Assessing the Public Health Benefits of Reduced Ozone Concentrations

Jonathan I. Levy,[1,2] Timothy J. Carrothers,[3] Jouni T. Tuomisto,[2,4] James K. Hammitt,[2,5] and John S. Evans[1,2]

[1]Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA; [2]Harvard Center for Risk Analysis, Boston, Massachusetts, USA; [3]Pharsight Corporation, Mountain View, California, USA; [4]Department of Environmental Health, National Public Health Institute, Kuopio, Finland; [5]Department of Health Policy and Management, Harvard School of Public Health, Boston, Massachusetts, USA

In this paper we examine scientific evidence and related uncertainties in two steps of benefit–cost analyses of ozone reduction: estimating the health improvements attributable to reductions in ozone and determining the appropriate monetary values of these improvements. Although substantial evidence exists on molecular and physiologic impacts, the evidence needed to establish concentration–response functions is somewhat limited. Furthermore, because exposure to ozone depends on factors such as air conditioning use, past epidemiologic studies may not be directly applicable in unstudied settings. To evaluate the evidence likely to contribute significantly to benefits, we focus on four health outcomes: premature mortality, chronic asthma, respiratory hospital admissions, and minor restricted activity days. We determine concentration–response functions for these health outcomes for a hypothetical case study in Houston, Texas, using probabilistic weighting reflecting our judgment of the strength of the evidence and the possibility of confounding. We make a similar presentation for valuation, where uncertainty is due primarily to the lack of willingness-to-pay data for the population affected by ozone. We estimate that the annual monetary value of health benefits from reducing ozone concentrations in Houston is approximately $10 per person per microgram per cubic meter (24-hr average) reduced (95% confidence interval, $0.70–$40). The central estimate exceeds past estimates by approximately a factor of five, driven by the inclusion of mortality. We discuss the implications of our findings for future analyses and determine areas of research that might help reduce the uncertainties in benefit estimation. *Key words*: **benefit–cost analysis, epidemiology, exposure assessment, monetary valuation, ozone, premature mortality.** *Environ Health Perspect* **109:1215–1226 (2001). [Online 24 November 2001]** ***http://ehpnet1.niehs.nih.gov/docs/2001/109p1215-1226levy/abstract.html***

In recent years, tropospheric ozone has been a primary regulatory focus of the U.S. Environmental Protection Agency (U.S. EPA). A revised National Ambient Air Quality Standard of 0.08 ppm for 8-hr average concentrations was finalized in 1997 (*1*), based in part on evidence of physiologic changes and health effects below the previous primary ozone standard (0.12 ppm, 1-hr average).

Although substantial evidence exists on the molecular and physiologic impacts of ozone exposure (*2*), the evidence needed to quantify the benefits of reducing ozone concentrations (for use in benefit–cost analyses) is surprisingly limited. A benefit–cost analysis of concentration reductions (leaving aside atmospheric dispersion modeling of ozone precursors) would need to incorporate, with a reasonable degree of certainty, the relationship between ambient concentrations and personal exposures; representative concentration–response functions for health outcomes for which causality can be reasonably inferred; and the economic valuations of these health outcomes.

For all three of these categories, significant uncertainty exists. Although personal exposures to ozone could be influenced by air conditioning and time spent indoors, possible geographic differences in concentration–response functions were not addressed in the prospective benefit–cost analysis of the Clean Air Act (CAABCA) (*3*) or the Regulatory Impact Analysis (RIA) of the Tier 2 motor vehicle standards (*4*). In these studies, ozone benefits were based largely on a limited number of studies of selected morbidity outcomes, and ozone effects on mortality were considered only in a sensitivity analysis. Economic valuation of premature death was based largely on studies of populations that arguably were not representative of those at risk from air pollution, and many morbidity valuations were based on limited studies or on only the direct economic costs of illness.

This is not to say that the CAABCA and the Tier 2 RIA did not represent a good understanding of the literature on ozone mitigation benefits; rather, these analyses demonstrate the relative lack of emphasis on ozone research relevant to the questions asked by benefit–cost analysis. A survey of the literature finds numerous recent meta-analyses (either qualitative or quantitative) of the particulate matter (PM) time-series literature (*5–11*) but few similar assessments for ozone (*12*). Given a limited number of primary studies and fewer critical assessments of these studies, there is a need for careful consideration of all elements of ozone benefit–cost analyses, to ensure that benefits of ozone reduction are not significantly underestimated or overestimated and to determine areas for future research.

Within this article, our approach is to focus on elements that would help us interpret a relatively limited body of literature. Because one of the overarching questions in evaluating health effects is determining causality, we construct our health effects arguments in light of some of Hill's causal criteria (*13*). We focus primarily on biologic plausibility, coherence, and strength/consistency of effect.

Clearly, the U.S. EPA criteria document and other similar publications cover these issues (as well as monetary valuation issues) extensively, and it is not our intent to summarize even approximately the full body of ozone literature. Rather, our goal is to interpret a limited number of studies that have provided the primary bases for past ozone damage estimations. Thus, we do not discuss some health outcomes (such as eye irritation or emergency room visits for asthma) that are commonly associated with ozone but that were not significant contributors to benefits in past analyses (*3,4*). In addition, we acknowledge that our analysis represents a preliminary look at these issues, based on our subjective judgments. We aim to raise questions related to uncertainty and the interpretation of the literature, but a broader evaluation by experts in the relevant fields might yield different estimates and characterizations of uncertainty.

Within this article, we draw conclusions regarding the interpretation of the current literature on health effects and monetary valuation, presenting our best estimates and estimates of uncertainty. We provide a hypothetical case study in Houston, Texas, to demonstrate one approach for applying past studies to different geographic locations. We conclude by discussing future research directions and the appropriate scope and framing of ozone benefit–cost analyses.

Address correspondence to J.I. Levy, Department of Environmental Health, Harvard School of Public Health, Landmark Center, P.O. Box 15677, Boston, MA 02215 USA. Telephone: (617) 384-8808, Fax: (617) 384-8859. E-mail: jilevy@hsph.harvard.edu

We thank G. Thurston, S. Moolgavkar, K. Ito, and P. Kinney for providing useful comments to help frame our analysis.

We performed this research as consultants to Exxon Chemical Americas. The opinions are those of the authors and should not be attributed to Exxon or Harvard.

Received 17 November 2000; accepted 7 May 2001.

Relevant Background Information

Biologic mechanisms. We briefly discuss the mechanisms of action for ozone in this section to help determine whether health effects derived from epidemiologic investigations are biologically plausible. We focus on review articles considering the molecular mechanisms of action (*14*) and physiologic effects in the mammalian lung (*15*).

Ozone is an oxidant gas with three oxygen atoms in the molecule. It is poorly water soluble, so it does not easily diffuse into tissues, but merely reacts with molecules at the air–fluid boundary. Ozone also reacts easily and rapidly with molecules that contain reactive groups, such as antioxidants or polyunsaturated fatty acids. There is fairly good agreement that ozone reactions with carbon double bonds in the lung lining fluid's polyunsaturated fatty acids represent the primary molecular mechanism for adverse physiologic effects. In pathologic conditions such as chronic obstructive pulmonary disease (COPD) or asthma, the thickness of the lung lining fluid may be reduced, and this may have some effect on the sensitivity to ozone among individuals with pre-existing respiratory disease (*14*).

The molecular effects of ozone are mediated somewhat by antioxidants in the lung lining fluid, which contains large amounts of urate, ascorbate, and reduced glutathione. This raises the possibility that there may be a threshold below which ozone would have few or no adverse effects, although the variability in individual sensitivities and antioxidant levels may imply that this putative threshold would not be seen at the population level. Interestingly, there are reports of compromised antioxidant status in asthmatics, which could sensitize the lung to further ozone exposures (*14,16*).

Ozone causes several changes in the airway epithelium. These include necrosis of ciliated cells and type I pneumocytes, deciliation, and degranulation of secretory cells. Also, tight junctions between epithelial cells are damaged, and this increases the permeability of the epithelium enabling outcomes such as protein leakage from the epithelium to the lung lining fluid and vice versa (*14*).

Along with an understanding of molecular mechanisms, there is a reasonable body of literature describing the physiologic effects of ozone. Numerous studies have detailed the fact that ozone exposure leads to short-term decreases in lung function (*12,14,17–19*), apparently caused by a decrease in inspiratory capacity secondary to sensitization of bronchial C-fibers (*20,21*). Inflammatory mechanisms seem to also be involved, as ibuprofen and indomethacin have been shown to reduce the ozone effect (*22,23*).

There is also evidence of increased airway resistance caused by small airway narrowing, through mechanisms such as increased smooth muscle tone, edema, localized inflammation, and mucus hypersecretion (*14*). This may involve ozone effects on the parasympathetic nervous system. In addition, ozone can increase reactivity to nonspecific bronchoconstrictors (*24,25*), which may (through inflammatory mechanisms) aggravate symptoms in individuals who already react to allergens or have obstructive diseases.

One key question for interpretation of epidemiologic findings is whether long-term exposure to ozone can lead to chronic health effects. Evidence from animal and human exposure studies shows that long-term exposure could produce sustained decrements in lung function, particularly in small airway measures (such as forced expiratory flow, which would be abnormal for individuals with COPD or asthma) (*15*). Studies of chronic ozone exposures (≥ 150 ppb) in monkeys and rats found thickening of the epithelium and interstitium of bronchioles (*26,27*). The respiratory epithelium was replaced by bronchial epithelium in the central acinar region in rats after long-term ozone exposure (*28*). In addition, increased collagen or fibroblast proliferation has been observed, suggesting a fibrotic process (*29,30*). There is also evidence from animal studies that exposure to ozone at an early age can lead to persistent developmental changes (*15*), including changes in tracheal mucociliar apparatus (*31*) and lesions in respiratory bronchioles (*32*). Thus, chronic exposure to ozone appears to cause bronchiolitis with remodeling of the bronchiolar epithelium leading to decreased diffusion capacity, fibrosis leading to reduced lung elasticity, and proliferation of type II pneumocytes. These changes have also been found in autopsied human lungs after long-term ozone exposure (*14,33*).

In conclusion, there are well-documented mechanisms for acute respiratory effects and limited evidence for chronic respiratory effects related to ozone exposure. Because the primary oxidative reactions of ozone seem to be related to universal properties of the mammalian respiratory tract, the animal-to-human extrapolations would be expected to have less uncertainty for ozone than for many other chemicals. However, animals are generally exposed to concentrations well above ambient levels, making definitive conclusions about effects at ambient levels difficult. Nevertheless, there appears to be sufficient evidence for the biologic plausibility of respiratory-related morbidity and mortality.

Exposure patterns. For benefit–cost analysis, we are interested in two dimensions of ozone exposure. First, to evaluate whether epidemiologic associations can be interpreted as causal relationships, we must determine the general relationship between ambient concentrations and personal exposures. Second, to extrapolate the epidemiologic results to unstudied regions, we must understand whether there are systematic differences in this relationship by location.

Individuals in developed countries generally spend most of their time indoors (*34*), implying that we need to understand the relationship between outdoor and indoor concentrations to evaluate personal exposures. In addition, ozone is a highly reactive secondary pollutant. This implies that indoor ozone generally is caused by penetration of outdoor ozone (*35*) and that ozone can be removed by interior surfaces or by pollutants generated indoors (*2*). As a result, indoor ozone concentrations are generally lower than ambient concentrations. Indoor–outdoor ratios in past studies have ranged between zero and one, with most values between 0.3 and 0.7 (*2*). Multiple recent analyses found that indoor exposures are lower in homes with air conditioning running (*35–37*).

These findings imply that the magnitude of the effect of ambient ozone on health would likely be influenced by activity patterns and air conditioning use. In the extreme, an individual who spends 24 hr per day in air-conditioned settings would be expected to have limited exposure to ozone, even if outdoor concentrations were substantial. This does not necessarily imply that the epidemiologic evidence is uninformative, because day-to-day variations in ambient concentrations may still be correlated with variations in levels of average personal exposures across a city. The implication for benefit–cost analysis is that bodies of epidemiologic literature may not be directly applicable in unstudied climates. Epidemiologic studies in cities in which residents spend greater amounts of time in air-conditioned environments would be expected to have lower concentration–response functions, even though the dose–response functions may be identical.

Concentration–Response Evaluation

Approach. As mentioned earlier, we focus on the health outcomes that contributed significantly to ozone benefits in past analyses. In the CAABCA (*3*), benefits were not presented independently for ozone. In the Tier 2 RIA, about 90% of ozone benefits were associated with minor restricted activity days and decreased worker productivity (*4*). Chronic asthma and respiratory hospital admissions provided most of the remaining benefits. We also evaluate ozone-related mortality because it would likely be a significant

contributor to benefits if a causal relationship existed.

To determine appropriate concentration–response functions, we gathered all relevant publications addressing each endpoint. Our approach is to use quantitative methods to pool studies that we judge to be adequate. In general, we exclude studies from our pooled estimate if they do not treat confounders appropriately or lack useful quantified coefficients or standard errors. However, we use the discarded studies to help interpret the complete body of literature and determine whether our quantitative estimates are representative. In addition, we focus on studies conducted in the United States when sufficient studies are available, to minimize variability related to differences in health care systems and population characteristics across countries.

Epidemiologic studies of ozone have considered numerous exposure periods, including 1-hr maximum, 8-hr average, or 24-hr average concentrations, with a range of lag structures and number of days averaged. Within our analysis, we consider all three averaging times with the application of constant conversion factors. We assume that 1-hr maximum concentrations will be 2.5 × 24-hr concentrations and 1.33 × 8-hr concentrations (*38*). In addition, we assume that 1 ppb ozone = 1.96 μg/m^3 (conversion at standard temperature and pressure), although this relationship will vary slightly in the locations studied (*12,38*). The application of these factors leads to associated uncertainties (because the relationships among these three measures vary from place to place and day to day). This is especially true if one exposure period is more representative of the true relationship between dose and effect.

We would expect that the observed concentration–response functions would differ by climate, given the importance of air conditioning for personal exposure. Thus, pooled literature estimates may not be directly applicable to our Houston case study. Ideally, we would use a methodology such as hierarchic linear modeling that can incorporate both systematic effects (e.g., time activity, air conditioning, temperature, humidity) and random effects (*11*). Given limited studies, we calculate pooled estimates and use some scaling factors to derive concentration–response functions for Houston.

Within this section, we first discuss the evidence from cohort studies, including both mortality and chronic asthma. We discuss general issues related to the time-series literature and focus on the evidence for mortality, hospital admissions, and minor restricted activity days.

Cohort mortality. Three major cohort studies have been published: the Six Cities study (*39*), the American Cancer Society (ACS) study (*40*), and the Adventist Health Study of Smog (AHSMOG) (*41*). For the former two studies, we focus on the results from a recent Health Effects Institute (HEI) reanalysis (*42*).

AHSMOG (*41*) evaluated the relationship between air pollution and mortality risks (lung cancer, cardiopulmonary, nonmalignant respiratory, and all-cause) among 6,338 Seventh Day Adventists in California from 1977 to 1992. Because Seventh Day Adventists largely abstain from smoking (validated through questionnaire), one would expect that respiratory disease rates would be lower than average. In single-pollutant models, the number of hours of ozone above 100 ppb was significantly associated with lung cancer in males [relative risk (RR) 4.19; 95% confidence interval (CI), 1.81–9.69] but not with lung cancer in females or any other cause of death. An increase in mean ozone concentrations was not significantly associated with any cause of death (with weak evidence for lung cancer in males). Multipollutant models were not reported, but the authors indicated that the ozone coefficient was reduced in magnitude with the inclusion of PM_{10} but was stronger than the PM_{10} coefficient. Ozone had a strong positive correlation with PM_{10}.

In the Six Cities study (*39*), which followed 8,111 white adults in six cities in the eastern half of the United States for approximately 14–16 years, there was little variation in ozone levels across cities (20–22 ppb annual average in four cities, 28 ppb in two cities). All relative risks for ozone were below one and not statistically significant in single-pollutant models (*42*). The negative relationship could be related to the inverse correlation between ozone and $PM_{2.5}$ (–0.53). Because of the small number of locations and high correlations between pollutants, no multipollutant model was tested, but ozone was the only pollutant that did not demonstrate an association with mortality in single-pollutant models.

The reanalysis of the ACS study (*42*), a retrospective analysis of a cohort of over 500,000 adults across the United States followed from 1982 to 1989, tested numerous statistical models that included ozone along with PM and other covariates. In one model accounting for spatial correlations, ozone was significantly associated with both all-cause and cardiopulmonary mortality. However, across all statistical models, ozone relative risks were often below one and were rarely statistically significant. Ozone was not significantly related with any cause of mortality in any models including sulfates rather than $PM_{2.5}$, and had no relationship with lung cancer in any model.

In summary, there is weak and inconsistent evidence of any long-term mortality effect from ozone. AHSMOG found ozone to be related to male lung cancer, but the ACS study (with a larger sample and a more geographically and demographically representative population) found no evidence of this relationship. The ACS study found moderately significant effects of ozone on all-cause and cardiopulmonary mortality in one statistical model, but these findings were contradicted by most reported models and were not supported by AHSMOG or Six Cities. We conclude that the current epidemiologic evidence does not support long-term mortality effects from ozone.

However, mechanistic studies demonstrate potential long-term lung function decrements associated with ozone exposure. A recent cohort study found that decrements in pulmonary function were significantly associated with mortality rates (*43*), a finding documented extensively elsewhere (*44–47*). Recently, a model of the relationship between lung function and age-specific survival probabilities found that small decrements in lung function associated with air pollution could plausibly explain cohort mortality findings (*48*). Thus, although there is no consistent evidence of long-term ozone mortality effects at current levels of exposure, the general notion that these effects could exist should not be dismissed.

Chronic asthma. Chronic asthma refers to the development of new cases of asthma. It was quantified in both CAABCA and the Tier 2 RIA, although with the stated caveat in the Tier 2 RIA that a causal mechanism had not been established (*4*). In both cases, the chronic asthma estimate was based on an analysis of a subset of the AHSMOG cohort, in which incident cases of doctor-diagnosed asthma were compared with 20-year mean 8-hr average ozone concentrations (*49*). In logistic regressions including parameters for age, education, smoking, and childhood pneumonia/bronchitis, a 27 ppb increase in ozone concentrations was significantly associated with increased incidence of asthma in males (RR 2.09; 95% CI, 1.03–4.16) but not in females (RR 0.86; 95% CI, 0.58–1.26). This relationship was unaffected by the inclusion of other pollutants in the model (PM_{10}, SO_4, NO_2, and SO_2).

Aside from issues of representativeness, the U.S. EPA raised other concerns about the inclusion of this study (*4*). Information on ozone levels over time was not used to determine the concentration–response functions, information on the accuracy of self-reported asthma incidence was not considered, and more than half of subjects dropped out of the study. Because of these uncertainties, we look at other relevant studies.

Two non-AHSMOG studies addressed asthma development and ozone: a cohort of children in Southern California (*50*) and the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) (*51*). In the Southern California investigation (*50*), a cohort of 3,676 children in 12 communities were surveyed by questionnaire in 1993 to provide a cross-sectional assessment of the relationship between respiratory morbidity and air pollution. Two-stage single-pollutant logistic regressions showed that high-hour ozone concentrations had little relationship with asthma prevalence (with a significant but negative relationship among females).

The SAPALDIA study (*51*) was a cross-sectional investigation of 9,651 adults at eight sites in Switzerland. Among never-smokers, there was a negative but statistically insignificant relationship between ozone concentrations and current asthma, with a significant negative relationship between asthma prevalence and frequency of 30-min excesses of ozone above 120 μg/m^3. Thus, although cross-sectional studies are less robust than cohort studies, these two investigations do not support the role of ozone in the development of asthma.

Although asthma development caused by chronic ozone exposure is biologically plausible, the existing epidemiologic evidence is weak and contradictory. We would consider it imprudent to omit this outcome entirely, but the negative studies (*50,51*) and the general uncertainty must be acknowledged. It is our judgment that the epidemiologic literature implies that, for adult males only, we should place a one-third weight on the concentration–response function from AHSMOG and a two-thirds weight on zero. These weights are our subjective judgments, based on the negative findings in two of three studies and the possible nonrepresentativeness of the AHSMOG cohort. The AHSMOG relative risk implies that the incidence rate of asthma among nonsmoking adult males increases by 23% (95% CI, 1–40%) per 10 μg/m^3 increase in annual average ozone concentrations. This is applied to the population of nonasthmatic and nonsmoking adults males given a baseline asthma incidence rate of 0.22% per year (*52*).

Acute health effects of ozone: general time-series issues. For time-series investigations, there are two potentially major confounders. PM has been linked with many of the health outcomes for which we wish to evaluate ozone effects (*5–11*). In locations where PM and ozone concentrations are positively correlated, it is difficult to determine the independent effects of ozone. The correlation between ozone and PM can be either positive or negative depending on the setting, implying that ozone effects could be either understated or overstated in single-pollutant (and perhaps multipollutant) models.

The second potential confounder for studies examining the relation between air pollution and human health is weather (*53*). Extremely hot or cold days are associated with greater mortality than occurs during average weather (*54*). Weather has also been associated with hospital admissions for asthma, a morbidity outcome also associated with ozone (*55*). Under hot and humid conditions, the human body has a decreased ability to cool itself by perspiration or vasodilation, which can increase the risk of elevated body temperature and potential hypotension or heat stroke. The effect of weather is a particular concern for ozone because ozone formation is greater under hot and humid conditions and is therefore more highly correlated with temperature than are most other air pollutants. Because both weather and ozone have plausible mechanisms to increase health risks on high-temperature days, it is difficult to determine whether the health risks are due to ozone (*53*). Complicating matters, the effects of weather differ somewhat with respect to the climate of the area; a 90°F day in May will have a different effect on health in Buffalo than in Houston. This difference is believed to be caused by a combination of human acclimation and activity patterns and differences in the built environment (i.e., the prevalence of air conditioning) (*56,57*).

Air pollution time-series studies have attempted to control for weather with varying degrees of complexity, using terms ranging from temperature indicators to linear and

Table 1. Summary of U.S. time-series studies of ozone mortality with quantitative multipollutant models including PM and nonlinear temperature controls.

Study	Location and dates	Reported relative risk and ozone measure	Copollutants in model	Change in mortality per 10 μg/m^3 of 24-hr average ozone
Moolgavkar et al., 1995 (*60*)	Philadelphia, PA 1973–1988	1.06 (95% CI, 1.02–1.11) per 100 ppb, 24-hr average, 1-day lag	TSP, SO_2	0.3% (95% CI, 0.1–0.5%)
Ito and Thurston, 1996 (*61*)	Cook County, IL 1985–1990	1.07 (95% CI, 1.01–1.12) per 100 ppb, 1-hr maximum, 2-day average	PM_{10}	0.9% (95% CI, 0.1–1.4%)
Kelsall et al., 1997 (*58*)	Philadelphia, PA 1974–1988	1.019 (95% CI, 1.007–1.031) per 20 ppb, 24-hr average, 2-day average	TSP, SO_2, NO_2, CO	0.5% (95% CI, 0.2–0.8%)
Moolgavkar et al., 2000 (*62*)	Cook County, IL 1987–1995	1.014 (95% CI, 1.006–1.023) per 10 ppb, 24-hr average, 1-day lag [a]	PM_{10}, SO_2	0.7% (95% CI, 0.3–1.1%)
Pooled estimate (random effects model)				0.5% (95% CI, 0.3–0.7%)

[a]Author reports results for lags between 0 and 5 days; reported result reflects maximum ozone impact (ozone was significant for 0–2 days, nonsignificant for 3 days and beyond).

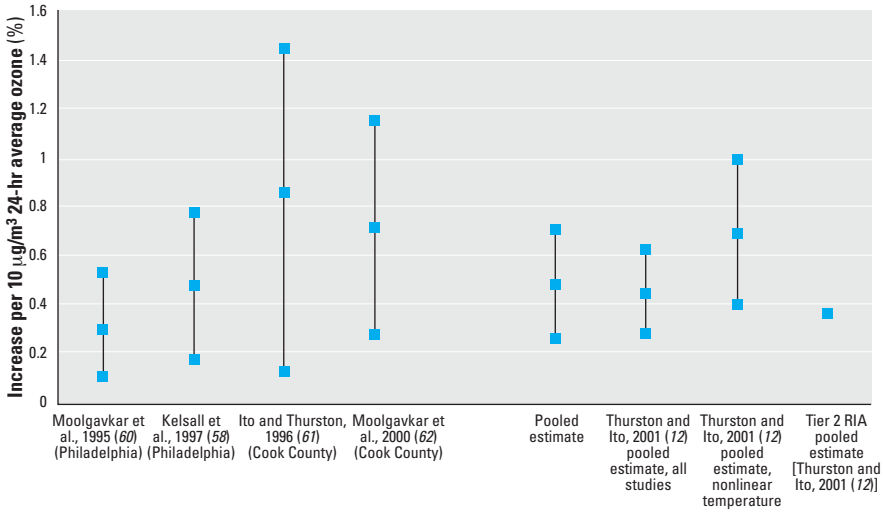

Figure 1. Time-series ozone mortality studies included in our quantitative analysis, along with pooled estimates from past investigations.

nonlinear temperature and humidity terms to synoptic air mass classification (*58,59*). Given the nonlinear relationships and complex interactions, simpler weather terms may not adequately characterize the true relationship between ozone and health. Interestingly, a recent study noted that past ozone time-series studies tended to report lower relative risks when simpler methods were used to control for temperature (*12*). Because this has significant implications for interpreting the epidemiologic literature, there is clearly a need for continued study of whether current statistical methods can rule out weather as a confounder of ozone health effects.

Time-series mortality. To determine the relationship between ozone and daily mortality, we conducted a broad survey of the time-series mortality literature. We evaluated 50 time-series studies from 39 published articles for their relevance and applicability, largely drawn from studies evaluated in a recent PM meta-analysis (*11*) and from a literature search on more recent publications. Our literature survey included all studies incorporated into the recent CAABCA and Tier 2 RIA (*3,4*) and is available from the authors upon request.

Of these 50 estimates, we eliminated all but four using simple screening criteria. Reasons for exclusion included no mention of ozone (19 estimates), studies outside the United States (13), use of linear temperature terms (1), lack of quantitative ozone estimates in any model (5) or in multipollutant models (3), lack of models for ozone that included PM (3), or lack of reported relative risks or standard errors (2). We are left with four studies of either Cook County, Illinois, or Philadelphia, Pennsylvania (*58,60–62*), with overlapping time periods. When we include studies outside the United States, we add two studies from Europe (*63,64*). By way of comparison, the Tier 2 RIA evaluated 28 studies and eliminated all but nine (*4*). Four of these studies were within the United States: the three studies cited above (*58,60,61*) that were published at the time of the Tier 2 RIA and a study that considered temperature as a linear term (*65*). Among our six applicable studies, only the two Cook County studies had PM_{10} as a particulate matter measure, with no studies using $PM_{2.5}$ and the remaining studies using either total suspended particles (TSP) or black smoke.

All four U.S. studies concluded that ozone was a statistically significant predictor of premature mortality (Table 1). We pool the four studies using a random effects model (*66*), yielding an estimated 0.5% increase in premature deaths per 10 μg/m^3 increase in 24-hr average ozone concentrations (95% CI, 0.3%, 0.7%) (Figure 1). If we included the two non-U.S. studies, our pooled estimate would increase slightly to 0.6% (95% CI, 0.4%, 0.9%). Although not stated explicitly, the Tier 2 RIA (and other recent U.S. EPA impact assessments) used a value of 2.9% per 100 ppb increase in 1-hr maximum ozone (*12*), which is similar to our pooled value given standard conversions. Our function can be applied to the all-age background annual mortality rate in the United States of 0.0086 (*67*).

Table 2. Summary of all U.S. time-series studies excluded from pooled analysis in Table 1 that included ozone mortality and used nonlinear temperature controls.

Study	Location and dates	Reported result and ozone measure	Problem	Correlation with PM term	Change in mortality per 10 mg/m^3 of 24-hr average ozone
Dockery et al., 1992 (*70*)	St. Louis, MO 1985–1986	β = 0.00029 per ppb, 24-hr average (95% CI, −0.0012–0.0018)[a]	No copollutants	—	0.1% (95% CI, −0.6–0.9%)
Dockery et al., 1992 (*70*)	Kingston, TN 1985–1986	β = –0.00065 per ppb, 24-hr average (95% CI, −0.0041–0.0028)[a]	No copollutants	—	−0.3% (95% CI, −2.1–1.5%)
Schwartz, 1991 (*69*)	Detroit, MI 1973–1982	Ozone "highly insignificant"	No copollutants, not quantified	—	0% (95% CI, −2–2%)[b]
Shumway et al., 1988 (*68*)	Los Angeles, CA 1970–1979	Ozone not significant in models, no quantitative estimates, highly correlated with temperature	Not quantified	−0.12 (KM)	0% (95% CI, −2–2%)[b]
Gwynn et al., 2000 (*72*)	Buffalo, NY 1988–1990	β = 0.000585 per ppb, 24-hr average, 2-day lag (95% CI, −0.00015–0.0013)[a]	No copollutants	0.68 (PM_{10})	0.3% (95% CI, −0.1–0.7%)
Mar et al., 2000 (*73*)	Phoenix, AZ 1995–1997	Ozone nonsignificant ($p < 0.10$)	Not quantified	−0.20 ($PM_{2.5}$)	0% (95% CI, −2–2%)[b]
Moolgavkar et al., 2000 (*62*)	Los Angeles, CA 1987–1995	Ozone nonsignificant	Not quantified	0.04 ($PM_{2.5}$)	0% (95% CI, −2–2%)[b]
Moolgavkar et al., 2000 (*62*)	Maricopa County, AZ 1987–1995	Ozone nonsignificant	Not quantified	0.00 (PM_{10})	0% (95% CI, −2–2%)[b]
Lippman et al., 2000 (*74*)	Detroit, MI 1985–1990	1.0247 (95% CI, 1.0025–1.0473) per 36 ppb 24-hr average, 1-day lag	No copollutants	0.36 (PM_{10})	0.3% (95% CI, 0.0–0.7%)
Lippman et al., 2000 (*74*)	Detroit, MI 1992–1994	1.04 (95% CI, 0.9667–1.1188) per 28 ppb 24-hr average, 1-day lag	No copollutants	0.49 ($PM_{2.5}$)	0.7% (95% CI, −0.6–2.0%)
Fairley, 1999 (*71*)	Santa Clara, CA 1989–1996	1.05 (nonsignificant) per 33 ppb 8-hr average	$PM_{2.5}$, CO, NO_2 in model; no CI given	−0.15 ($PM_{2.5}$)	1.4% (95% CI, −0.4–3.2%)[c]
Pooled estimate from Table 1					0.5% (95% CI, 0.3–0.7%)
Pooled estimate including above studies					0.4% (95% CI, 0.3–0.5%)
Pooled estimate, minimum variance in unquantified studies					0.3% (95% CI, 0.1–0.6%)

KM, optical measure of carbonaceous particles.
[a]Regression coefficient reported; RR = exp(βx), where x is the concentration increment. [b]We assume 0% for central estimate given no quantified effect; variance assumed to be maximum of all studies in table (minimally informative). [c]Eight-hour average converted to 24-hr average using ratio of 2.5/1.33; variance assumed to be maximum of all studies in table (minimally informative).

Although these four studies provide weak epidemiologic support for ozone mortality, our estimate could be biased because it excludes studies that found ozone to be insignificant but did not fulfill our inclusion criteria. Studies that found ozone to be insignificant in single-pollutant models would have excluded ozone from multipollutant analyses, and it would be inappropriate to discount this information. Similarly, studies that focused on other pollutants and considered ozone as a confounder provide relevant information. Thus, we examine the excluded estimates that used nonlinear temperature terms to determine whether they significantly influence our pooled estimate.

In Table 2, we present an expanded list of U.S. studies with their reported findings and limitations (*62,68–74*). For the studies in which ozone was stated to be insignificant without quantified estimates (*62,68,69,73*), we assume a central estimate of zero and test variances equivalent to both the minimum and the maximum reported in the studies in Table 2. Including the insignificant studies with the above assumptions does not materially influence either the central estimate or the confidence intervals. However, the fact that nearly all of the studies in Table 2 find ozone not to be a significant predictor of premature mortality (including all studies in warmer climates) gives one pause in using our pooled estimate as a representative measure of ozone mortality risks. The lack of significance could demonstrate either that no causal relationship exists or that the low indoor–outdoor ratios imply that many studies have insufficient statistical power to detect the population effects of ozone.

In summary, the time-series mortality literature shows a significant relationship between ozone and premature mortality when PM and nonlinear temperature terms are incorporated, but limited information is available in warmer climates. Possible confounding by weather leaves lingering doubt about whether the ozone findings are causal, an issue that would be difficult to resolve epidemiologically. Evidence of biologic mechanisms and the documented morbidity effects lend credence to the possibility of premature deaths from ozone exposure, but the uncertainties are greater than reflected in pooled literature estimates.

Hospital admissions. Analysts have looked at both respiratory and cardiovascular categories of hospital admissions to determine whether an association with ozone exists. The major respiratory outcomes include acute bronchitis, pneumonia and influenza, COPD, and asthma. Categories examined for cardiovascular outcomes include ischemic heart disease, dysrhythmias, and heart failure. For a control, analysts have examined outcomes believed to be completely unrelated to air pollution, such as appendicitis.

Unlike PM and CO, ozone has not shown a consistent association with cardiovascular hospital admissions (*75–78*), and we do not consider this outcome further. However, significant associations have been observed for respiratory outcomes, especially in the spring and summer. As identified by Thurston and Ito (*79*), three main categories of studies exist: a group of studies conducted in New York, Ontario, and Montreal looking at major respiratory outcomes for all ages, the same group of studies restricted to asthma, and a group of Medicare-based studies in the United States. The identified studies included all studies incorporated into past benefit–cost analyses, except a recent study of Toronto that found risks similar to those in past studies (*80*). The National Morbidity, Mortality, and Air Pollution Study (*81*) did not evaluate ozone as an independent predictor of hospital admissions but found it to be insignificant as a stage-2 parameter in PM models.

Thurston and Ito (*79*) combined the studies in each category using a random effects model, with each contributing study representing a different population in location or time. Since daily 1-hr maximum ozone was the variable most often used, they converted studies using other measures based on information reported in each study or using default conversion factors as described earlier.

All three categories showed similar results. The "all respiratory/all age" category of studies yielded a combined RR of 1.18 (95% CI, 1.10–1.26) per 100 ppb increase in daily 1-hr maximum ozone. The "asthma/all age" category yielded a combined RR of 1.18 (95% CI, 1.07–1.30), with Medicare-based studies yielding a combined RR of 1.19 (95% CI, 1.1–1.26). Although hospital admission patterns could differ between the United States and Canada (given differences in health care systems), the pooled estimates in all categories were similar for both countries.

Because these relative risks are almost identical, we consider only "all respiratory/all age" for benefit–cost analysis (because asthma admissions or admissions for the elderly are a subset of this category). The pooled relative risk implies a 2% increase in respiratory hospital admissions (RHA) per 10 $\mu g/m^3$ increase in 24-hr average ozone concentrations (95% CI, 1–3%). If only the U.S. estimates were used, the estimate would be reduced slightly to 1.7% (95% CI, 1.1–2.3%). Because the estimates are similar, we use the U.S.-based estimate for our case study for simplicity and consistency. As for time-series mortality, this estimate is based exclusively on studies in cold climates. Two Medicare-based studies listed by Thurston and Ito (*79*) were based in a warmer climate (Birmingham, Alabama), and both found no significant relationship. The all-age background annual hospital admission rate for the respiratory categories in the epidemiologic studies is 0.009 (*82*).

Restricted activity days. The term "restricted activity day" (RAD) is defined as any day in which an individual is forced to reduce his or her normal activities because of acute or chronic conditions (*83*). Minor restricted activity days (MRAD) are days with reduced activity that do not result in work or school loss or bed disability, and respiratory restricted activity days (RRAD) are RADs when acute respiratory symptoms were reported.

Only one published study used in past benefit–cost analyses evaluated the relationship between RAD and ozone (*84*). This study determined RAD between 1976 and 1981 from the annual Health Interview Survey, a nationally representative cross-sectional sample of 50,000 households. Restricted activities were taken from 2-week recall surveys of working adults and were regressed against $PM_{2.5}$ (derived from airport visibility data) and ozone in each year. Ozone concentrations were highly correlated with the temperature term but not with $PM_{2.5}$. For RRAD, ozone was not statistically significant in any year. For MRAD, in multipollutant models the authors reported that an inverse-variance weighting yielded a 0.2% increase per microgram per cubic meter increase in 2-week average 1-hr maximum ozone concentrations. No uncertainty bounds were reported, but a simple variance estimate based on reported standard deviations by year yields a 95% confidence interval of 0.1–0.3%.

Although this study found a significant and plausible relationship, some statistical issues make the estimate somewhat uncertain. First, temperature is incorporated linearly and is highly correlated with ozone, which decreases our certainty that we are properly measuring the independent ozone effect. In addition, the reported pooled value is based on the assumption that the three years without positive and significant estimates should be assigned a value of zero (the regression coefficient is significantly negative in 1977 and 1981 and is positive but nonsignificant in 1976). There is reason to believe that nonsignificant slopes should be included as calculated because a regression across all 6 years would incorporate these data. Using the reported central estimates and standard deviations for all years reduces the concentration–response to 0.1% (95% CI, 0.05–0.2%).

Although no other studies have evaluated MRAD, other epidemiologic studies of

respiratory symptoms have been used for comparison. In the Tier 2 RIA (*4*), a study by Krupnick and colleagues (*85*) was pooled with the MRAD estimate to yield a single estimate of ozone restricted activities. This study found that a 1% increase in high-hour ozone concentrations corresponded with a 0.073% increase in any of 19 respiratory symptoms (a 0.04% increase per microgram per cubic meter increase in high-hour ozone). Comparability with the MRAD estimate is impaired by the differences in averaging time, symptom severity, and study population. However, the concentration–response is reported to be greater for MRAD, the more severe health outcome. Because of differences in health effects, study populations, and treatment of confounders, pooling these two studies does not seem appropriate.

In summary, the magnitude of the impact of ozone on MRAD should be considered somewhat uncertain, given that only one older study with statistical issues is available. Alternative methods to pool the six years of data tend to decrease the effect estimate, whereas incorporation of nonlinear temperature terms could increase the effect estimate (*79*). It is our judgment that a 0.1% increase in MRAD per $\mu g/m^3$ increase in 2-week average 1-hr maximum ozone concentrations (equivalent to a 3% increase per 10 $\mu g/m^3$ increase in 24-hr concentrations) is an appropriate best estimate. A 0.2% increase, reflecting the reported estimate (*84*) or the possible influence of linear temperature controls, would be an upper bound. A lower bound of 0.05% would reflect the 19 symptom findings (*85*). We place probability weights of 50% on the central estimate and 25% on the upper and lower bounds, and we use a background MRAD rate of 7.8 per person per year (*84*).

Case Study: Estimation of Concentration–Response Functions for Houston

For a case study of benefits from ozone reductions in Houston, no epidemiologic studies are currently available for the city or for cities with similar climates. Because of differences in exposure patterns, it may not be appropriate to directly apply findings from colder locations. Our approach is to determine "scaling factors" that represent personal exposures per unit concentration, which can be used to extrapolate findings from studies in different climates. Our model is a first approximation, and we provide broad uncertainty bounds to reflect this fact.

Based on the exposure assessment literature for ozone, key components of an exposure-related scaling factor are time spent indoors versus outdoors and time spent indoors with and without air conditioning. For simplicity, we derive our central estimate of mean personal exposure using a simplified microenvironmental model (*37*). In our model,

$$E = C_o F_o + (I_o \times C_o) F_i \Rightarrow SF = F_o + I_o F_i,$$

where E = mean personal exposure concentration (micrograms per cubic meter); C_o = outdoor ozone concentration (micrograms per cubic meter); F_o = fraction of time spent outdoors; F_i = fraction of time spent indoors without air conditioning; I_o = indoor/outdoor ratio without air conditioning; SF = scaling factor. This model assumes that time spent indoors with air conditioning results in minimal ozone exposure (*2,37*).

We assume that the indoor-outdoor ratio without air conditioning (I_0) equals 0.5 (*2*). For simplicity, we assume that ozone exposures while in transport are equivalent to outdoor concentrations and that all time spent indoors is equivalent to residential indoors. We use national average time-activity pattern data (given small regional differences) to estimate that F_o = 0.14 (*34*). To determine F_i, we need to know both the prevalence of air conditioning and the frequency of its use. We assume that air conditioning is used any day when the maximum temperature exceeds 90°F (a simplification that ignores humidity).

Thus, our final scaling factor formula is

$$SF = 0.14 + (0.5)(0.86) \times [(1–AC) + AC(1 – HOT)],$$

where AC = prevalence of air conditioning and HOT = fraction of days with maximum temperature above 90°F. This formula reflects the fact that time can be spent in non–air-conditioned homes either when a home lacks air conditioning or when the outside temperature is low.

To derive the scaling factors, we estimated the prevalence of air conditioning from the American Housing Survey for a year representative of the epidemiologic study dates for all U.S. studies (*86*). Temperature values were taken from National Climatic Data Center reports from each city for all study dates (*87*).

Using the derived scaling factors (Table 3), we found the personal exposures per unit concentration to be almost identical in every location but Houston, where the scaling factor is approximately 25% lower. This difference is perhaps less than anticipated or indicated by the limited epidemiologic evidence. The small difference is largely related to our assumption that air conditioning is used across only a fraction of the year in all settings. To bound our scaled concentration–response estimates for Houston appropriately, we consider two extremes. As an upper bound, we assume that no scaling is required. As a lower bound, we assume that air conditioning is on at all times when present, which makes our scaling factor equal to 0.14 + 0.43(1–AC).

For time-series mortality and RHA in Houston, our central estimate is the central estimate when studies are pooled using the scaling factor adjustment. Our lower bound is the 5% confidence value with the lower bound scaling factor, and our upper bound is the 95% confidence value with no scaling factor. We assign probability weights of 50% to the central estimate and 25% to the extremes. Similarly, for MRAD, we apply no scaling, the central scaling factor, and the lower bound scaling factor to the derived upper bound, central estimate, and lower bound (respectively), assigning the same probability weights. For chronic asthma, zero remains our lower bound with a two-thirds weight, and we consider the lower bound scaling factor applied to the AHSMOG central estimate to be our central estimate, with an upper bound as the unscaled AHSMOG central estimate. All values and weights are presented in Table 4.

Monetary Valuation

Premature mortality. There are two primary competing philosophies about the appropriate approach for valuing reductions in premature deaths. The value of statistical life (VSL) approach theoretically represents a "willingness-to-pay" (WTP) framework, in which the dollar amount an individual is willing to pay to avoid a small increase in pollution-based risk is used to value changes in population deaths caused by pollution. The VSL approach is well grounded in economic theory and has been the primary approach used in recent integrated assessments (*3,4,88–90*), but the lack of a market for mortality risks from air pollution implies that WTP in this context must be extrapolated from estimates for other settings.

Alternatively, the medical decision-making field has used measures such as quality-adjusted life years (QALYs) to compare the cost-effectiveness of different medical interventions. QALYs account for self-reported health status and life expectancy, allowing characteristics of at-risk populations to be considered, but QALYs are not directly applicable to benefit–cost comparisons. Values of approximately $100,000 per QALY are often used as a rough upper bound for the desirability of interventions (*91*). There is an active debate about the relative merits of VSL and QALY frameworks, given numerous implications about the relative values of health outcomes and risks to subpopulations. Because resolution of this issue is beyond the scope of our article, we

present mortality valuations under both frameworks.

For VSL, recent assessments have used an estimate derived from a group of 26 "policy-relevant" studies summarized in Viscusi (*92*), which had values ranging from $1 million to $11 million (in 1997 dollars). Twenty-one of the 26 studies consider the additional compensation demanded in the labor market for riskier jobs, with the remaining five studies directly surveying individuals (contingent valuation studies). Although U.S. EPA has recognized the possible importance of adjusting these estimates, its recent benefit–cost studies (*3,4*) have used an unadjusted VSL pooling the 26 studies (mean of $5.8 million, standard deviation of $3.2 million).

For the application of these VSL estimates to be appropriate, they must accurately represent what people who are likely to be affected by air pollution would be willing to pay to reduce their risk of dying within a specified time period. There is considerable uncertainty regarding the appropriate way to adjust VSL between labor market or general population contingent valuation (CV) studies and air pollution applications (*93–95*). This uncertainty is predicated largely on the assumptions that *a*) people who are dying from air pollution differ from the populations studied in the labor market and CV literature; and *b*) that VSL will be different for these populations (because of age, current health status, willingness to accept risk, or other factors).

On the first point, the populations studied in the labor market and CV literature are likely much younger and healthier than the populations affected by air pollution. Recent literature has demonstrated that elderly individuals with serious pre-existing pulmonary or cardiovascular disease are at greater risk from PM (*96*). Although we are not aware of a similar investigation for ozone, the fact that ozone likely has a disproportionate impact on individuals with COPD or other respiratory diseases lends credence to this argument.

For the second point, we must be able to extrapolate from young-to-middle-aged workers who accept hazardous jobs (and therefore might have lower VSL than those who do not) to older individuals who are likely in worse health. Several researchers (*97–100*) have examined how tradeoffs between income and mortality risk are expected to vary over the life cycle (*91*). This pattern would be influenced by two opposing factors: The number of future life-years at risk declines with age, but so does the opportunity cost of spending on risk reduction. Shepard and Zeckhauser (*98*) estimate that VSL is about half the level at age 65 as at age 40. On the other hand, Ng (*100*) argues that people discount their future utility at a rate smaller than the market interest rate, and therefore that VSL could conceivably rise until a relatively old age (e.g., 65 or so) before it would begin to fall.

Given this uncertainty, it is difficult to support a specific adjustment to the VSL reported by the EPA based on any possible diminished length or quality of life. An age-adjusted VSL would clearly be more appropriate than an unadjusted value, but given uncertainties regarding the magnitude and even direction of this effect, the EPA mean value of $5.8 million is one reasonable estimate for the valuation of premature mortality.

Alternatively, a QALY-based approach would take into account the remaining life expectancy and health status of individuals at risk from air pollution. We focus only on estimating the average length of life lost in ozone-related deaths, which is quite uncertain. This is similar to using the method of value of statistical life year (VSLY). Using this concept, we assign a constant value per year of life lost, although the idea that VSLY would be constant is inconsistent with standard economic theory (because the opportunity cost of spending depends on age).

An upper bound on life-years lost would assume that persons dying from acute ozone exposure have a life expectancy equal to their age cohort. We make a simplifying assumption that these are all individuals with COPD. Given U.S. life expectancies of 14 years at age 70, 8 years at age 80, and 4 years at age 85, this approach would yield an estimate of approximately 10 years of lost life per death given the age distribution of deaths for COPD in the U.S. population (*101*). Because individuals with COPD would be expected to have a shorter life expectancy than their age cohort, this is likely an overestimate.

A more realistic estimate of life expectancy loss would take into account the poor health of at-risk persons relative to their age cohort. A recent statistical analysis concluded that the life expectancy loss associated with acute PM exposure is at least several months for

Table 3. Derivation of scaling factors for a hypothetical case study of ozone concentration reductions in Houston, TX.

Health effect, study site/years	Residential air conditioning prevalence (year of data)	Percentage of days with maximum temperature > 90°F	Scaling factor (lower bound estimate)
Time-series mortality			
Philadelphia, PA;1973–1988	69% (1982)	7%	0.96 (0.41)
Cook County, IL;1985–1995	71% (1987)	5%	0.97 (0.39)
Chronic asthma			
San Francisco, San Diego, Los Angeles, CA; 1977–1992	34%[a]	1%[a]	1.00 (0.71)
Respiratory hospital admissions			
Buffalo, NY; 1988	27% (1988)	5%	0.99 (0.77)
New York City; 1988	57% (1987)	7%	0.97 (0.51)
Minor restricted activity days			
United States,1976–1981	50% (1978)	10% (estimated)	0.96 (0.57)
Houston, TX	96% (1995)	30%	0.75 (0.17)

[a]Average across all three cities, given no information about number of participants in each location. Air conditioning prevalence taken from 1985 San Francisco (19%), 1989 Los Angeles (50%), and 1987 San Diego (33%) data.

Table 4. Concentration–response functions for a hypothetical case study of ozone concentration reductions in Houston (% increase in outcome per 10 μg/m^3 increase in 24-hr average ozone concentrations).

Outcome	Affected population	Lower bound (weight)	Central value (weight)	Upper bound (weight)
Time-series mortality	All ages	0.2% (0.25)	0.4% (0.50)	0.7% (0.25)
Chronic asthma incidence[a]	Nonasthmatic, nonsmoking males, age ≥ 27	0% (0.67)	6% (0.17)	23% (0.17)
Respiratory hospital admissions	All ages	0.4% (0.25)	1% (0.50)	2% (0.25)
Minor restricted activity days[b]	Age ≥ 18	0.4% (0.25)	2% (0.50)	5% (0.25)

Weights are subjectively determined by authors, based on strength of literature, consistency, and representativeness. [a]Based on twenty-year average concentrations; percentage increase refers to incident cases of asthma (baseline rate of 0.22%). [b]Based on two-week average concentrations.

Table 5. Summary of derived monetary valuations of ozone-related health outcomes (in 1997 dollars).

Outcome	Lower bound (weight)	Central value (weight)	Upper bound (weight)
Time-series mortality	$100,000 (0.5)	–	$5,800,000 (0.5)
Chronic asthma incidence	$15,000 (0.25)	$31,000 (0.5)	$60,000 (0.25)
Respiratory hospital admissions	$10,000 (0.25)	$20,000 (0.5)	$40,000 (0.25)
Minor restricted activity days	$20 (0.25)	$47 (0.5)	$75 (0.25)

all-cause mortality, but on the order of weeks for COPD (*102*). Even if the all-cause mortality finding holds for ozone, current statistical methods cannot distinguish whether the air pollution deaths involve an average loss of only three months or a longer loss of life. Another relevant data point: If the average person dying from ozone exposure had previously been admitted to an ICU for COPD, then evidence from the medical literature tells us that the life expectancy loss would be on the order of months (*103*).

Given the uncertainties in the loss of life, it is difficult to provide a definitive QALY-based value. A reasonable estimate would be that the life expectancy lost per death is on the order of a year, implying that a QALY approach would yield an economic value of approximately $100,000 per ozone-related death. This may be an underestimate for elderly individuals who have a reduced opportunity cost of spending, as illustrated by a recent CV study that found VSL among individuals over age 70 to be approximately $500,000, with similar values for those in poorer health (*104*). Furthermore, because this study was conducted on Canadian individuals (and converted to U.S. currency), the existence of national health care may imply that the study subjects may be willing to pay less for risk reduction than would U.S. subjects.

It is clear that there is a broad range between our lower bound QALY-based estimate ($100,000) and our upper bound VSL-based estimate ($5.8 million), with each estimate having significant uncertainties. Clearly, the degree of belief placed on the appropriate valuation framework will strongly influence any benefit estimation and policy decision. For simplicity, we assign each estimate a weight of 50%, but we strongly encourage that any benefit–cost analysis evaluate this weighting carefully and determine whether policy formulations are driven by the weights placed on these valuations.

Chronic asthma. For chronic asthma, two valuation studies were cited by U.S. EPA (*105,106*). In the first investigation, both dichotomous choice and bidding game methods were used to determine WTP for a cure for asthma, with mean monthly values of $343 and $189, respectively. In dichotomous choice, the respondent accepts or rejects single prices for a risk reduction, with the WTP estimated by varying the price across respondents. Bidding game changes the price for the respondent until the maximum WTP is reached (either by increasing or decreasing the price). U.S. EPA (*4*) used the bidding game value, assuming a 5% discount rate and average male life expectancy, to yield a value of $37,000 per case (in 1997 dollars). In the second study (*106*), the authors reported WTP values ranging from $1,000 to $3,700 per year (depending on model form), with a value of $1,500 selected by the U.S. EPA (corresponding to $23,000 per case). The U.S. EPA then used a triangular distribution centered at $31,000 for its benefit–cost evaluation.

We feel that this triangular distribution underestimates the uncertainty in the valuation of chronic asthma, partly because of significant issues related to the generalizability of the two WTP studies. The former analysis considered a convenience sample of 69 patients in Kentucky, whereas the latter study included 51 individuals from the same region of Kentucky as well as 95 people recruited from an internet newsgroup for asthma sufferers. Because of this, O'Conor and Blomquist (*106*) state explicitly that "the sample was convenience-based and not readily suitable for drawing inferences regarding the general population" (p. 673). In addition, there are uncertainties associated with the statistical model, the discount rates, and the time horizons.

We select the U.S. EPA estimate of $31,000 as our central estimate, given a lack of systematic bias in the uncertainties described above (Table 5). As our lower bound, we consider a cost-of-illness (COI) estimate, which we would expect to be less than the WTP to cure the disease. A recent assessment of U.S. medical costs found that adults with asthma incur an average of approximately $800 per year in direct (doctor visits and medication) and indirect (work days lost) expenses (*107*). If we assume this cost to remain across the lifetime of the individual, then a reasonable COI estimate for the elimination of asthma in an adult would be approximately $15,000 (in 1997 dollars, 5% discount rate). Our upper bound is taken from the highest central value reported by O'Conor and Blomquist (*106*), which translates to approximately $60,000 per case.

Hospital admissions. For hospital admissions, no WTP studies were included in the U.S. EPA assessments or were identified in our literature search. Thus, the U.S. EPA assessments (*3,4*) estimated the COI associated with "all cause" RHA to be $10,000, based on medical costs and lost work time. However, direct application of COI values likely underestimates the total social costs of hospitalization. Studies of both WTP and COI for changes in asthma symptoms (*108,109*) or angina (*110*) found that the ratio of WTP to COI ranged from 1.3 to 4. Thus, although the U.S. EPA opted not to apply a scaling factor to the RHA COI estimates, a realistic best estimate would likely be a factor of two greater than the COI ($20,000). We consider the COI ($10,000) as a lower bound and place an upper bound at four times the COI ($40,000) (Table 5).

Minor restricted activity days. To our knowledge, no studies have directly evaluated the WTP to avoid an MRAD. The estimate generally used is based on WTP estimates for a three-symptom combination of coughing, throat congestion, and sinusitis (*111*). In 1997 dollars, the WTP estimate was $47, and this estimate was bounded by considering a lower bound of $20 for the mildest symptom evaluated (eye irritation) and selecting an upper bound of $75 to fit a triangular distribution (*52*). The upper bound is somewhat arbitrary, but it is argued (*52*) that an MRAD should be valued as less than a work-loss day ($104 in 1997 dollars). Although there are uncertainties associated with the application of WTP for selected symptoms rather than specific restrictions of activity, the U.S. EPA distribution seems appropriate, and an accurate WTP estimate for MRAD would be unlikely to extend beyond this range (Table 5). It is worth noting that WTP is generally a concave function of duration of morbidity, which may imply that these estimates could vary somewhat for episodes with different durations.

Discussion

Our overview of the relevant literature for ozone benefit–cost analyses raises a few major issues. Although the epidemiologic literature yields coherent and plausible findings, interpretation and extrapolation are impaired by the small number of available studies and the lack of geographic diversity. Since time–activity patterns and the presence of air conditioning can influence ozone exposures, it is difficult to determine whether study findings are applicable across settings. Based on the exposure assessment literature and limited information from epidemiologic investigations, the benefits of ozone concentration reductions appear to be lower in hot and humid climates with prevalent air conditioning.

There are a few disquieting implications of this conclusion. First, although it appears that ozone can influence respiratory health given sufficient exposure, benefit–cost analyses based on values reflecting air conditioning levels may conclude that controls are not cost-effective. However, individuals in these warmer climates who spend most of their day outdoors or who do not have air conditioning (likely lower-income individuals) would be placed at risk from a policy limiting ozone controls. This has equity concerns and it violates the Clean Air Act concept of protection of "sensitive or susceptible individuals or groups" (*112*). Furthermore, an optimal policy based on the premise of lower indoor exposures might argue that susceptible individuals should stay indoors as much as possible to avoid known health impacts in

the outdoor environment. Most policy makers would feel some unease with that conclusion, and the ubiquity of indoor air pollution might imply that these individuals would ultimately be worse off.

Using the estimates and probability weights in Tables 4 and 5, we can calculate a simple distribution of health benefits and the leading contributors to uncertainty (Figure 2). Our central estimate is that a 1-μg/m^3 decrease in annual average ozone concentrations would lead to an annual benefit of approximately $10 per individual (95% CI, $0.70–40). Nearly 90% of this total is related to premature mortality, with MRAD as the next largest effect. By way of comparison, in the Tier 2 RIA, annual health benefits projected for 2030 for ozone-related endpoints were approximately $260 million [Table VII-12 (*4*)]. The population average concentration reduction from May to September was 0.5 ppb, which translates to 0.4 μg/m^3 annual average if formation is minimal in other months. Given a projected at-risk population of 345 million (*4*), health benefits are approximately $2/person/μg/m^3 annual average. Our central estimate is greater due to the inclusion of mortality. Although the probability distribution has limited interpretability given our discrete weighting approach, it is apparent that the uncertainty regarding the appropriate monetary value for mortality contributes most to overall uncertainty, followed by the concentration–response function for mortality (Figure 2).

Future research should focus on those health outcomes and topics for which reduced uncertainty or different values could lead to different policy options. Although it is difficult to determine the key areas of research without a comprehensive value-of-information analysis, our initial benefit estimation and preliminary evaluation of uncertainty lead us to conclude that the following studies are warranted:

- Willingness-to-pay studies targeted at individuals susceptible to air pollution health risks (e.g., elderly individuals with COPD)
- Further research on the life expectancy loss associated with ozone-related mortality
- Epidemiologic investigations centered on ozone in a range of climates, especially time-series studies of premature mortality and minor restricted activity days (including issues of the relevant exposure window/averaging time)
- Investigations of indoor/outdoor/personal exposure patterns in a range of geographic settings, to strengthen our knowledge of the relationship between concentration and exposure as a function of air conditioning, climate, and activity patterns.

As mentioned earlier, these conclusions are based on our interpretation of the existing literature. Although we feel that the general conclusions of our analysis are supported by the literature we surveyed, other researchers might derive different quantitative estimates and characterizations of uncertainty. The goal of our investigation was to flag the important questions and to make a first attempt at addressing these questions, but a larger-scale effort involving experts from all disciplines is warranted to refine this analysis.

Although we have broadly considered the major issues related to ozone benefit estimation, a comprehensive benefit–cost analysis should consider multiple additional dimensions. Because ozone is a secondary product of reactions between NO_x and volatile organic compounds, any control strategy must focus on one or both of these. Reduced NO_x emissions will also influence concentrations of pollutants other than ozone, including reduced formation of secondary nitrate particles, acidic precipitation, and gaseous NO_2. A comprehensive benefit–cost analysis should account for the health benefits associated with these pollutants, along with visibility and other nonhealth endpoints. On the other hand, it has been argued that tropospheric ozone can be protective, through reductions in UV-β radiation and associated reductions in skin cancer and cataracts (*113,114*). It is unclear whether any of these endpoints would materially influence control decisions for ozone precursors, but any benefit–cost analysis of ozone mitigation should include these ancillary benefits and risks.

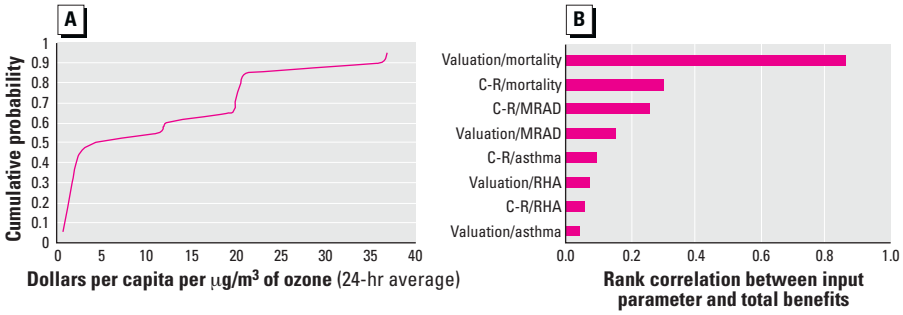

Figure 2. Distribution of health benefits from ozone concentration reductions (dollars/person/year/μg/m^3 decrease in 24-hr average concentration) and major contributors to uncertainty. C-R, concentration–response function.

Conclusions

Our objective in this paper was to survey the limited evidence used to estimate benefits of ozone mitigation and to discuss some of the underlying uncertainties. We found biologically plausible evidence of mortality and respiratory morbidity from ozone exposure, but the limited number of studies and possible geographic variations in concentration–response functions lead to uncertainties in specific applications. Uncertainties regarding the approach for valuation of premature death are substantial, partly because past studies of willingness to pay have not focused on the populations most affected by ozone. We determined that the benefits of ozone reduction may be greater than previously estimated because of the possible independent effect of ozone on premature mortality, but this conclusion is contingent on the economic value placed on mortality. Future research should focus on ozone-related mortality, both refining the monetary valuation and evaluating the evidence in varied climates to confirm hypothesized exposure-related trends.

References and Notes

1. U.S. Environmental Protection Agency. National Ambient Air Quality Standards for Ozone; final rule. 40 CFR Part 50. Fed Reg 62(138):1–37 (1997).
2. U.S. EPA. Air Quality Criteria for Ozone and Related Photochemical Oxidants. EPA/600/P-93/004cF. Washington, DC:U.S. Environmental Protection Agency, Office of Research and Development, 1996.
3. U.S. EPA. The Benefits and Costs of the Clean Air Act: 1990 to 2010. EPA-410-R99-001. Washington, DC:U.S. Environmental Protection Agency, Office of Air and Radiation, 1999.
4. U.S. EPA. Regulatory Impact Analysis – Control of Air Pollution from New Motor Vehicles: Tier 2 Motor Vehicle Emissions Standards and Gasoline Sulfur Control Requirements. EPA420-R-99-023. Washington, DC:U.S. Environmental Protection Agency, Office of Air and Radiation, 1999.
5. Dockery DW, Pope CA III. Acute respiratory effects of particulate air pollution. Annu Rev Public Health 15:107–132 (1994).
6. Moolgavkar SH, Luebeck EG. A critical review of the evidence on particulate air pollution and mortality. Epidemiology 7:420–428 (1996).
7. Pope CA III, Bates DV, Raizenne M. Health effects of particulate air pollution: time for reassessment? Environ Health Perspect 103:472–480 (1995).
8. Pope CA III, Dockery DW, Schwartz J. Review of epidemiologic evidence of health effects of particulate air pollution. Inhal Toxicol 7:1–18 (1995).
9. Schwartz J. Air pollution and daily mortality. Environ Res 64:36–52 (1994).
10. Thurston GD. A critical review of PM_{10}-mortality time-series studies. J Exp Anal Environ Epidemiol 6:3–21 (1996).
11. Levy JI, Hammitt JK, Spengler JD. Estimating the mortality impacts of particulate matter: what can be learned from between-study variability? Environ Health Perspect 108:109–117 (2000).
12. Thurston GD, Ito K. Epidemiologic studies of acute ozone exposures and mortality. J Exp Anal Environ Epidemiol 11:286–294 (2001).
13. Hill AB. The environment and disease: association or causation? Proc R Soc Med 58:295–300 (1965).

14. Mudway IS, Kelly FJ. Ozone and the lung: a sensitive issue. Mol Aspects Med 21:1–48 (2000).
15. Paige RC, Plopper CG. Acute and chronic effects of ozone in animal models. In: Air Pollution and Health (Holgate ST, Samet JM, Koren HS, Maynard RL, eds). London:Academic Press, 1999;531–557.
16. Powell CV, Nash AA, Powers HJ, Primhak RA. Antioxidant status in asthma. Pediatr Pulmonol 18:3–38 (1994).
17. Kinney PL, Thurston GD, Raizenne M. The effects of ambient ozone on lung function in children: a reanalysis of six summer camp studies. Environ Health Perspect 104:170–174 (1996).
18. Korrick SA, Neas LM, Dockery DW, Gold DR, Allen GA, Hill LB, Kimball KD, Rosner BA, Speizer FE. Effects of ozone and other pollutants on the pulmonary function of adult hikers. Environ Health Perspect 106:93–99 (1998).
19. Spektor DM, Lippmann M, Thurston GD, Lioy PJ, Stecko J, O'Connor G, Garshick E, Speizer FE, Hayes C. Effects of ambient ozone on respiratory function in healthy adults exercising outdoors. Am Rev Respir Dis 138:821–828 (1988).
20. Hazucha MJ, Bates DV, Bromberg PA. Mechanism of action of ozone on the human lung. J Appl Physiol 67:1535–1541 (1989).
21. Passanante AN, Hazucha MJ, Bromberg PA, Seal E, Folinsbee L, Koch G. Nociceptive mechanisms modulate ozone-induced human lung function decrements. J Appl Physiol 85:1863–1870 (1998).
22. Schelegle ES, Adams WC, Siefkin AD. Indomethacin pretreatment reduces ozone-induced pulmonary function decrements in human subjects. Am Rev Respir Dis 136:1350–1354 (1987).
23. Ying RL, Gross KB, Terzo TS, Eschenbacher WL. Indomethacin does not inhibit the ozone-induced increase in bronchial responsiveness in human subjects. Am Rev Respir Dis 142:817–821 (1990).
24. Folinsbee LJ, McDonnell WF, Horstman DH. Pulmonary function and symptom responses after 6.6-hour exposure to 0.12 ppm ozone with moderate exercise. J Air Pollut Control Assoc 38:28–35 (1988).
25. Horstman DH, Folinsbee LJ, Ives PJ, Abdul-Salaam S, McDonnell WF. Ozone concentration and pulmonary response relationship for 6.6-hour exposures with five hours of moderate exercise to 0.08, 0.10, and 0.12 ppm. Am Rev Respir Dis 142:1158–1159 (1990).
26. Harkema JR, Plopper CG, Hyde DM, St. George JA, Wilson DW, Dungworth DL. Response of macaque bronchiolar epithelium to ambient concentrations of ozone. Am J Pathol 143:857–866 (1993).
27. Plopper CG, Harkema JR, Last JA, Pinkerton KE, Tyler WS, St. George JA, Wong VJ, Nishio SJ, Weir AS, Dungworth DL, et al. The respiratory system of nonhuman primates responds more to ambient concentrations of ozone than does that of rats. In: Tropospheric Ozone and the Environment (Berglund RL, Lawson DR, McKee DJ, eds). Pittsburgh, PA:Air and Waste Management Association, 1991;137–150.
28. Pinkerton KE, Dodge DE, Cederdahl-Demmler J, Wong VJ, Peake J, Haselton CJ, Mellick PW, Singh G, Plopper CG. Differentiated bronchial epithelium in alveolar ducts of rats exposed to ozone for 20 months. Am J Pathol 142:947–956 (1993).
29. Chang LY, Huang Y, Stockstill BL, Graham JA, Grose EC, Menache MG, Miller FJ, Costa DL, Crapo JD. Epithelial injury and interstitial fibrosis in the proximal alveolar regions of rats chronically exposed to a simulated pattern of urban ambient ozone. Toxicol Appl Pharmacol 115:241–252 (1992).
30. Last JA, Gelzleichter T, Harkema J, Parks WC, Mellick P. Effects of 20 months of ozone exposure on lung collagen in Fisher 344 rats. Toxicology 84:83–102 (1993).
31. Mariassy AT, Abraham WM, Phipps RJ, Sielczak MW, Wanner A. Effects of ozone on the postnatal development of lamb mucociliary apparatus. J Appl Physiol 68:2504–2510 (1990).
32. Tyler WS, Tyler NK, Last JA, Gillespie MJ, Barstow TJ. Comparison of daily and seasonal exposures of young monkeys to ozone. Toxicology 50:131–144 (1988).
33. Sherwin RP, Richters V. Centriacinar (CAR) disease in the lungs of young adults: a preliminary report. In: Tropospheric Ozone and the Environment (Berglund RL, Lawson DR, McKee DJ, eds). Pittsburgh, PA:Air and Waste Management Association, 1991;178–196.
34. U.S. EPA. Descriptive Statistics Tables from a Detailed Analysis of the National Human Activity Pattern Survey (NHAPS) Data. EPA/600/R-95/148. Washington, DC:U.S. Environmental Protection Agency, Office of Research and Development, 1996.
35. Zhang J, Lioy PJ. Ozone in residential air: concentrations, I/O ratios, indoor chemistry, and exposures. Indoor Air 4:95–105 (1994).
36. Avol EL, Navidi WC, Colome SD. Modeling ozone levels in and around Southern California homes. Environ Sci Technol 32:463–468 (1998).
37. Liu L-JS, Delfino R, Koutrakis P. Ozone exposure assessment in a Southern California community. Environ Health Perspect 105:58–65 (1997).
38. Schwartz J. Health effects of air pollution from traffic: ozone and particulate matter. In: Health at the Crossroads: Transport Policy and Urban Health (Fletcher T, McMichael AJ, eds). New York:John Wiley, 1997.
39. Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. An association between air pollution and mortality in six US cities. N Engl J Med 329:1753–1759 (1993).
40. Pope CA III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Health CW Jr. Particulate air pollution as a predictor of mortality in a prospective study of US adults. Am J Respir Crit Care Med 151:669–674 (1995).
41. Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knutsen SF, Beeson WL, Yang JX. Long-term inhalable particles and other air pollutants related to mortality in nonsmokers. Am J Respir Crit Care Med 159:373–382 (1999).
42. Krewski D, Burnett RT, Goldberg MS, Hoover K, Siemiatycki J, Jarrett M, Abrahamowicz M, White WH, et al. Particle Epidemiology Reanalysis Project. Part II: Sensitivity Analyses. Cambridge, MA:Health Effects Institute, 2000.
43. Schunemann HJ, Dorn J, Grant BJB, Winkelstein W Jr, Trevisan M. Pulmonary function in a long-term predictor of mortality in the general population: 29-year follow-up of the Buffalo Health Study. Chest 118:656–664 (2000).
44. Beaty TH, Newill CA, Cohen BH, Tockman MS, Bryant SH, Spurgeon HA. Effects of pulmonary function on mortality. J Chronic Dis 38:703–710 (1985).
45. Lange P, Nyboe J, Appleyard M, Jensen G, Schnohr P. Spirometric findings and mortality in never-smokers. J Clin Epidemiol 43:867–873 (1990).
46. Hole DJ, Watt GC, Davey-Smith G, Hart CL, Gillis CR, Hawthorne VM. Impaired lung function and mortality risk in men and women: findings from the Renfrew and Paisley prospective population study. Br Med J 313:711–715 (1996).
47. Ryan G, Knuiman MW, Divitini ML, James A, Musk AW, Bartholomew HC. Decline in lung function and mortality: the Busselton Health Study. J Epidemiol Community Health 53:230–234 (1999).
48. Evans J, Wolff S. Modeling of air pollution impacts: one possible explanation of the observed cohort mortality. In: Particles in Our Air (Wilson R, Spengler J, eds). Cambridge, MA:Harvard University Press, 1996;189–204.
49. McDonnell WF, Abbey DE, Nishino N, Lebowitz MD. Long-term ambient ozone concentration and the incidence of asthma in nonsmoking adults: the AHSMOG study. Environ Res 80:110–121 (1999).
50. Peters JM, Avol E, Navidi W, London SJ, Gauderman WJ, Lurmann F, Linn WS, Margolis H, Rappaport E, Gong H Jr, et al. A study of twelve Southern California communities with differing levels and types of air pollution. I. Prevalence of respiratory morbidity. Am J Respir Crit Care Med 159:760–767 (1999).
51. Zemp E, Elsasser S, Schindler C, Kunzli N, Perruchoud AP, Domenighetti G, Medici T, Ackermann-Liebrich U, Leuenberger P, Monn C, et al. Long-term ambient air pollution and respiratory symptoms in adults (SAPALDIA study). Am J Respir Crit Care Med 159:1257–1266 (1999).
52. Abt Associates. Final Tier 2 Rule: Air Quality Estimation, Selected Health and Welfare Benefits Methods, and Benefits Analysis Results. EPA420-R-99-032. Research Triangle Park, NC:U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, 1999.
53. Kalkstein LS, Barthel CD, Ye H, Smoyer KE, Cheng S. The differential impact of weather and pollution on human mortality. Publication in Climatology 50. Newark, DE:Department of Geography, Center for Climatic Research, University of Delaware, 1997.
54. Larson U. The effects of monthly temperature fluctuations on mortality in the United States from 1921–1985. Int J Biometeorol 34:136–145 (1990).
55. Jamason PF, Kalkstein LS, Gergen PJ. A synoptic evaluation of asthma hospital admissions in New York City. Am J Respir Crit Care Med 156:1781–1788 (1997).
56. Kalkstein LS, Davis RE. Weather and human mortality: an evaluation of demographic and interregional responses in the United States. Annals Assoc Am Geogr 79:44–64 (1989).
57. Kalkstein LS, Greene JS. An evaluation of climate/mortality relationships in large U.S. cities and the possible impact of a climate change. Environ Health Perspect 105:84–93 (1997).
58. Kelsall JE, Samet JM, Zeger SL, Xu J. Air pollution and mortality in Philadelphia, 1974–1988. Am J Epidemiol 146:750–762 (1997).
59. Pope CA III, Kalkstein LS. Synoptic weather modeling and estimates of the exposure–response relationship between daily mortality and particulate air pollution. Environ Health Perspect 104:414–420 (1996).
60. Moolgavkar SH, Luebeck EG, Hall TA, Anderson EL. Air pollution and daily mortality in Philadelphia. Epidemiology 6:476–484 (1995).
61. Ito K, Thurston GD. Daily PM_{10}/mortality associations: an investigation of at-risk subpopulations. J Expo Anal Environ Epidemiol 6:79–95 (1996).
62. Moolgavkar SH. Air pollution and daily mortality in three U.S. counties. Environ Health Perspect 108:777–784 (2000).
63. Hoek G, Schwartz JD, Groot B, Eilers P. Effects of ambient particulate matter and ozone on daily mortality in Rotterdam, the Netherlands. Arch Environ Health 52:455–463 (1997).
64. Touloumi G, Katsouyanni K, Zmirou D, Schwartz J, Spix C, Ponce de Leon A, Tobias A, Quennel P, Rabczenko D, Bacharova L, et al. Short-term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project. Am J Epidemiol 146:177–185 (1997).
65. Kinney PL, Ito K, Thurston GD. A sensitivity analysis of mortality/PM_{10} associations in Los Angeles. Inhal Toxicol 7:59–69 (1995).
66. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 7:177–188 (1986).
67. Murphy SL. Deaths: Final data for 1998. National Vital Statistics Reports 48(11). Hyattsville, MD:National Center for Health Statistics, 2000.
68. Shumway RH, Azari AS, Pawitan Y. Modeling mortality fluctuations in Los Angeles as functions of pollution and weather effects. Environ Res 45:224–241 (1988).
69. Schwartz J. Particulate air pollution and daily mortality in Detroit. Environ Res 56:204–213 (1991).
70. Dockery DW, Schwartz J, Spengler JD. Air pollution and daily mortality: associations with particulates and acid aerosols. Environ Res 59:362–373 (1992).
71. Fairley D. Daily mortality and air pollution in Santa Clara County, California: 1989–1996. Environ Health Perspect 107:637–641 (1999).
72. Gwynn RC, Burnett RT, Thurston GD. A time-series analysis of acidic particulate matter and daily mortality and morbidity in the Buffalo, New York, region. Environ Health Perspect 108:125–133 (2000).
73. Mar TF, Norris GA, Koenig JQ, Larson TV. Associations between air pollution and mortality in Phoenix, 1995–1997. Environ Health Perspect 108:347–353 (2000).
74. Lippmann M, Ito K, Nádas A, Burnett RT. Association of Particulate Matter Components with Daily Mortality and Morbidity in Urban Populations. Cambridge, MA:Health Effects Institute, 2000.
75. Schwartz J, Morris R. Air pollution and hospital admissions for cardiovascular disease in Detroit, Michigan. Am J Epidemiol 142:23–35 (1995).
76. Burnett RT, Dales RE, Brook JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. Epidemiology 8:162–167 (1997).
77. Schwartz J. Air pollution and hospital admissions for cardiovascular disease in Tucson. Epidemiology 8:371–377 (1997).
78. Schwartz J. Air pollution and hospital admissions for heart disease in eight U.S. counties. Epidemiology 10:17–22 (1999).
79. Thurston GT, Ito K. Epidemiologic studies of ozone exposure effects. In: Air Pollution and Health (Holgate ST, Samet JM, Koren HS, Maynard RL, eds). London:Academic Press, 1999;485–510.
80. Burnett RT, Smith-Doiron M, Stieb D, Cakmak S, Brook

JR. Effects of particulate and gaseous air pollution on cardiorespiratory hospitalizations. Arch Environ Health 54:130–139 (1999).
81. Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. The National Morbidity, Mortality, and Air Pollution Study Part II: Morbidity, Mortality, and Air Pollution in the United States. Cambridge, MA:Health Effects Institute, 2000.
82. Owings MF, Lawrence L. Detailed diagnoses and procedures: National Hospital Discharge Survey, 1997. Vital Health Stat 13(145). Hyattsville, MD:National Center for Health Statistics, 1999.
83. Benson V, Marano MA. Current estimates from the National Health Interview Survey, 1993. Vital Health Stat 10(190). Hyattsville, MD:National Center for Health Statistics, 1995.
84. Ostro BD, Rothschild S. Air pollution and acute respiratory morbidity: an observational study of multiple pollutants. Environ Res 50:238–247 (1989).
85. Krupnick AJ, Harrington W, Ostro B. Ambient ozone and acute health effects: evidence from daily data. J Environ Econ Manag 18:1–18 (1990).
86. U.S. Department of Commerce, Bureau of the Census. American Housing Survey, MSA Files. Washington, DC. Available: http://www.icpsr.umich.edu [cited 24 September 2000].
87. U.S. National Climatic Data Center. Annual Climatological Summary. Asheville, NC. Available: http://nndc.noaa.gov [cited 14 October 2000].
88. U.S. EPA. Regulatory Impact Analysis for the Particulate Matter and Ozone National Ambient Air Quality Standards and Proposed Regional Haze Rule. Research Triangle Park, NC:U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, 1997.
89. National Acid Precipitation Assessment Program. 1996 Biennial Report to Congress: An Integrated Assessment. Washington, DC:National Science and Technology Council, Committee on Environment and Natural Resources, 1998.
90. Burtraw D, Krupnick A, Mansur E, Austin D, Farrell D. The Costs and Benefits of Reducing Acid Rain. Discussion Paper 97-31-REV. Washington, DC:Resources for the Future, 1997.
91. Hammitt JK. Valuing mortality risk: theory and practice. Environ Sci Technol 34:1396–1400 (2000).
92. Viscusi WK. Fatal Tradeoffs: Public and Private Responsibilities for Risk. New York:Oxford University Press, 1992.
93. Cropper ML, Subramanian U. Public Choices between Lifesaving Programs. How Important Are Lives Saved? World Bank Policy Research Working Paper 1497. Washington, DC:World Bank, 1995.
94. Revesz RL. Environmental regulation, cost-benefit analysis, and the discounting of human lives. Columbia Law Rev 99:941–1017 (1999).
95. Advisory Council on Clean Air Compliance Analysis. Final Advisory by the Advisory Council on Clean Air Compliance Analysis on the 1999 Prospective Study of Costs and Benefits of Implementation of the Clean Air Act Amendments (CAAA). EPA-SAB-COUNCIL-ADV-00-003, November 19, 1999.
96. Zanobetti A, Schwartz J, Gold D. Are there sensitive subgroups for the effects of airborne particles? Environ Health Perspect 108:841–845 (2000).
97. Arthur WB. The economics of risks to life. Am Econ Rev 71:54–64 (1981).
98. Shepard DS, Zeckhauser RJ. Survival versus competition. Manage Sci 30:423–439 (1984).
99. Rosen S. The value of changes in life expectancy. J Risk Uncertainty 1:285–304 (1988).
100. Ng Y-K. The older the more valuable: divergence between utility and dollar values of life as one ages. J Econ 55:1–16 (1992).
101. Hoyert DL, Kockanek KD, Murphy SL. Deaths: Final Data for 1997. National Vital Statistics Report 47 (19). Hyattsville, MD:National Center for Health Statistics, 1999.
102. Schwartz J. Harvesting and long term exposure effects in the relation between air pollution and mortality. Am J Epidemiol 151:440–448 (2000).
103. Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of COPD. JAMA 274:1852–1857 (1995).
104. Krupnick A, Alberini A, Cropper M, Simon N, O'Brien B, Goeree R, Heintzelman M. Age, health, and the willingness to pay for mortality risk reductions: a contingent valuation survey of Ontario residents. Washington, DC: Resources for the Future, 2000.
105. Blumenschein K, Johannesson M. Relationship between quality of life instruments, health state utilities, and willingness to pay in patients with asthma. Ann Allergy Asthma Immunol 80:189–194 (1998).
106. O'Conor RM, Blomquist GC. Measurement of consumer-patient preferences using a hybrid contingent valuation method. J Health Econ 16:667–683 (1997).
107. Weiss KB, Sullivan SD, Lyttle CS. Trends in the cost of illness for asthma in the United States, 1985–1994. J Allergy Clin Immunol 106:493–499 (2000).
108. Rowe RD, Chestnut LG. Oxidants and Asthmatics in Los Angeles: A Benefits Analysis. Prepared by Energy and Resource Consultants, Inc for U.S. EPA. EPA-230-09-86-018. Washington, DC:Office of Policy Analysis, 1986.
109. Rowe RD, Chestnut LG, Shaw WD. Oxidants and asthmatics in Los Angeles: A benefits analysis. In: Evaluation of the Ozone/Oxidants Standards (Lee SD, ed). Houston:Air Pollution Control Association, 1984.
110. Chestnut LG, Colome SD, Keller LR, Lambert WE, Ostro B, Rowe RD. Wojciechowski SL. Heart Disease Patients' Averting Behavior, Costs of Illness, and Willingness to Pay to Avoid Angina Episodes. EPA 230-10-88-042. Washington, DC:Office of Policy Analysis, 1988.
111. Tolley GS, Babcock L, Berger M, Bilotti A, Blomquist G, Fabian R, Fishelson G, Kahn C, Kelly A, Kenkel D, et al. Valuation of reductions in human health symptoms and risks. Prepared at the University of Chicago. Final Report for the U.S. Environmental Protection Agency, Grant #CR-811053-01-0, January 1986.
112. U.S. Code. Clean Air Act. Section 108, Air Quality Criteria and Control Techniques. U.S.C. 42:7408–7409, 1991.
113. Dudley SE, Gramm WL. Perspective: EPA's ozone standard may harm public health and welfare. Risk Anal 17:403–405 (1997).
114. Lutter R, Wolz C. UV-B screening by tropospheric ozone: implications for the National Ambient Air Quality Standard. Environ Sci Technol 31:142A–146A (1997).