed population and divide them by different denominators. The *ex ante* measure divides the total life-years lost by the total population exposed; the *ex post* measure divides the same total life-years lost by only a small subset of the total population exposed, namely, those who died from PM. The average per exposed individual is therefore much smaller than the average per affected individual. Because both types of average may be reported, and both are valid measurements, it is important to understand that, although the numbers will be very dissimilar, they are consistent with each other and are simply different measures of the estimated mortality impact of PM.

To illustrate the different measures of life-years lost and the effects of various input assumptions on these measures, death rates from the 1992 U.S. Statistical Abstract were used to follow a cohort of 100,000 U.S. males from birth to age 90 in a "dirty" scenario and a "clean" scenario, under various assumptions. Death rates were available for ages less than 1, ages 1-4, and for ten-year age groups thereafter. The ten-year age groups were divided into five-year age groups, applying the death rate for the ten-year group to each of the corresponding five-year age groups. *Ex ante* and *ex post* measures of life-years lost among those individuals who survive to the 25-29 year old category (96,947 individuals) were first calculated under the assumptions in the World Health Organization (WHO) 1996 report. These assumptions were that the relative risk of mortality in the "dirty" scenario versus the "clean" scenario is 1.1; that exposure does not begin until age 25; that the effect of exposure effects observed throughout the fifteen year exposure period can be summed and attributed (for mathematical convenience) to the 15th year of exposure; that individuals at the beginning of

[8] Even in the absence of cumulative effects of exposure, exposure of a population for many years will result in a greater total number of pollution-related deaths than exposure for only a year or two, because the same relative risk is applied repeatedly, year after year, to the population, rather than for only a year or two.

each age grouping either survive to the next age grouping or live zero more years; and that all individuals age 85 live exactly five more years. Under these assumptions, the expected life-years lost per exposed individual in the 25-29 year old cohort is 1.32 years, while the expected life-years lost per affected individual (i.e., for each of the 7,646 expected PM-related deaths) is 16.44 years.

Ozone and Mortality

The literature investigating the relationship between ozone and mortality has been rapidly evolving over the last several years. Of the 31 time-series epidemiology studies identified in the literature that report quantitative results on a possible association between daily ozone concentrations and daily mortality, 25 were published or presented since 1995. These studies were conducted in various urban areas throughout the world: sixteen in the United States or Canada, nine in Europe, two in Australia, and four in Latin America. Seventeen of the studies report a statistically significant relationship between ozone and mortality, with the more recent studies tending to find statistical significance more often than the earlier studies.

While the growing body of epidemiological studies suggests that there may be a positive relationship between ozone and premature mortality, there is still substantial uncertainty about this relationship. Because the evidence linking premature mortality and particulate matter is currently stronger than the evidence linking premature mortality and ozone, it is important that models of the relationship between ozone and mortality include a measure of particulate matter as well. Because of the lack of monitoring data on fine particulates or its components, however, the measure of particulate matter used in most studies was generally either PM_{10} or TSP or, in some cases, Black Smoke. If a component of PM, such as $PM_{2.5}$ or sulfates, is more highly correlated with ozone than with PM_{10} or TSP, and if this component is also related to premature mortality, then the apparent ozone effects on mortality could be at least partially spurious.

Even if there is a true relationship between ozone and premature mortality, after taking particulate matter into account, there would be a potential problem of double counting in this analysis if the ozone effects on premature mortality were added to the PM effects estimated by Pope et al., 1995, because, as noted above, the Pope study does not include ozone in its model. Because of this, the potential ozone-mortality relationship is not included in the primary analysis. Instead the benefits associated with ozone reductions are estimated in a sensitivity analysis. The results of this sensitivity analysis should be reviewed with the appropriate caution, however, in view of the above-noted uncertainties surrounding a potential ozone-mortality relationship.

To synthesize the results of multiple studies on the relationship between ozone and premature mortality, a modified meta-analysis method was used. Because of differences in the averaging times used in the underlying studies (some use daily average ozone levels, while others use 1-hour daily maximum values), the meta-analysis approach was applied to the predicted mortality incidence changes estimated by each of the studies rather than to the coefficients of ozone in the C-R functions.

A study was included in the meta-analysis if it (1) is in or has been accepted by a peer-reviewed publication; (2) reports quantitative results for daily mortality and ozone (rather than for other measures such as total oxidants); (3) considers the entire population (rather than only a subset of the population) in the study location; (4) considers the whole year (rather than only a season or seasons); (5) considers all non-accidental or total mortality; (6) considers only one location (rather than a pooling of results across multiple locations); and (7) reports results from a copollutant model, that includes PM or some proxy for PM in the model with ozone, as well as some measure of temperature and season. The selection of a single result from among multiple ozone results reported in the same study was facilitated by the following three additional selection criteria: (8) PM (PM_{10} or $PM_{2.5}$) is preferable to other measures of particulate matter; (9) more pollutants in the model is preferable to fewer pollutants; and (10) Poisson

regression is preferred to other specifications.[9] Nine studies were chosen using these criteria. To minimize benefits transfer problems, the meta-analysis was limited to the four of these nine studies that were conducted in the United States. Table D-2a briefly describes the four studies included in the meta-analysis.

[9] Almost all the models in the literature used Poisson regression. This final criterion was therefore included to impose consistency, if there was no other means by which to select a model from among several models in a study.

Table D-2a
Studies and Results Selected for Meta-Analysis of the Relationship between Daily Mortality and Exposure to Ambient Ozone in the United States

Study	Study Location/ Duration	Copollutants in model	O_3 Concentration Measure (ppb)	Relative Risk and 95% CI for a 25 ppb Increase in O_3
Ito and Thurston (1996) [a]	Cook County, Illinois 1985-1990	PM_{10}	average of same day and previous day 1-hr maxima	1.016 (1.004 — 1.029)
Kinney et al. (1995)	Los Angeles County 1985-1990	PM_{10}	daily 1-hr max	1.000 (0.989 — 1.010)
The following studies were used to generate a single distribution for Philadelphia:				
Moolgavkar et al. (1995)	Philadelphia 1973-1988	TSP, SO_2	daily avg	1.015 (1.004 — 1.026)
Samet et al. (1997)	Philadelphia 1974-1988	TSP, SO_2, NO_2, Lagged CO	2-day avg	1.024 (1.008 — 1.039)

[a] Relative risks derived from the ozone coefficient and standard error from the copollutant model were provided by personal communication with Dr. Kazuhiko Ito.

Carbon Monoxide and Mortality

Research work presents some evidence that CO may be significantly linked to mortality, although it is not clear to what extent CO may have an effect independent of PM. Burnett et al. (1998) studied mortality in association with CO, NO_2, O_3, SO_2, coefficient of haze, TSP, sulfates and estimated $PM_{2.5}$ and PM_{10} from 1980-1994 in metropolitan Toronto. In models that included the day of the week, weather, CO and one of the other pollutants, they found that daily average CO and all of the PM measures contributed a significant fraction of the daily number of non-accidental deaths. The measure for coefficient of haze had the strongest impact on the relative risk for CO. The relative risk associated with a 1.4 ppm change (i.e., 95th to the 5th CO percentile) was 1.070 in the single pollutant model; with the addition of COH, it fell to 1.043 (Burnett et al., 1998, Table 2). Nevertheless, the impact of CO is still quite large, and it is reported to occur in all seasons, age, and disease groupings. The model with the best fit included CO and TSP. With both CO and TSP in the model and using the mean levels of the pollutants reported for Toronto, CO contributed, on average, 4.7% of daily non-accidental deaths and TSP contributed 1% (Burnett et al., 1998, p. 689).

A review of three articles suggests that Burnett et al.'s results may not be consistent with other published results (Table D-2b).[10] In a model with CO and PM_{10}, Kinney et al. (1995, Figure 3) reported a relative risk of 1.05 for a 10 ppm CO increase (with a 95% confidence interval of 0.98-1.12). This is not statistically significant at the usual significance level of 5%, and the implied relative risk (1.007) for a 1.4 ppm change is about six times smaller than that reported by in Burnett et al's two-pollutant model.[11] Saldiva (1995, Table 4) reported a positive and significant CO regression coefficient in a model with just CO. Estimated at the mean, this suggests a relative risk of 1.039 per 1.4 ppm of CO, or about half the size of that reported in Burnett et al.'s single pollutant model (RR = 1.070).[12] Saldiva et al. also reported a model with CO along with all of the other measured

[10] A fourth study, by Gwynn, Burnett, and Thurston, cited as being submitted for publication, was not considered here.

[11] The underlying coefficient equals the logarithm of the relative risk divided by the change in pollution.

[12] The regression coefficient, β, = 1.69 (Saldiva et al., 1995, Table 4) and the mean mortality rate per day = 62.6 (1995, Table 1). Estimated mortality after reducing CO by 1.4 ppm = 60.23 deaths per day. The relative risk = (62.9/60.23) = 1.039.

pollutants: PM_{10}, SO_2, NO_x, and O_3. In this model, the PM_{10} coefficient remained significant and unchanged from its single-pollutant model value, but the CO coefficient dropped substantially and became insignificant (1995, Table 4). Touloumi et al. (1996, Table 4) estimated a single pollutant model with a reported relative risk of 1.05 for a 7.6 mg/m^3 rise in CO. Assuming a conversion of 1 ppm = 1.145 mg/m^3 (U.S. EPA, 1991, Table 3-1), this suggests a relative risk (1.015) that is about five times smaller than the relative risk (1.070) in Burnett et al.'s single pollutant model value.

In 1991, the EPA (1991, p. 1-12) concluded that the results of CO epidemiological work "is suggestive, but not conclusive evidence" that CO may lead to sudden death in persons with coronary artery disease. Since that time, studies by Morris et al. (1995) and Schwartz and Morris (1995) reported that ambient CO concentrations increase the likelihood of hospitalization for cardiovascular disease. It is not unlikely that a certain fraction of these admittances will die, and thus indirectly one might estimate the impact of CO on mortality. However, there does not appear to be a study from which one may develop with confidence a C-R function to directly estimate CO-related mortality.[13] The results from Burnett et al. (1998) suggest that CO may have an effect on mortality independent of other pollutants, but it is premature to base an estimate of CO-related mortality with the relative risk published in their study.

[13]This difficulty may be related in part to the highly variable CO concentrations that are typically found in an urban area.

Table D-2b
Selected Studies and Results for Carbon Monoxide and Mortality

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Burnett et al. (1998)	Toronto, Canada 1980-1994	All ages, metropolitan Toronto	non-accidental mortality	CO,NO_2, SO_2, O_3, SO_4, TSP, COH, PM_{10}, $PM_{2.5}$	Significant CO effect found in all two pollutant models. Controlling for CO, significant effect found for SO_4, TSP, COH, PM_{10}, and $PM_{2.5}$.	Association with cardiac-related mortality is stronger, but CO is also significantly related to non-cardiac mortality. PM_{10} and $PM_{2.5}$ estimated from SO_4, TSP, and COH.
Kinney et al. (1995)	Los Angeles County 1985-1990	All ages	non-accidental mortality	CO, O_3, PM_{10}	In single pollutant models, CO significant, and PM_{10} and O_3 are marginally significant. In model with CO and PM_{10}, both CO and PM_{10} are not significant.	Magnitude of single pollutant CO relationship drops modestly with inclusion of PM_{10}.
Saldiva et al. (1995)	Sao Paulo, Brazil 1990 to 1991	Elderly (+65 years)	mortality from natural causes	CO, O_3, PM_{10}, SO_2, NO_x	CO significant in single pollutant model. CO not significant in model with all other pollutants.	
Touloumi et al. (1996)	Athens, Greece 1987-1991	All ages	total mortality	CO, SO_2, black smoke	CO, SO_2, and black smoke significant in single pollutant models.	Deaths during a one month summertime heat wave were excluded from analysis

Post-Neonatal Mortality

In a recent study of four million infants in 86 U.S. metropolitan areas, Woodruff et al. (1997) linked PM_{10} exposure in the first two months of an infant's life with the probability of dying between the ages of 28 days and 364 days. In addition to the work by Woodruff et al., recent work in Mexico City (Loomis et al., 1999), the Czech Republic (Bobak and Leon, 1992), Sao Paulo (Pereira et al., 1998; Saldiva et al., 1994), and Beijing (Wang et al., 1997) provides additional evidence that particulate levels are significantly related to infant or child mortality, low birth weight or intrauterine mortality (Table D-3).

Conceptually, neonatal or child mortality could be added to the premature mortality predicted by Pope et al. (1995), because the Pope function covers only the population over 30 years old. Predicted neonatal mortality could not be added to the premature mortality predicted by the daily (short-term exposure) mortality studies, however, because these studies cover all ages. The EPA Clean Air Council recently advised the Agency not to include post-neonatal mortality in this analysis because the study is of a new endpoint and the results have not been replicated in other studies (U.S. EPA, 1999, p. 12). The estimated avoided incidences of neonatal mortality are estimated and presented as a sensitivity analysis, but are not included in the aggregate benefits analysis results.

Table D-3
Studies and Results Selected for Adverse Effects in Fetuses, Infants, and Young Children

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings
Bobak and Leon (1992)	45 of 86 administrative districts in the Czech Republic 1986-1988	neonates (0-1 month); post-neonates (1-12 months)	all-cause mortality; respiratory mortality	TSP, SO_2, NO_x	Controlling for SO_2 and NO_x, TSP linked to all-cause and respiratory post-neonatal mortality; weaker, insignificant effect found for neonatal. Controlling for TSP and SO_2, NO_x marginally significant for all-cause and respiratory post-neonatal mortality; no effect for neonatal mortality. No effect found for SO_2.
Loomis et al. (1999)	southwestern Mexico City 1/93-7/95	infants <1 year old	all cause mortality	$PM_{2.5}$, O_3, NO_2, SO_2	$PM_{2.5}$ and NO_2 significant in single pollutant models. $PM_{2.5}$ and NO_2 both not significant in two pollutant model; $PM_{2.5}$ coefficient changed little from single pollutant; NO_2 coefficient dropped substantially. O_3 not significant. SO_2 not analyzed since ambient levels were negligible.
Pereira et al. (1998)	Sao Paulo, Brazil 1/91-12/92	fetuses over 28 weeks of pregnancy age	intrauterine mortality	PM_{10}, O_3, NO_2, SO_2, CO	In single pollutant models, NO_2, SO_2, and CO significantly related to intrauterine mortality. PM_{10} and O_3 not significant. Considering all pollutants simultaneously, NO_2 is the only significant pollutant.
Ritz and Yu (1999)	Los Angeles, CA 1989-1993	gestational age 37-44 weeks	low birth weight	CO	Average CO exposure in the last trimester associated with low birth weight.
Saldiva et al. (1994)	Sao Paulo, Brazil 5/90-4/91	children <5	respiratory mortality	PM_{10}, O_3, NO_x, SO_2, CO	NO_x significantly related to respiratory mortality. No effect found for the other pollutants.
Wang et al. (1997)	Beijing, China 1988-1991	gestational age 37-44 weeks	low birth weight	TSP, SO_2	TSP and SO_2 exposure in the final trimester significantly related to low birth weight. Both pollutants highly correlated (r=0.92).
Woodruff et al. (1997)	86 metropolitan areas in the U.S. 1989-1991	post-neonates (1-12 months)	all-cause mortality; respiratory mortality	PM_{10}	PM_{10} exposure in the first two months of life significant for all-cause mortality. PM_{10} significant for respiratory mortality in average birth-weight infants, but not low birth-weight infants.
Xu et al. (1995a)	Beijing, China 1988	25,370 pregnant women	pre-term delivery	TSP, SO_2	TSP and SO_2 exposure significant for pre-term delivery.

Chronic Illness

There are a limited number of studies that have estimated the impact of air pollution on chronic bronchitis (Table D-4). An important hindrance is the lack of health data and the associated air pollution levels over a number of years. Schwartz (1993) and Abbey et al. (1995; 1993) provide evidence that PM exposure over a number of years gives rise to the development of chronic bronchitis in the U.S., and a recent study by McDonnell et al. (1999) provides evidence that ozone exposure is linked to the development of asthma in adults. These results are consistent with research that has found chronic exposure to pollutants leads to declining pulmonary functioning (Abbey et al., 1998; Ackermann-Liebrich et al., 1997; Detels et al., 1991).

Schwartz (1993) examined survey data collected from 3,874 adults ranging in age from 30 to 74, and living in 53 urban areas in the U.S. The survey was conducted between 1974 and 1975, as part of the National Health and Nutrition Examination Survey, and is representative of the non-institutionalized U.S. population. Schwartz (1993, Table 3) reported chronic bronchitis prevalence rates in the study population by age, race, and gender. Non-white males under 52 years old had the lowest rate (1.7%) and white males 52 years and older had the highest rate (9.3%). The study examined the relationship between the prevalence of reported chronic bronchitis and annual levels of TSP, collected in the year prior to the survey.

Abbey et al. (1995; 1993) are part of a series of studies of an ongoing prospective cohort tracking research project that began in 1977. These two studies on the development of chronic respiratory illness are based on a ten year follow-up examination of adult Seventh-Day Adventists living in California. Abbey et al. (1993) examined 3,914 adults, and estimated the relationship between annual mean ambient TSP, ozone and SO_2 and the presence of certain chronic respiratory symptoms (including airway obstructive disease (AOD), chronic bronchitis, and asthma) that were not present at the beginning of the study. TSP was significantly linked to new cases of AOD and chronic bronchitis, but not to asthma or the severity of asthma. Ozone was not linked to the incidence of new cases of any endpoint, but ozone was linked to the severity of asthma. No effect was found for SO_2. Abbey et al. (1995) examined the relationship between estimated $PM_{2.5}$ (annual mean from 1966 to 1977), PM_{10} (annual mean from 1973 to 1977) and TSP (annual mean from 1973 to 1977) and the same chronic respiratory symptoms in a sample population of 1,868 Californian Seventh-Day Adventists. In this single-pollutant study, there was a statistically significant $PM_{2.5}$ relationship with development of chronic bronchitis, but not for AOD or asthma; PM_{10} was significantly associated with chronic bronchitis and AOD; and TSP was significantly associated with all cases of all three chronic symptoms.

The McDonnell et al. (1999) study used the same cohort of Seventh-Day Adventists, and examined the association between air pollution and the onset of asthma in adults between 1977 and 1992. Males who did not report doctor-diagnosed asthma in 1977, but reported it in 1987 or 1992, had significantly higher ozone exposures, controlling for other covariates; no significant effect was found between ozone exposure and asthma in females. No significant effect was reported for females or males due to exposure to PM, NO_2, SO_2, or SO_4.

We estimate the changes in the new cases of chronic bronchitis using the studies by Schwartz (1993), Abbey et al. (1993), and Abbey et al. (1995); also, we estimate the onset of asthma in adult males using the work by McDonnell et al. (1999). The Schwartz study is somewhat older and uses a cross-sectional design; however, it is based on a national sample, unlike the Abbey et al. studies which are based on a sample of California residents who were non-smokers. We first pool the estimates from the two studies by Abbey et al. – since they are based on the same sample population and simply use different measures of PM – and then pool this estimate with that from Schwartz.

The Abbey et al. (1995; 1993) studies are based on the incidence of new cases of chronic bronchitis,

however, Schwartz (1993) is based on the *prevalence* of chronic bronchitis, not its *incidence*. To use Schwartz's study and still estimate the change in incidence, there are at least two possible approaches. The first is to simply assume that it is appropriate to use the baseline *incidence* of chronic bronchitis in a C-R function with the estimated coefficient from Schwartz's study, to directly estimate the change in incidence. The second is to estimate the percentage change in the prevalence rate for chronic bronchitis using the estimated coefficient from Schwartz's study in a C-R function, and then to assume that this percentage change applies to a baseline incidence rate obtained from another source. (That is, if the prevalence declines by 25 percent with a given decrease in PM, then baseline incidence drops by 25 percent with the same drop in PM). This analysis uses the latter approach, and estimates the change in incidence by first estimating the percentage change in prevalence.

Table D-4
Summary of Selected Studies for Chronic Illness

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Abbey et al. (1993)	California initial survey: 1977 final survey: 1987	3,914 Seventh Day Adventists	AOD; chronic bronchitis; asthma	TSP, O_3, SO_2	TSP linked to new cases of AOD and chronic bronchitis, but not to asthma or the severity of asthma. O_3 not linked to the incidence of new cases of any endpoint, but O_3 was linked only to the severity of asthma. No effect found for SO_2.	Emphysema, chronic bronchitis, and asthma comprise AOD.
Abbey et al. (1995)	California initial survey: 1977 final survey: 1987	1,868 Seventh Day Adventists	AOD; chronic bronchitis; asthma	$PM_{2.5}$	$PM_{2.5}$ related to new cases of chronic bronchitis, but not to new cases of AOD or asthma.	$PM_{2.5}$ estimated from visibility data.
Chapman et al. (1985)	4 Utah communities 1976	5,623 young adults	persistent cough and phlegm	SO_2, SO_4, NO_3, TSP	Persistent cough and phlegm is higher in the community with higher SO_2, SO_4, and TSP concentrations.	
McDonnell et al. (1999)	California initial survey: 1977 final survey: 1992	3,091 Seventh Day Adventists	asthma	O_3, PM_{10},, SO_4, SO_2, NO_2	Single pollutant models: O_3 significantly linked to new asthma cases in males, but not in females; other pollutants not significantly linked to new asthma cases in males or females. Two pollutant models estimated for ozone with another pollutant; little impact found on size of ozone coefficient.	Average pollution level from 1973-1992 used. Prior to 1987, PM_{10} estimated from TSP.
Portney and Mullahy (1990)	Nationwide sample from the 1979 U.S. National Health Interview Survey	1,318 persons age 17-93	sinusitis, hay fever, AOD	O_3, TSP	Controlling for TSP, O_3 significantly related to the initiation (or exacerbation) of sinusitis and hay fever; no effect on AOD. TSP not significantly related to any endpoint, although it is marginally significant for AOD.	

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Schwartz (1993)	Nationwide sample from the National Health and Nutrition Examination Survey 1974-1975	6,138 individuals ages 30-74	chronic bronchitis; asthma; shortness of breath (dyspnea); respiratory illness	TSP	TSP significantly related to the prevalence of chronic bronchitis, and marginally significant for respiratory illness. No effect on asthma or dyspnea.	Respiratory illness defined as a significant condition, coded by an examining physician as ICD8 code (460-519)
Xu et al. (1993)	Beijing, China Survey conducted August-September 1986	1,576 never smokers	chronic bronchitis; asthma	TSP; SO_2	Chronic bronchitis significantly higher in the community with the highest TSP level. TSP not linked to the prevalence of asthma.	
Zemp et al. (1999)	Eight sites in Switzerland 1991	9,651 individuals ages 18-60	chronic phlegm, chronic cough, breathlessness, asthma, dyspnea on exertion	TSP, PM_{10}, NO_2, O_3	Single pollutant models: PM_{10} and NO_2 significantly associated with chronic phlegm, chronic cough or phlegm, breathlessness and dyspnea. Similar though less significant associations found for TSP. No significant effect found for O_3.	

Hospital Admissions

There is a wealth of epidemiological information on the relationship between air pollution and hospital admissions for various respiratory and cardiovascular diseases; in addition, some studies have examined the relationship between air pollution and emergency room (ER) visits. Because most emergency room visits do not result in an admission to the hospital -- the majority of people going to the ER are treated and return home -- we treat hospital admissions and ER visits separately, taking account of the fraction of ER visits that do get admitted to the hospital, as discussed below.

Hospital admissions require the patient to be examined by a physician, and on average may represent more serious incidents than ER visits (Lipfert, 1993, p. 230). The two main groups of hospital admissions estimated in this analysis are respiratory admissions and cardiovascular admissions. There is not much evidence linking air pollution with other types of hospital admissions. The only types of ER visits that have been linked to air pollution in the U.S. or Canada are asthma-related visits.

To estimate the number of hospital admissions for respiratory illness, we pool the incidence estimates from a variety of U.S. and Canadian studies, using a random effects weighting procedure. These studies differ from each other in two important ways: (1) Some studies considered people of all ages while others considered only people ages 65 and older; and (2) The International Classification of Diseases - 9th revision (ICD-9) codes included in studies of respiratory hospital admissions and air pollution vary substantially.

The broadest classification used (for example, in Schwartz, 1996) includes ICD-9 codes 460-519. Other studies, however, considered only subsets of the broader classification. For example, Burnett et al. (1997b) consider ICD-9 codes 466, 480-486, 490-494, and 496. The correct set of ICD codes for this study is difficult to determine. If the broadest category (460-519) is too broad, including respiratory illnesses that are not linked to air pollution, we would expect the estimated pollutant coefficients to be biased downward; however, they would be used in combination with a larger baseline incidence in estimating changes in respiratory hospital admissions associated with changes in pollutant concentrations. If the broadest category is correct (i.e., if all the respiratory illnesses included are actually associated with air pollution), then studies using only subsets of ICD codes within that category would presumably understate the change in respiratory hospital admissions. It is likely, however, that all the studies have included the most important respiratory illnesses, and that the impact of differences in the definition of "all respiratory illnesses" may be less than that of other study design characteristics. We therefore treat each study equally, at least initially, in the pooling process, assuming that each study gives a reasonable estimate of the impact of air pollution on respiratory hospital admissions.

There are several steps in our estimation process:

- Develop study-specific estimates of respiratory admissions incidence change;
- Develop C-R functions for each pollutant in a model from a given study: e.g., Burnett et al. (1997b) included $PM_{2.5-10}$, O_3, NO_2, and SO_2 in their final model for respiratory admissions (ICD-9 codes 464-466, 480-486, 490-494, 496);
- Estimate the change in incidence associated with the change in each air pollutant considered in the model, and aggregate these incidence changes across the pollutants in the model: e.g., for Burnett et al. (1997b) we sum the incidence changes associated with $PM_{2.5-10}$, O_3, NO_2, and SO_2;
- If a study estimated separate models for non-overlapping respiratory illness categories, sum the estimated incidence changes across these non-overlapping categories: e.g., Delfino et al. (1994) estimated two separate models: one for asthma (ICD code 493) and one for all respiratory non-asthma (ICD codes 462-466,

480-487, 490-492, 494, and 496); we estimated and summed incidences for these two categories.

Aggregate estimates across non-overlapping age categories:

- Seven studies estimated C-R functions for respiratory admissions for people ages 65 and older. One study, Sheppard et al. (1999), estimated a C-R function for asthma only for people under 65. Using a Monte Carlo procedure, we aggregate the results from the Sheppard study with those from each of the over-65 respiratory admissions studies.

Pool estimates of respiratory hospital admissions changes:

- Four studies estimated C-R functions for respiratory admissions for people of all ages. With the seven "all ages" estimates developed in step 2, there are eleven separate estimates of the change in respiratory hospital admissions associated with a change in air pollutant concentrations. Using Monte Carlo procedures, the results of these eleven studies are pooled.

Table D-5 summarizes the studies used in estimating respiratory admissions; Table D-6 provides more detailed information on these studies, and other studies that were not chosen for this analysis.

Similar issues of definition arise for cardiovascular hospital admissions. The broadest classification we have seen in the epidemiological literature includes ICD codes 390-429 (see, for example, Schwartz, 1999). Some studies, however, use a much more narrow definition, including only subsets of the larger group of ICD codes. We use a similar procedure for cardiovascular admissions as we used for respiratory hospital admissions. Table D-7 summarizes the studies used in estimating cardiovascular admissions; Table D-8 provides more detailed information on these studies, and other studies that were not chosen this analysis.

Because we are estimating ER visits as well as hospital admissions for asthma, we must avoid counting twice the ER visits for asthma that are subsequently admitted to the hospital. To avoid double-counting, the baseline incidence rate for emergency room visits is adjusted by subtracting the percentage of patients that are admitted into the hospital. Three studies provide some information to do this: Richards et al. (1981, p. 350) reported that 13% of children's ER visits ended up as hospital admissions; Lipfert (1993, p. 230) reported that ER visits (for all causes) are two to five times more frequent than hospital admissions; Smith et al. (1997, p. 789) reported 445,000 asthma-related hospital admissions in 1987 and 1.2 million asthma ER visits. The study by Smith et al. seems the most relevant since it is a national study and looks at all age groups. Assuming that air-pollution related hospital admissions first pass through the ER, the reported incidence rates suggest that 37% (=445,000/1,200,000) of ER visits are subsequently admitted to the hospital, or that ER visits for asthma occur 2.7 times as frequently as hospital admissions for asthma. The baseline incidence of asthma ER visits is therefore taken to be 2.7 times the baseline incidence of hospital admissions for asthma. To avoid double-counting, however, only 63% of the resulting change in asthma ER visits associated with a given change in pollutant concentrations is counted in the ER visit incidence change.

Table D-9 summarizes the studies used in estimating ER visits for asthma; Tables D-10 and D-11 provide more detailed information on these studies and other ER studies that were not used in the analysis.

Table D-5
Studies Used to Develop Respiratory Admissions Estimates

Location	Study	Endpoints Estimated [a] (ICD code)	Pollutants Used in Final Model	Study Population
Toronto, Canada	Burnett et al. (1997b)	all respiratory (464-466, 480-486, 490-494, 496)	$PM_{2.5-10}$, O_3, NO_2, SO_2	all ages
Toronto, Canada	Burnett et al. (1999)	asthma (493); respiratory infection (464, 466, 480-487, 494); non-asthma COPD (490-492, 496)	O_3, CO, $PM_{2.5-10}$ (asthma); O_3, NO_2, $PM_{2.5}$ (respiratory infection); O_3, CO, $PM_{2.5-10}$ (COPD).	all ages
Toronto, Canada	Thurston et al. (1994)	all respiratory (466, 480-482, 485, 490-493)	O_3, $PM_{2.5}$	all ages
Minneapolis-St. Paul, MN	Moolgavkar et al. (1997)	pneumonia (480-487); COPD (490-496)	O_3, SO_2, NO_2, PM_{10} (pneumonia); O_3, CO, PM_{10} (COPD)	>64
Minneapolis-St. Paul, MN	Schwartz (1994c)	pneumonia (480-486); COPD (490-496)	O_3, PM_{10} (pneumonia); PM_{10} (COPD)	>64
Birmingham, AL	Schwartz (1994a)	pneumonia (480-487); COPD (490-496)	PM_{10}	>64
Detroit, MI	Schwartz (1994b)	pneumonia (480-486); non-asthma COPD (491-492, 494-496)	O_3, PM_{10}	>64
Spokane, WA	Schwartz (1996)	all respiratory (460-519)	PM_{10}	>64
New Haven, CT	Schwartz (1995)	all respiratory (460-519)	O_3, PM_{10}	>64
Tacoma, WA	Schwartz (1995)	all respiratory (460-519)	O_3, PM_{10}	>64
Seattle, WA	Sheppard et al. (1999)	asthma (493)	CO, $PM_{2.5}$	<65

[a] Monetized benefits of non-overlapping endpoints within each study are aggregated. Monetized benefits for asthma among people age <65 (Sheppard et al., 1999) are aggregated with the benefits in studies of people age >64.

Table D-6
Summary of Hospital Admissions Studies – Respiratory Illnesses

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Anderson et al. (1997)	Barcelona, Paris Amsterdam, Rotterdam, Milano Period varies by city from 5-13 years	all ages; >64	COPD (490-492, 496)	NO_2, BS (black smoke), TSP, SO_2, O_3	COPD: Single pollutant models: meta-analysis of city specific results found significant effect for BS, NO_2, O_3, and SO_2 in the all age group; similar results reported for ages >64. Strongest effect found for O_3. TSP not significant in meta-analysis. For a given pollutant, results varied considerably by city.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Burnett et al. (1995)	southern Ontario, Canada 1/83-12/88	<65; >64	all respiratory (466, 480-486, 490-494, 496)	SO_4, O_3	All respiratory: SO_4 significantly related to respiratory admissions in ages <65 and >64. O_3 significant impact from May-September; no effect the rest of the year.	May-September results also discussed in Burnett et al. (1994). *Study not used to estimate incidence: no study specific conversion available between* SO_4 *and* $PM_{2.5}$ *or* PM_{10}.
Burnett et al. (1997b)	Toronto, Canada summers in 1992-1994	all ages	all respiratory (464-466, 480-486, 490-494, 496)	O_3, CO, NO_2, SO_2, COH (coefficient of haze), H^+, SO_4, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10},	All respiratory: COH and O_3 linked to respiratory admissions; other PM measures less strongly linked. Two pollutant models: CO, NO_2, and SO_2 not significant, controlling for COH; O_3 significant, controlling for COH. Four pollutant models: COH and O_3 significant; no effect for NO_2 and SO_2; other PM measures not significant, controlling for O_3, NO_2, and SO_2.	*Four pollutant model ($PM_{2.5-10}$, O_3, NO_2, and SO_2) used to estimate all respiratory incidence.*
Burnett et al. (1997a)	16 Canadian cities 3/81-12/91	<65; >64	all respiratory (466, 480-486, 490-494, 496)	O_3, CO, SO_2, NO_2, COH	All respiratory: Multiple pollutant models: O_3 significantly related to admissions, controlling for CO and COH; significant effect also reported for CO and COH; no significant effect found for NO_2 and SO_2 after controlling for O_3 and CO. Montreal and Vancouver decreased the size of the effect of O_3 substantially. O_3 significant with and without these cites in the model.	*Study not used to estimate incidence: no study specific conversion available between COH and* $PM_{2.5}$ *or* PM_{10}.

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Burnett et al. (1999)	Toronto, Canada 1980-1994	all ages	asthma (493); respiratory infection (464, 466, 480-487, 494); COPD (490-492, 496)	O_3, CO, NO_2, SO_2, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10},	Multiple pollutant models estimated, where pollutants for best fitting model chosen using stepwise regression based on AIC criterion. Asthma: O_3, CO, $PM_{2.5-10}$ significantly related to asthma admissions; other pollutants not chosen in stepwise regression. Respiratory infection: O_3, NO_2, and $PM_{2.5}$ chosen in stepwise regression COPD: O_3 and $PM_{2.5-10}$ chosen in stepwise regression.	$PM_{2.5}$, $PM_{2.5-10}$, and PM_{10} estimated from TSP, COH, and SO_4 data. *Multiple pollutant models used to estimate incidence of: asthma (O_3, CO, $PM_{2.5-10}$), respiratory infection (O_3, NO_2, $PM_{2.5}$), and COPD (O_3, CO, $PM_{2.5-10}$).*
Delfino et al. (1994)	Montreal, Canada May-October in 1984-1988. July-August subset used to examine all respiratory admissions.	all ages	asthma (493); all respiratory (462-466, 480-487, 490-494, 496); all respiratory non-asthma	O_3, SO_4, PM_{10}	Asthma: Two pollutant model: marginally significant effect for PM_{10}, controlling for O_3. No effect for O_3 and SO_4. All respiratory and all respiratory non-asthma: PM_{10} suggestive but not significant, after controlling for temperature. Significant link between all respiratory non-asthma and SO_4. No effect for O_3.	SO_4 and PM_{10} were both estimated from COH and other variables. *Study not used to estimate incidence*
Lipfert and Hammerstrom (1992)	Southern Ontario, Canada January-February and July-August in 4/79-3/85	all ages	all respiratory (466, 480-482, 485, 490-493)	O_3, SO_4, NO_4, SO_4, COH, TSP	All respiratory: SO_2, SO_4, and O_3 found to be significant predictors of respiratory admissions in July-August.	*Study not used to estimate incidence: estimated coefficients not reported.*

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Moolgavkar et al. (1997)	Minneapolis-St. Paul, MN; Birmingham, AL 1/86-12/91	>64	pneumonia (480-487); COPD (490-496); all respiratory (480-487, 490-496)	O_3, CO, SO_2, NO_2, PM_{10}	Pneumonia: Four pollutant model: O_3 significant (NO_2, SO_2, and PM_{10} not significant) in Minneapolis-St. Paul; no significant effect found for any pollutant in Birmingham. COPD: No significant effect found in Birmingham or Minneapolis-St. Paul for any pollutant. All respiratory: Single pollutant models: O_3, NO_2, and PM_{10} significant in Minneapolis-St.Paul. Multiple pollutant models (results presented in graph): O_3 significant, controlling for other pollutants; PM_{10} significant controlling for O_3, but not significant controlling for O_3, SO_2, and NO_2 together. No significant effect found in Birmingham for admissions with O_3, CO, or PM_{10}; NO_2 and SO_2 data not available for Birmingham.	*Multiple pollutant models used to estimate pneumonia incidence (O_3, SO_2, NO_2, PM_{10}) and COPD incidence (O_3, CO, PM_{10}) in Minneapolis-St. Paul. No model estimated for Birmingham: coefficients and standard errors not reported.*
Morgan et al. (1998)	Sydney, Australia 1/90-12/94	1-14; 15-64; >64	asthma; COPD (490-492,494 496)	O_3, NO_2, bscat (measure of light scattering)	Asthma: Single pollutant models: NO_2 significant for ages 1-14 but not other age groups. O_3 and bscat not significant for any age group. Three pollutant model: NO_2 remains significantly related to asthma admission in ages 1-14. COPD: No pollutant significantly related to COPD admissions.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Pantazopoulou et al. (1995)	Athens, Greece 1988	all ages	all respiratory (not defined by ICD code)	BS, CO, NO_2	All respiratory: Single-pollutant models: BS, CO, NO_2 significantly related to respiratory admissions in the winter time. No significant effect found any pollutant in the summer.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Ponce de Leon et al. (1996)	London, England 4/87-2/92	0-14; 15-64; >64	all respiratory (460-519)	BS, SO_2, O_3, NO_2	All respiratory: O_3 significantly related to admissions in ages >14. No significant effect found for SO_2, O_3, and NO_2.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Ponka and Virtanen (1994)	Helsinki, Finland 1/87-12/89	<65; >64	COPD (491-492)	NO_2, SO_2, O_3, TSP	COPD: Single pollutant models: SO_2 linked to (491-492) admissions in ages <65; NO_2 linked to admissions in ages >64; no significant effect seen for O_3 and TSP.	*Study not used to estimate incidence: study outside U.S. and Canada.*

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Schwartz (1994a)	Birmingham, AL 1/86-12/89	>64	pneumonia (480-487); COPD (490-496)	PM_{10}, O_3	Pneumonia: PM_{10} significant and O_3 not significant in single pollutant models. COPD: PM_{10} significant and O_3 not significant in single pollutant models.	*Single pollutant models (PM_{10}) used to estimate pneumonia incidence and COPD incidence.*
Schwartz (1994b)	Detroit, MI 1/86-12/89	>64	asthma (493); pneumonia (480-486); non-asthma COPD (491-492, 494-496)	PM_{10}, O_3	Asthma: admissions not associated with either pollutant; coefficients and standard errors not reported. Pneumonia: Two pollutant model: PM_{10} and O_3 both significant for pneumonia. Non-asthma COPD: Two pollutant model: PM_{10} and O_3 both significant.	*Two pollutant models (PM_{10} and O_3) used to estimate pneumonia incidence and non-asthma COPD incidence.*
Schwartz (1996)	Spokane, WA 1/88-12/90	>64	pneumonia (480-487); COPD (490-496); all respiratory (460-519)	PM_{10}, O_3	Pneumonia: PM_{10} marginally significant and O_3 not significant for pneumonia in single pollutant models. COPD: PM_{10} significant and O_3 not significant in single pollutant models. All respiratory: Single pollutant models: PM_{10} and O_3 both significant. Two pollutant model not estimated because of limited overlap between PM_{10} and O_3 data.	*Single pollutant model (PM_{10}) used to estimate all-respiratory incidence.*
Schwartz (1994c)	Minneapolis-St. Paul, MN 1/86-12/89	>64	pneumonia (480-486); COPD (490-496)	PM_{10}, O_3	Pneumonia: Two pollutant model: PM_{10} significantly related to pneumonia; O_3 weakly linked to pneumonia. COPD: Single pollutant models: PM_{10} significant and O_3 not significant.	*Two pollutant model (PM_{10}, O_3) used to estimate pneumonia incidence; single pollutant model (PM_{10}) used to estimate COPD incidence.*
Schwartz (1995)	New Haven, CT; Tacoma, WA 1/88-12/90	>64	all respiratory (460-519)	PM_{10}, O_3, SO_2	All respiratory: Single pollutant models: PM_{10}, O_3, SO_2 significant, except O_3 in New Haven. Two pollutant model results varied by city: O_3 significant (3 of 4 models) and stable coefficient estimates PM_{10} significant (3 of 4 models), but less stable estimates. SO_2 significant (1of 4 models).	*Two pollutant model (PM_{10}, O_3) used to estimate all respiratory incidence.*

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Sheppard et al. (1999)	Seattle, WA 1/87-12/94	<65	asthma (493)	CO, SO_2, O_3, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10}	Asthma: Single pollutant models: each pollutant significantly related to asthma, except SO_2. Multiple pollutant models: $PM_{2.5}$ and CO reported to have best fit in models without O_3. Both $PM_{2.5}$ and CO are significant when included together in a model.	In most years, O_3 data was available only from April through October. O_3 reported to have the best fit, but authors did not consider O_3 further because of limited data. *Two pollutant model (CO, $PM_{2.5}$) used to estimate asthma incidence.*
Spix et al. (1998)	London, Amsterdam, Rotterdam, Paris, Milano Period varies by city from 5-13 years	15-64; >64	all respiratory (460-519)	NO_2, SO_2, O_3, TSP, BS	All respiratory: Single pollutant models: O_3 significantly related to admissions in ages 15-64 and >64. BS significantly related to admissions in ages 15-64. SO_2 significantly related to admissions in ages >64.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Sunyer et al. (1997)	Barcelona, Helsinki, London, Paris Period varies by city from 3-6 years	0-14; 15-64	asthma	NO_2, SO_2, O_3, BS	Asthma: Two pollutant models: NO_2 significant in ages 15-64, controlling for BS; NO_2 had no effect on ages 0-14. SO_2 significant in ages 0-14, controlling for either BS or NO_2; SO_2 had no effect on ages 15-64.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Tenias et al. (1998)	Valencia, Spain 1/93-12/95	>14	asthma	NO_2, SO_2, O_3, BS	Asthma: Two pollutant models: O_3 and NO_2 both significant. No significant effect found for SO_2 and BS.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Thurston et al. (1994)	Toronto, Canada six weeks in July and August 1986-1988	all ages	asthma (493); all respiratory (466, 480-482, 485, 490-493)	H^+, SO_4, O_3, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10}, TSP	Asthma: Single pollutant models: O_3, H^+, SO_4, O_3, and TSP linked to all respiratory admissions; $PM_{2.5}$, $PM_{2.5-10}$, PM_{10} not significant. Two pollutant models: O_3 significant, but PM measures no longer significant. Best fitting PM measure is H^+. All respiratory: Single pollutant models: O_3 and various measures of PM linked to all respiratory admissions. Two pollutant models: with O_3 and PM together, O_3 still significant, but PM often not significant (only H^+ significant).	*Two pollutant model (O_3, $PM_{2.5}$) used to estimate all respiratory incidence.*

Study	Location and Period	Population	Endpoint	Pollutants [a]	Main Findings	Comment
Thurston et al. (1992)	Buffalo, NY; New York City June-August in 1988-1989	all ages	all respiratory (466, 480-486, 490-493)	H^+, SO_4, O_3	All respiratory: Three pollutant model: H^+, SO_4, and O_3 are all significant. This result is found in both Buffalo and New York City.	*Study not used to estimate incidence: no study specific conversion available between study pollutants (H^+ and SO_4) and $PM_{2.5}$ or PM_{10}.*
Vigotti et al. (1996)	Milan, Italy 1/89-12/89	15-64; >64	all respiratory (460-519)	TSP, SO_2	All respiratory: Single pollutant models: TSP and SO_2 linked to admissions.	*Study not used to estimate incidence: study outside U.S. and Canada.*

[a] Not all pollutants considered in a study are necessarily included in the model used to develop C-R functions.

Table D-7
Studies Used to Develop Cardiovascular Admissions Estimates

Location	Study	Endpoints Estimated (ICD code)	Pollutants Used in Final Model	Study Population
Toronto, Canada	Burnett et al. (1997b)	cardiac (410-414, 427-428)	O_3, $PM_{2.5-10}$	all ages
Toronto, Canada	Burnett et al. (1999)	ischemic heart disease (410-414); dysrhythmias (427); congestive heart failure (428)	NO_2, SO_2 (ischemic heart disease); $PM_{2.5}$, CO, O_3 (dysrhythmias); CO, NO_2 (heart failure incidence)	all ages
Detroit, MI	Schwartz and Morris (1995)	ischemic heart disease (410-414); congestive heart failure (428)	CO, PM_{10}	>64
Eight U.S. counties 1/88-12/90	Schwartz (1999)	cardiovascular disease (390-429)	CO, PM_{10}	>64
Tucson, AZ 1/88-12/90	Schwartz (1999)	cardiovascular disease (390-429)	CO, PM_{10}	>64

Table D-8
Summary of Hospital Admissions Studies – Cardiovascular Illnesses

Study	Location and Period	Population	Endpoint (ICD code)	Pollutants	Main Findings	Comment
Burnett et al. (1995)	southern and central Ontario, Canada 1/83--12/88	all ages	cardiac (410, 413, 427-428)	SO_4, O_3	Cardiac: Two pollutant model: SO_4 significantly related to cardiac admissions; O_3 not significant, in any season or over the whole year.	*Study not used to estimate incidence: no study specific conversion available between* SO_4 *and* $PM_{2.5}$ *or* PM_{10}*.*
Burnett et al. (1997b)	Toronto, Canada summers 1992-1994	all ages	cardiac (410-414, 427-428)	O_3, CO, NO_2, SO_2, COH (coefficient of haze), H^+, SO_4, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10},	Cardiac: COH and O_3 linked to cardiac admissions; other PM measures less strongly linked. Two pollutant models: CO, NO_2, and SO_2 not significant, controlling for COH. O_3 significant, controlling for COH. Four pollutant models: COH and O_3 significant; no effect for NO_2 and SO_2. Other PM measures not significant, controlling for O_3, NO_2, and SO_2.	*Two pollutant model (*O_3*,* $PM_{2.5-10}$*) used to estimate cardiac incidence.*
Burnett et al. (1997c)	10 Canadian cities 1/81-12/91	>64	congestive heart failure (428)	O_3, CO, NO_2, SO_2, COH	Congestive heart failure: Single pollutant models: CO, NO_2, SO_2, COH are significant; no effect for O_3. CO and NO_2 have the best fit. Two pollutant models: Controlling for NO_2, CO significant, with only small reduction in coefficient size; NO_2 insignificant in this model.	*Study not used to estimate incidence: limited endpoint.*
Burnett et al. (1999)	Toronto, Canada 1980-1994	all ages	ischemic heart disease (410-414); dysrhythmias (427); congestive heart failure (428)	O_3, CO, NO_2, SO_2, $PM_{2.5}$, $PM_{2.5-10}$, PM_{10},	Multiple pollutant model, where pollutants for best fitting model chosen using stepwise regression based on AIC criterion. Ischemic heart disease: NO_2 and SO_2, chosen by stepwise regression. Other pollutants not chosen. Dysrhythmias: polluO_3, CO, and $PM_{2.5}$ chosen by stepwise regression. Other pollutants not chosen. Congestive heart failure: NO_2 and CO chosen by stepwise regression procedure. other pollutants not chosen in stepwise regression.	$PM_{2.5}$, $PM_{2.5-10}$, and PM_{10} estimated from TSP, COH, and sulfate (SO_4) data. *Multiple pollutant models used to estimate ischemic heart disease (*NO_2*,* SO_2*), dysrhythmias (*$PM_{2.5}$*, CO,* O_3*), and congestive heart failure incidence (CO,* NO_2*).*

Study	Location and Period	Population	Endpoint (ICD code)	Pollutants	Main Findings	Comment
Morgan et al. (1998)	Sydney, Australia 1/90-12/94	0-64; >64	heart disease (410,413, 427-428)	O_3, NO_2, bscat (measure of light scattering)	Single pollutant models: bscat significant for ages >64; NO_2 significant in ages 0-64 and >64. Three pollutant model: NO_2 significant in ages >64; O_3 and bscat not significant.	Results from three pollutant model for ages 0-64 not presented. *Study not used to estimate incidence: study outside U.S. and Canada.*
Morris et al. (1995)	seven U.S. cities 1/86-12/89	>64	congestive heart failure (428)	O_3, CO, NO_2, SO_2	Single pollutant models: CO, NO_2, and SO_2 significant in single pollutant models. Four pollutant model: CO is significant in five of the seven cities; NO_2 is significant in one city; SO_2 and O_3 are not significant in any cities.	*Study not used to estimate incidence: no PM measure used in the study, plus limited endpoint.*
Morris and Naumova (1998)	Chicago, IL 1/86-12/89	>64	congestive heart failure (428)	O_3, CO, NO_2, SO_2, PM_{10}	Single pollutant models: CO, NO_2, SO_2, and PM_{10} significant. Five pollutant model: CO significant (CI for RR=1.03-1.12); PM_{10} borderline significant (CI for RR=0.99-1.06); other pollutants not significant.	*Study not used to estimate incidence: limited endpoint.*
Pantazopolou et al. (1995)	Athens, Greece 1988	all ages	cardiac (not defined by ICD code)	BS (black smoke), CO, NO_2	Single pollutant models: BS, CO, NO_2 significantly related to cardiac admissions in the winter. No significant effect found for any pollutant in the summer.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Schwartz and Morris (1995)	Detroit, MI 1/86-12/89	>64	ischemic heart disease (410-414); dysrhythmias (427); congestive heart failure (428)	O_3, CO, SO_2, PM_{10}	Ischemic heart disease: Two pollutant models: PM_{10} and CO both significant; no effect seen for SO_2 and O_3. Dysrhythmias: Air pollutants did not have a significant effect. Congestive heart failure: Single pollutant models: PM_{10} and CO significant; SO_2 and O_3 not significant. Two pollutant models: PM_{10} significant, controlling for CO and SO_2. Controlling for PM_{10}, CO significant.	*Two pollutant models (PM_{10}, CO) used to estimate ischemic heart disease and congestive heart failure incidence.*

Study	Location and Period	Population	Endpoint (ICD code)	Pollutants	Main Findings	Comment
Schwartz (1999)	Eight U.S. counties 1/88-12/90	>64	cardiovascular disease (390-429)	CO, PM_{10}	Two pollutant model: CO and PM_{10} both significant.	*Two pollutant model (PM_{10}, CO) used to estimate incidence of cardiovascular admissions.*
Schwartz (1997)	Tucson, AZ 1/88-12/90	>64	cardiovascular disease (390-429)	O_3, CO, SO_2, NO_2, PM_{10}	In a model with the two pollutants, CO and PM_{10} were both significant. No effect seen for O_3, SO_2, and NO_2.	*Two pollutant model (PM_{10}, CO) used to estimate incidence of cardiovascular admissions.*
Yang et al. (1998)	Reno/Sparks, NV 1/89-12/94	all ages	cardiovascular illness (390-459)	CO	Reported significant relationship between CO and admissions.	*Study not used to estimate incidence: no PM measure used in the study.*

Table D-9
Studies Used to Develop Asthma Emergency Room Visits

Location	Study	Endpoints Estimated	Pollutants Used in Final Model	Study Population
central and northern NJ	Cody et al. (1992)	asthma	O_3	all ages
central and northern NJ	Weisel et al. (1995)	asthma	O_3	all ages
Seattle, WA	Schwartz et al. (1993)	asthma	PM_{10}	<65
St. John, New Brunswick, Canada	Stieb et al. (1996)	asthma	O_3	all ages

Table D-10
Summary of Selected Studies for Emergency Room Visits -- Asthma and Acute Wheezing

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Atkinson et al. (1999)	London, England 1/92-12/94	0-14; 15-64; >64; all ages	asthma	NO_2, BS (black smoke), PM_{10}, SO_2, CO, O_3	Single pollutant models: PM_{10} and NO_2 significantly related to asthma visits in all age groups. SO_2 significant in ages 0-14. BS is significant for ages 15-64. No effect seen for O_3. Two pollutant results only for ages 0-14: NO_2 and SO_2 significant; other pollutants not significant.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Bates et al. (1990)	Vancouver, Canada 7/84-10/86	1-14; 15-60; >60	asthma	NO_2, SO_2, SO_4, O_3	SO_4 correlated with asthma in all age groups with some variation by season. SO_2 correlated with asthma visits in ages 15 and up. No effect found for NO_2 and O_3.	*Study not used to estimate incidence: correlations only presented.*
Buchdahl et al. (1996)	London, England 3/92-2/93	<17	acute wheezing	NO_2, SO_2, O_3	SO_2 significantly related to acute wheezing. O_3 has a significant, U-shaped result, suggesting that the optimal level of ozone is not zero. NO_2 not significant.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Castellsague et al. (1995)	Barcelona, Spain January-March and July-September in 1985-1989	>14	asthma	NO_2, BS, SO_2, O_3	Single pollutant models: NO_2 significant in both July-September and January-March. BS linked to asthma ER visits in July-September. No significant effect found for SO_2 and O_3.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Cody et al. (1992)	central and northern NJ May-August in 1988-1989	all ages	asthma	PM_{10}, SO_2, O_3	Two pollutant model: O_3 linked to asthma visits; SO_2 not significant. No significant effect seen for PM_{10}; PM_{10} considered in separate analysis, because of limited (every sixth day) sampling.	*Single pollutant model (O_3) used to estimate incidence of asthma visits.*
Goldstein and Weinstein (1986)	New York City 1/69-2/72	all ages	asthma	SO_2	No significant correlation found between SO_2 and asthma ER visits.	*Study not used to estimate incidence: only SO_2 in the analysis.*

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Lipsett et al. (1997)	Santa Clara County, CA November-January in 1988-1992	all ages	asthma	PM_{10}, COH (coefficient of haze), O_3, NO_2	Single pollutant models: NO_2, PM_{10}, and COH significant; O_3 not significant. Two pollutant models: PM_{10} and COH linked to ER visits controlling for NO_2; NO_2 not significant. PM_{10} reported to provide a slightly better fit than COH	PM_{10} estimated from COH observations. *Study not used to estimate incidence: results depend on temperature interaction that we cannot model.*
Richards et al. (1981)	Los Angeles, CA 8/79-1/80	children (median age =6)	asthma and bronchiolitis (92% asthma only)	COH, HC (hydrocar-bons), NO, NO_2, O_3, SO_2, SO_4, TSP	COH, HC, NO, and NO_2 have positive and significant correlation with ER visits; O_3 and SO_2 have negative significant correlation; SO_4 and TSP have insignificant correlation.	13% of reported visits subsequently admitted to the hospital. *Study not used to estimate incidence: correlations only presented.*
Romieu et al. (1995)	Mexico City, Mexico 1/90-6/90	<16	asthma	SO_2, O_3	Two pollutant model: O_3 significant and SO_2 marginally significant.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Rosas et al. (1998)	Mexico City, Mexico 1991	<15; 16-59; >59	asthma	O_3, SO_2, NO_2, PM_{10}, TSP	Little effect found for air pollutants. Strong effect found for aeroallergens, such as grass pollen.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Schwartz et al. (1993)	Seattle, WA 9/89-9/90	<65; >64	asthma	SO_2, PM_{10}, O_3	Single pollutant models: PM_{10} linked to ER visits in ages <65, with no effect in ages >64. No effect for SO_2 and O_3 on ER visits in either age group.	O_3 only available May-September. *Single pollutant model (PM_{10}) used to estimate incidence of asthma visits.*
Stieb et al. (1996)	St. John, New Brunswick, Canada May-September in 1984-1992	0-15; >15; all ages	asthma	NO_2, TSP, SO_2, SO_4, O_3	O_3 linked to ER visits in ages >15, especially when O_3 levels exceed 75 ppb; O_3 not significant in ages 0-15. No significant effect seen for the other pollutants.	TSP and SO_4 gathered every sixth day. *Single pollutant model (O_3) used to estimate incidence of asthma visits.*
Weisel et al. (1995)	central and northern NJ May-August in 1986-1990	all ages	asthma	O_3	O_3 linked to ER visits.	*Single pollutant model used.*

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
White et al. (1994)	Atlanta, GA 6/90-8/90	1-16	asthma and restrictive airway disease	O_3, SO_2, PM_{10}	O_3 linked to ER visits when O_3 levels exceeded 110 ppb. No significant effect reported for SO_2 or PM_{10}.	PM_{10} estimated from visibility levels. *Study not used to estimate incidence: limited study data.*

Table D-11
Summary of Selected Studies for Emergency Room Visits -- All-Cause, All-Respiratory, Chronic Obstructive Pulmonary Disease (COPD), and Bronchitis

Study	Location and Period	Population	Endpoint (ICD code)	Pollutants	Main Findings	Comment
Atkinson et al. (1999)	London, England 1/92-12/94	0-14; 15-64; >64; all ages	all respiratory (not defined by ICD code)	NO_2, BS (black smoke), PM_{10}, SO_2, CO, O_3	Single pollutant models: PM_{10} significant in ages 0-14 and 15-64. BS and SO_2 significant in ages 0-14. CO and NO_2 significant in ages >64. O_3 not significant.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Bates et al. (1990)	Vancouver, Canada 7/84-10/86	1-14; 15-60; >60	all respiratory (466, 480-486, 491-493, 496)	NO_2, SO_2, SO_4, O_3	SO_2 correlated with respiratory visits in all age groups. SO_4 correlated in ages >14. NO_2 correlated in ages 15-60. O_3 not significant.	Results varied somewhat by season. *Study not used to estimate incidence: correlations only presented.*
Cody et al. (1992)	central and northern New Jersey May-August 1988-1989	all ages	bronchitis (466, 490, 491, 496)	PM_{10}, SO_2, O_3	No significant effect seen for PM_{10}, O_3, or SO_2 on bronchitis admissions.	PM_{10} sampled every sixth day, so limited dataset. PM_{10} considered in separate analysis. *Study not used to estimate incidence.*
Delfino et al. (1997)	Montreal, Canada June-September 1992-1993	<2; 2-64; >64	all respiratory (not defined by ICD code)	O_3, PM_{10}, $PM_{2.5}$, SO_4, H^+	Single pollutant models: H^+ and SO_4 significant in ages <2; no effect in ages 2-64 for any pollutants; O_3, PM_{10}, $PM_{2.5}$, and SO_4 significant in ages >64. Two pollutant model: O_3 significant and $PM_{2.5}$ not significant in ages >64.	Limited number of results presented for two pollutant models. *Study not used to estimate incidence: all respiratory not defined by ICD code.*
Delfino et al. (1998)	Montreal, Canada June-August 1989-1990	>64	all respiratory (not defined by ICD code)	$PM_{2.5}$, O_3	Two pollutant model: O_3 significant; $PM_{2.5}$ has consistent link but not significant.	$PM_{2.5}$ measured every sixth day, with rest of daily observations estimated from visibility and other data. *Study not used to estimate incidence: all respiratory not defined by ICD code.*
Samet et al. (1981)	Steubenville, Ohio March-April and October-November 1974-1977	all ages	all respiratory (not defined by ICD code)	NO_2, TSP, SO_2, CO, O_3	Single pollutant models: TSP and SO_2 significant; NO_2,, CO, or O_3 were not significant.	*Study not used to estimate incidence: all respiratory not defined by ICD code.*

Study	Location and Period	Population	Endpoint (ICD code)	Pollutants	Main Findings	Comment
Pantazopolou et al. (1995)	Athens, Greece 1988	all ages	all outpatient visits	BS, CO, NO_2	Single-pollutant models: NO_2 significant in the winter. No effects found for any pollutant in the summer.	*Study not used to estimate incidence: study outside U.S. and Canada.*
Sunyer et al. (1993)	Barcelona, Spain 1985-1989	>14	COPD (not defined by ICD code)	SO_2, BS	SO_2 correlated with ER visits in the summer and winter. BS significant in the winter only	*Study not used to estimate incidence: study outside U.S. and Canada.*
Xu et al. (1995b)	Beijing, China 1990	all ages	all causes	SO_2, TSP	SO_2 and TSP both linked to ER visits.	*Study not used to estimate incidence: study outside U.S. and Canada.*

Minor Illness

In addition to chronic illnesses and hospital admissions, there is a considerable body of scientific research that has estimated significant relationships between elevated air pollution levels and other morbidity health effects. Chamber study research has established relationships between specific air pollution chemicals and symptoms such as coughing, pain on deep inspiration, wheezing, eye irritation and headaches. In addition, epidemiological research has found air pollution relationships with acute infectious diseases (e.g., bronchitis, sinusitis) and a variety of "symptom-day" categories. Some "symptom-days" studies examine excess incidences of days with identified symptoms such as wheezing, coughing, or other specific upper or lower respiratory symptoms. Other studies estimate relationships for days with a more general descriptions of days with adverse health impacts, such as "respiratory restricted activity days" or work loss days.

A major challenge in preparing an analysis of the minor morbidity effects is identifying a set of effect estimates that reflects the full range of identified adverse health effects but avoids double counting. From the definitions of the specific health effects examined in each research project, it is possible to identify a set of effects that are non-overlapping, and can be ultimately treated as additive in the monetary benefits analysis. This section primarily focuses on the set of effect relationships that have been identified that make up a non-overlapping set. Table D-12 summarizes the studies used in estimating minor illnesses; Tables D-13 and D-14 provide more detailed information on these studies and other studies that were not used in the analysis.

Acute Bronchitis

Dockery et al. (1996) examined the relationship between PM and other pollutants on the reported rates of asthma, persistent wheeze, chronic cough, and bronchitis, in a study of 13,369 children ages 8-12 living in 24 communities in U.S. and Canada. Health data were collected in 1988-1991. Single-pollutant models were used in the analysis. Annual levels of sulfates and particle acidity were significantly related to bronchitis, and $PM_{2.5}$ and PM_{10} were marginally significant. Earlier work, based on six U.S. cities, by Dockery et al. (1989) found acute bronchitis and chronic cough significantly related to PM_{15}. Because it is based on a larger sample, the Dockery et al. (1996) study is used to develop a C-R function linking $PM_{2.5}$ with acute bronchitis.

Upper Respiratory Symptoms (URS)

Using logistic regression, Pope et al. (1991) estimated the impact of PM_{10} on the incidence of a variety of minor symptoms in 55 subjects (34 "school-based" and 21 "patient-based") living in the Utah Valley from December 1989 through March 1990. The children in the Pope et al. study were asked to record respiratory symptoms in a daily diary, and the daily occurrences of upper respiratory symptoms (URS) and lower respiratory symptoms (LRS), as defined above, were related to daily PM_{10} concentrations. Pope et al. describe URS as consisting of one or more of the following symptoms: runny or stuffy nose; wet cough; and burning, aching, or red eyes. Levels of ozone, NO_2, and SO_2 were reported low during this period, and were not included in the analysis. The sample in this study is relatively small and is most representative of the asthmatic population, rather than the general population. The school-based subjects (ranging in age from 9 to 11) were chosen based on "a positive response to one or more of three questions: ever wheezed without a cold, wheezed for 3 days or more out of the week for a month or longer, and/or had a doctor say the 'child has asthma' (Pope et al., 1991, p. 669)." The patient-based subjects (ranging in age from 8 to 72) were receiving treatment for asthma and were referred by local physicians. Regression results for the school-based sample (Pope et al., 1991, Table 5) show PM_{10} significantly associated with both upper and lower respiratory symptoms. The patient-based sample did not find a significant PM_{10} effect. The results from the school-based sample are used here.

Lower Respiratory Symptoms (LRS)

Schwartz et al. (1994) used logistic regression to link lower respiratory symptoms in children with SO_2, NO_2, ozone, PM_{10}, $PM_{2.5}$, sulfate and H^+ (hydrogen ion). Children were selected for the study if they were exposed to indoor sources of air pollution: gas stoves and parental smoking. The study enrolled 1,844 children into a year-long study that was conducted in different years (1984 to 1988) in six cities. The students were in grades two through five at the time of enrollment in 1984. By the completion of the final study, the cohort would then be in the eighth grade (ages 13-14); this suggests an age range of 7 to 14.

Respiratory Illness

Several epidemiological studies report that NO_2 exposure increases risk of respiratory illness in children. The results of many of the studies are not statistically significant. In addition, many of the studies do not provide ambient NO_2 measurements, having focused on the presence or absence of gas stoves as surrogates for exposure. However, there are data available from a well-designed study with adequate ambient exposure measurements. Based on work by Melia et al. (1980; 1982), Hasselblad et al. (1992) examined data from 103 children in homes where gas stoves were present and where bedroom NO_2 measurements were taken. A significant increase in respiratory illness was found to be a function of bedroom NO_2 levels, independent of social class, age, gender, or the presence of a smoker in the house. Hasselblad et al. used a multiple logistic model fitted to the Melia data with a linear slope for NO_2 and separate intercepts for boys and girls. This analysis uses the average slope of these two estimates.

Work Loss Days (WLD)

Ostro (1987) estimated the impact of PM on the incidence of work-loss days (WLD) in a national sample of the adult working population, ages 18 to 65, living in metropolitan areas. Separate coefficients were developed for each year in the analysis (1976-1981); we then combined these coefficients for use in this analysis using a weighted average based on the inverse of the variances.

Minor Restricted Activity Days (MRAD) / Any of 19 Respiratory Symptoms

Two studies by Ostro and Rothschild (1989b) and Krupnick et al. (1990) cover a variety of minor respiratory symptoms. To avoid double counting, we treat these two studies as alternative measures of the same health effect, and pool the incidence estimates.

Ostro and Rothschild (1989b) estimated the impact of ozone and $PM_{2.5}$ on the incidence of minor restricted activity days (MRAD) in a national sample of the adult working population, ages 18 to 65, living in metropolitan areas. We developed separate coefficients for each year in the analysis (1976-1981), which were then combined for use in this analysis. The coefficient used in this analysis is a weighted average of the coefficients using the inverse of the variance as the weight.

Krupnick et al. (1990) estimated the impact of coefficient of haze (COH, a measure of particulate matter concentrations), ozone and SO_2 on the incidence of any of 19 respiratory symptoms or conditions.[14] They used a logistic regression model that takes into account whether a respondent was well or not the previous day. A key difference between this and the usual logistic model is that the model they used includes a lagged value of the dependent variable.

Moderate or Worse Asthma

This health endpoint comes from Ostro et al. (1991), a study in which asthmatics, ages 18 to 70, were asked to record daily a subjective rating of their overall asthma status each day (0=none, 1=mild, 2=moderate, 3=severe, 4=incapacitating). Ostro et al.

[14]Krupnick et al. (1990) list 13 specific "symptoms or conditions": head cold, chest cold, sinus trouble, croup, cough with phlegm, sore throat, asthma, hay fever, doctor-diagnosed ear infection, flu, pneumonia, bronchitis, and bronchiolitis. The other six symptoms or conditions are not specified.

then examined the relationship between moderate (or worse) asthma and H^+, sulfate, SO_2, $PM_{2.5}$, estimated $PM_{2.5}$, PM_{10}, nitrate, and nitric acid. The published results used in the prospective analysis are from a single-pollutant linear regression model where the log of the pollutant is used.

Asthma "attacks" associated with ozone are estimated using the study by Whittemore and Korn (1980). Symptoms in asthmatic children associated with SO_2 are from Linn et al. (1987; 1988; 1990) and Roger et al. (1985).

Shortness of Breath

Using a logistic regression estimation, Ostro et al. (1995) estimated the impact of PM_{10}, ozone, NO_2, and SO_2 on the incidence of coughing, shortness of breath, and wheezing in 83 African-American asthmatic children ages 7-12 living in Los Angeles from August through September 1992. Regression results show both PM_{10} and ozone significantly linked to shortness of breath; the beginning of an asthma episode was also significantly linked to ozone. Results for single-pollutant models only were presented in the published paper.

Restricted Activity Days (RADs)

Ostro (1987) used a log-linear regression to estimate the impact of $PM_{2.5}$ on the incidence of restricted activity days (RAD) in a national sample of the adult population, ages 18 to 65, living in metropolitan areas. Separate coefficients were developed for each year in the analysis (1976-1981); these coefficients were pooled. The coefficient used in the concentration-response function used here is a weighted average of the coefficients in Ostro (1987, Table III) using the inverse of the variance as the weight.

Table D-12
Studies Used to Develop Minor Illness Estimates

Endpoints Estimated	Study Population Age	Study	Pollutants Used in Final Model
acute bronchitis	8-12	Dockery et al. (1996)	$PM_{2.5}$
upper respiratory symptoms	9-11	Pope et al. (1991)	PM_{10}
lower respiratory symptoms	7-14	Schwartz et al. (1994)	$PM_{2.5}$
respiratory illness	6-7	Hasselblad et al. (1992)	NO_2
any of 19 respiratory symptoms	18-65	Krupnick et al. (1990)	O_3, PM_{10}
moderate or worse asthma	all ages (asthmatics)	Ostro et al. (1991)	$PM_{2.5}$
asthma attacks	all ages (asthmatics)	Whittemore and Korn (1980)	O_3, PM_{10}
chest tightness, shortness of breath, or wheeze	all ages (asthmatics)	Linn et al. (1987; 1988; 1990) and Roger et al. (1985)	SO_2
shortness of breath	7-12 (African-American asthmatics)	Ostro et al. (1995)	PM_{10}
work loss days	18-65	Ostro (1987)	$PM_{2.5}$
minor restricted activity days	18-65	Ostro and Rothschild (1989b)	$PM_{2.5}$, O_3
restricted activity days	18-65	Ostro (1987)	$PM_{2.5}$

Table D-13
Summary of Selected Studies for Minor Illness

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Dockery et al. (1996)	24 communities in U.S. and Canada 1988-1991	13,369 children ages 8-12	asthma, persistent wheeze, chronic cough, bronchitis	particle acidity, SO_4, $PM_{2.1}$, PM_{10}, HNO_2, HNO_3, O_3	Annual level of sulfates and particle acidity related to bronchitis. HNO_2 and HNO_3 linked to asthma. SO_2 linked to chronic phlegm.	Study examined annual pollution exposures, and the authors did not rule out that acute (daily) exposures could be related to asthma attacks and other acute episodes.
Dockery et al. (1989)	Six U.S. cities 1980-1981	5,422 children ages 10-12	bronchitis, chest illness, cough, wheeze, asthma	SO_2, NO_2, O_3, $PM_{2.5}$, PM_{15}, TSP, SO_4	Annual level of PM_{15} significantly related to bronchitis and chronic cough. Annual O_3 significantly related to asthma.	
Hasselblad et al. (1992)	Meta-analysis of 11 studies from the U.S. and Europe	children ages 5-12	lower respiratory tract illness	NO_2	Annual NO_2 change of 30 µg/m^3 associated with lower respiratory tract illness.	
Hoek and Brunekreef (1995)	Two rural towns in the Netherlands. Spring-Summer 1989	300 children ages 7-11	symptoms including: cough, phlegm, wheeze, runny nose, throat pain, headache, eye irritation, physician visit	SO_2, NO_2, O_3, $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$, SO_4, NO_3	Daily pollutant levels not associated with any of the symptoms studied.	
Krupnick et al. (1990)	Three communities in Los Angeles County, California 9/78-3/79	570 adults and 756 children	any of 19 respiratory symptoms including cough with phlegm	O_3, COH (coefficient of haze), SO_2, NO_2	In single pollutant models, daily O_3, COH, and SO_2 related to respiratory symptoms in adults. O_3 significant controlling for other pollutants. Results more variable for COH and SO_2, perhaps due to collinearity. NO_2 had no significant effect. No effect seen in children for any pollutant.	
Ostro (1987)	Nationwide sample from U.S. Health Interview Survey 1976-1981	Adults ages 18-65	work-loss days restricted activity days (RADs), respiratory-related RADs	$PM_{2.5}$	Two-week average $PM_{2.5}$ levels significantly linked to work-loss days, RADs, and respiratory-related RADs. Some year-to-year variability in results.	$PM_{2.5}$ estimated from visibility data.

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Ostro et al. (1993)	Three communities in Los Angeles County, California 9/78-3/79	321 non-smoking adults	lower respiratory symptoms, upper respiratory symptoms, eye irritation	O_3, COH, SO_4, SO_2, NO_2	In single pollutant model, daily O_3 linked to lower and upper respiratory symptoms. SO_4 linked to lower respiratory symptoms. No significant effects seen for COH, SO_2, and NO_2.	
Ostro and Rothschild (1989b)	Nationwide sample from U.S. Health Interview Survey 1976-1981	Adults ages 18-65	respiratory-related RADs, minor RADs.	O_3, $PM_{2.5}$	Controlling for $PM_{2.5}$, two-week average O_3 has highly variable association with respiratory-related and minor RADs. Controlling for O_3, two-week average $PM_{2.5}$ significantly linked to both health endpoints in most years.	$PM_{2.5}$ estimated from visibility data.
Peters et al. (1999)	Twelve communities in southern California 1994	3,676 fourth, seventh, tenth grade students	asthma, wheeze, bronchitis, cough	SO_2, NO_2, O_3, $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$, SO_4, NO_3, NH_4, gaseous acids	Wheeze in males, linked to annual average NO_2 and acid in 1994 (similar link for exposure averaged over 1986-1990). Peak ozone reported associated with decreased asthma prevalence in females. No other reported effects.	
Pope and Dockery (1992)	Utah Valley 12/90-3/91	79 children ages 10-12	upper respiratory symptoms, lower respiratory symptoms, cough	PM_{10}	PM_{10} linked to daily reported incidences of upper and lower respiratory symptoms and cough. Effect seen in symptomatic sample. Only cough in symptomatic sample linked to PM_{10}.	Of the 79 children in the sample, 39 were symptomatic, and the other 40 were asymptomatic.
Pope et al. (1991)	Utah Valley 12/89-3/90	34 children ages 9-11, and 21 asthmatics ages 8-72	upper respiratory symptoms, lower respiratory symptoms, took asthma medication	PM_{10}	PM_{10} significantly linked to upper and lower respiratory symptoms in sample of 34 children. PM_{10} linked only to increased asthma medication use in the asthmatic sample.	

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Schwartz et al. (1994)	Six U.S. cities April-August in one year between 1984 and 1988 (year varies by city)	1,844 children	upper respiratory symptoms, lower respiratory symptoms, cough	SO_2, NO_2, O_3, $PM_{2.5}$, PM_{10}, SO_4, H^+	In single pollutant models SO_2, NO_2, $PM_{2.5}$, and PM_{10} significantly linked to cough. In two-pollutant models, PM_{10} has most consistent effect; other pollutants not significant, controlling for PM_{10}. In single pollutant models, SO_2, O_3, $PM_{2.5}$, PM_{10}, SO_4, and H^+ linked to lower respiratory symptoms. No effect seen for upper respiratory symptoms.	
Schwartz and Zeger (1990)	Los Angeles, CA 1961-1964	110 student nurses	cough, phlegm, sore throat, headache, chest discomfort, eye irritation	CO, SO_2, NO_2, O_x	NO_2 linked to sore throat, phlegm, and eye irritation. Oxidants (O_x) linked to chest discomfort and eye irritation. CO linked to headache.	Results presented as a mix of single pollutant and dual pollutant models. Stepwise selection used to pick significant covariates.
von Mutius et al. (1995)	Leipzig, Germany 10/91-7/92	1,500 children ages 9-11	upper respiratory symptoms	SO_2, NO_x, PM	In single pollutant models, SO_2, NO_x, and PM linked to upper respiratory symptoms in winter (high pollution season). In the summer, only NO_x linked to respiratory symptoms.	PM measured by beta-absorption. The limited modeling results presented for models with more than one pollutant were similar to single pollutant results.

Table D-14
Summary of Selected Studies for Asthmatics

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Forsberg et al. (1993)	Pitea, Sweden about sixty days	31persons ages 9-71	shortness of breath, wheeze, cough, phlegm	BS (black smoke), SO_2, NO_2	Controlling for other pollutants, daily levels of BS linked to shortness of breath. No link between pollutants and wheeze, cough, and phlegm.	Black smoke is an indirect measure of PM.
Gielen et al. (1997)	Amsterdam, Netherlands summer 1995	61 children ages 7-13	upper respiratory symptoms, lower respiratory symptoms, medication use	O_3, PM_{10}, BS	In single pollutant model, daily levels of BS significantly linked to lower and upper respiratory symptoms and medication use. PM_{10} linked to lower respiratory symptoms and medication use. O_3 linked to upper respiratory symptoms.	Results in the model highly dependent on the lag length used. The five-day mean black smoke and PM_{10} yielded significant results, but current, one and two day lags did not. Current day O_3 significant.
Hiltermann et al. (1998)	Leiden University, Netherlands 7/3/95-10/6/95	60 adults ages 18-55	symptoms include: shortness of breath, cough, phlegm, wheeze, runny nose, throat pain, headache, eye irritation, physician visit	O_3, PM_{10}, BS, NO_2, SO_2	In single pollutant models, daily levels of O_3, PM_{10}, BS, and NO_2 linked to shortness of breath. Some significant negative associations reported for nasal symptoms and levels of PM_{10}, BS, and NO_2. No significant effect reported for SO_2.	
Linn et al. (1987; 1988; 1990) and Roger et al. (1985)	Chamber studies.	Exercising, young asthmatics	chest tightness, shortness of breath, or wheeze	SO_2	SO_2 exposure linked to moderate symptoms in these studies of moderately exercising young asthmatics.	

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Neukirch et al. (1998)	Paris, France 11/92-5/93	40 persons (mean age of sample was 46)	asthma, wheeze, shortness of breath, cough, respiratory infection	PM_{13}, BS, NO_2, SO_2	In single pollutant models, daily levels of PM_{13}, BS, NO_2, and SO_2 were each significantly associated with asthma attacks, wheeze, cough, respiratory infections, and shortness of breath.	PM_{13} used rather than the more common PM_{10}.
Ostro et al. (1991)	Denver, CO 12/87-2/88	207 persons ages 18-70	severity of asthma symptoms, cough, wheeze, shortness of breath, chest tightness	SO_2, $PM_{2.5}$, SO_4, NO_3, H^+, nitric acid	Daily levels of H^+ linked to cough, asthma, and shortness of breath. $PM_{2.5}$ linked to asthma. SO_4 linked to shortness of breath. No effects seen for other pollutants.	Some $PM_{2.5}$ estimated. Exclusion of estimated data removes significant link to asthma. Only single pollutant models reported.
Ostro et al. (1995)	Los Angeles, CA 8/92-11/92	83 children ages 7-12	cough, shortness of breath, wheeze	O_3, NO_2, SO_2, PM_{10}	In single pollutant models, daily levels of O_3 and PM_{10} linked only to shortness of breath. No effect seen for NO_2 and SO_2.	
Peters et al. (1996)	Three cities in East Germany and the Czech Republic 9/90-6/92	155 children ages 7-15 and 102 adults ages 32-80	symptom score based on a variety of respiratory symptoms	TSP, SO_2, SO_4, particle acidity	Daily SO_2 linked to the respiratory symptom score. No link between the other pollutants and the symptom score.	
Roemer et al. (1998)	28 locations in Europe winter 1993-1994	2,010 children ages 6-12	symptoms include: shortness of breath, cough, phlegm, wheeze, runny nose, sore throat, headache, eye irritation	PM_{10}, BS, NO_2, SO_2	Daily pollutant levels not related to adverse health symptoms.	
Romieu et al. (1996)	Mexico City	71 children ages 5-7	cough, phlegm, difficulty breathing, wheezing, lower respiratory illness	PM_{10}, $PM_{2.5}$, O_3, NO_2, SO_2	Controlling for $PM_{2.5}$, daily levels of O_3 linked to cough and lower respiratory illness. Controlling for O_3, $PM_{2.5}$ linked to cough, phlegm, and lower respiratory symptoms.	PM_{10} also linked adverse symptoms. Published results focused on O_3 and $PM_{2.5}$. Results for NO_2 and SO_2 not reported.

Study	Location and Period	Population	Endpoint	Pollutants	Main Findings	Comment
Whittemore and Korn (1980)	Six communities in southern CA Three 34-week periods 1972-1975	443 children and adults	asthma	O_x, TSP	In a two pollutant model, daily levels of both TSP and O_x were significantly related to reported asthma attacks.	Respirable PM, NO_2, SO_2 were highly correlated with TSP and excluded from the analysis.