Technical Memorandum

November 15, 2009

To: Jim DeMocker, OAR/OPAR

From: Neal Fann, OAR/OAQPS

Re: Estimating PM$_{2.5}$ and Ozone-related Premature Mortality Based on Risk Estimates from the Jerrett et al. (2009) and Krewski et al. (2009) Studies

The recent Jerrett et al. (2009) publication provides new evidence that long-term exposure to ozone is associated with premature mortality, while Krewski et al. (2009) reinforces earlier findings of an association between long-term PM$_{2.5}$ exposure and premature mortality. Below we: (1) summarize Jerrett, Krewski and colleagues' analytical approach; (2) present the results of an illustrative health impact analysis using risk coefficients drawn from each article; (3) summarize our current approach for presenting the results of ozone and PM-related mortality impacts and (4) raise key science policy questions regarding the application of these risk estimates in EPA health impact assessments supporting air quality policy. In the appendix to this document we summarize the key policy-relevant findings of each analysis.

Overview of analytical approach

These studies assess the relationship between long-term exposure to air pollutants and premature mortality among members of the American Cancer Society (ACS) cohort. In each case the authors assess the long-term PM$_{2.5}$ and ozone-related mortality based on the ACS cohort with an extended follow-up period through 2000 (for a total of 18 years). The Krewski et al. (2009) analysis includes an extensive spatial analysis designed to better estimate population-level exposure to PM$_{2.5}$. The Jerrett et al. (2009) analysis finds an association between respiratory-related premature mortality and long-term exposures to ozone, after having controlled for PM$_{2.5}$. In both cases the authors apply a random effects Cox proportional hazards model and incorporate 44 individual and 7 ecological co-variates.

Results of an illustrative health impact analysis

As a means of placing the risk estimates from these two studies in a policy context, below we estimate the excess numbers of PM$_{2.5}$ and ozone-related mortality projected to occur as a result of national-scale air quality changes.

Illustrative ozone health impact analysis using Jerrett et al. (2009)

Below we present the results of an illustrative analysis of the estimated ozone-related premature mortalities avoided resulting from a national modeled air quality scenario of a regional emission control strategy developed for the 2008 ozone NAAQS RIA. This air quality modeling projects ozone values at 12km grid cells nationwide for the months of May to September. For this assessment we apply the estimate of respiratory mortality risk based on the two-pollutant model reported in table 3 (RR = 1.040, 95% CI: 1.013—1.067). Figure 1 contrasts this ACS-based long-term respiratory mortality estimate with results based on risk coefficients drawn from the all-cause short-term mortality studies that EPA current applies. These studies include Bell et al. (2004) NMMAPS-based analysis and three meta-analyses by Bell et al. (2005), Ito et al. (2005) and Levy et al. (2005). The ACS-based estimate falls well above the NMMAPS-based estimate and within the range of the three meta-analyses.

## Figure 1: Comparing Alternate Estimates of Ozone-Related Premature Mortality
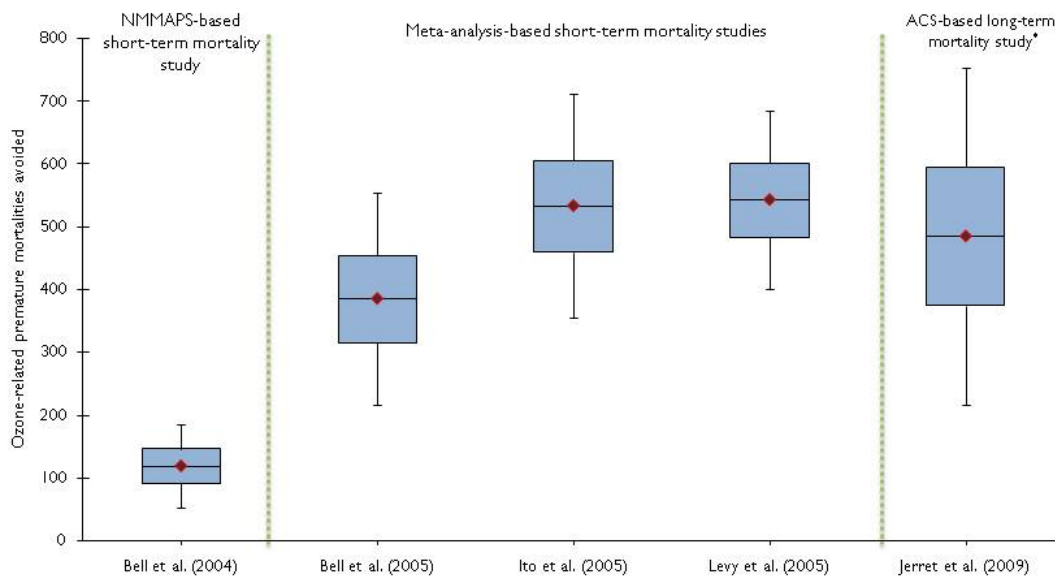
*Respiratory mortality based on two-pollutant model controlling for $PM_{2.5}$. Exposure metric adjusted from 1hr daily maximum to 8hr daily maximum to maintain consistency with results based on short-term studies
Ozone impacts modeled using air quality impacts nationwide from May to September

Illustrative $PM_{2.5}$ analysis

Below are the results of an illustrative $PM_{2.5}$ mortality analysis based on CMAQ-modeled annual mean $PM_{2.5}$ concentrations at 36km grid cells nationwide for a regional emissions control strategy produced for the 2006 PM NAAQS RIA. The Krewski et al. (2009) study reports a large number of risk estimates

according to an array of statistical models. For this illustrative analysis we apply effect coefficients drawn from commentary table 4. Specifically, we incorporate all-cause, ischemic heart disease and lung cancer risk estimates based on the follow-up air quality period (1999—2000), using the random effects Cox model that incorporates the 44 individual and 7 ecological variables. To place these estimates in context, in Figure 2 below we contrast the results of each Krewski-based estimate with the all-cause estimates reported in the Laden et al. (2006) and Pope et al. (2002) studies. The mean estimate of the all-cause Krewski estimate is consistent with the all-cause estimate based on Pope, though the confidence intervals around the Krewski estimate are narrower. The sum of the Krewski IHD and Lung cancer mortality estimates is about 90% as large as the all-cause estimate.

Figure 2: Comparing Alternate Estimates of $PM_{2.5}$-Related Premature Mortality
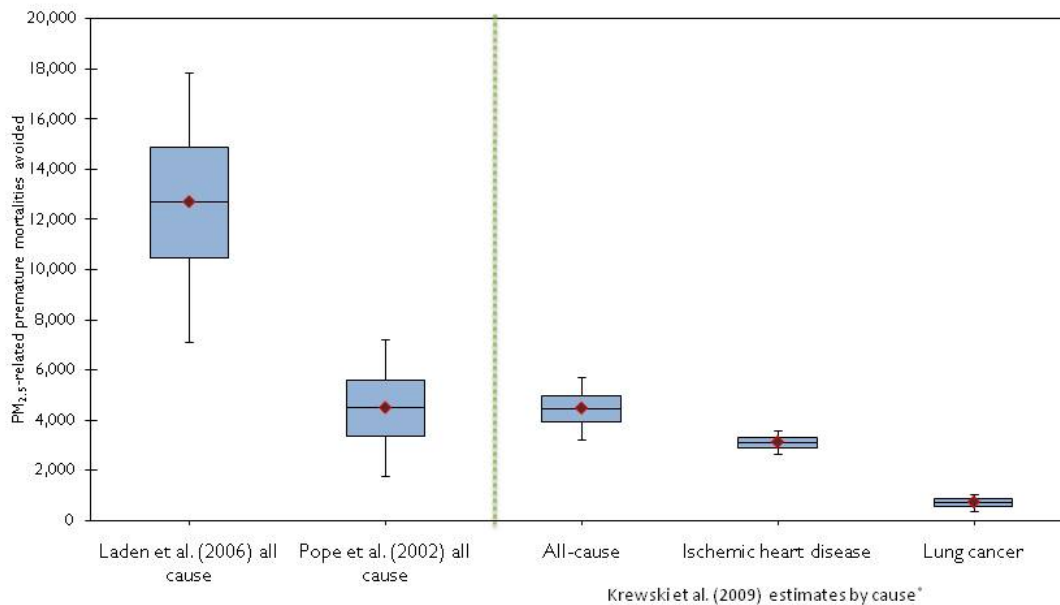
*Effect coefficients drawn from table 4 of HEI commentary

## OAR's approach to presenting ozone and $PM_{2.5}$ mortality estimates in regulatory analyses

When presenting estimates of ozone and $PM_{2.5}$-related premature mortality we report results based on each risk estimates; we do not pool the incidence estimates or perform any other meta-analysis. Table 1 reflects the format in which we present ozone-related premature mortalities. In this example, the estimates represent the number of avoided excess mortalities resulting from full attainment of three alternate ozone NAAQS levels in 2020. The addition of mortality estimates based on Jerrett et al., clearly identified as being based on a long-term mortality estimate, would be added to this same table.

Table 1: Ozone-related premature mortalities of Alternate Ozone NAAQS in 2020 (3% discount rate, in millions of 2006$)

Mortality study		0.075 ppm	0.070 ppm	0.065 ppm
Multi-city studies	Bell et al. (2004)	74 (36—120)	250 (130—410)	450 (240—730)
	Schwartz (2005)	110 (54—190)	380 (190—630)	700 (350—1,100)
	Huang et al. (2004)	130 (66—200)	420 (230—670)	770 (420—1,200)
Meta-analyses	Bell et al. (2005)	240 (410—350)	800 (490—1,200)	1,500 (910—2,200)
	Ito et al. (2005)	330 (230—450)	1,100 (790—1,500)	2,000 (1,400—2,800)
	Levy et al. (205)	340 (260—430)	1,100 (870—1,500)	2,100 (1,600—2,600)

Figure 3 illustrates our approach to presenting monetized $PM_{2.5}$ -related benefits calculating using risk estimates drawn from two epidemiological studies based on the ACS and H6C cohorts and the 12 expert-derived estimates. This figure reports the benefits estimated to occur as a result of attaining a new NO_2 standard. OAR has historically developed independent, un-pooled, estimates of $PM_{2.5}$ - mortality estimates corresponding to the concentration-response function provided by each of the twelve experts, to better characterize the degree of variability in the expert responses.

Figure 3: PM-related monetized benefits of attaining an NO_2 standard of 50ppb nationwide in 2020

PM$_{2.5}$ mortality benefits estimates derived from 2 epidemiology functions and 12 expert functions
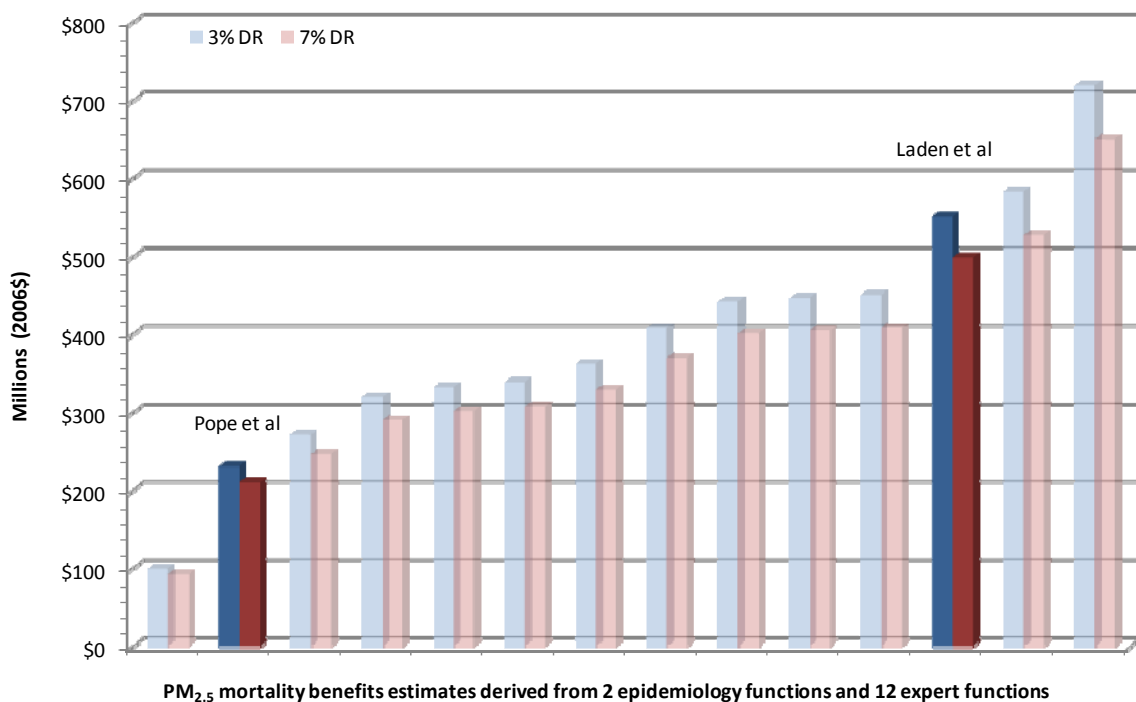
The Krewski et al. (2009) analysis considers an extended follow-up period, incorporates new ecological variables and utilizes an extensive spatial analysis to better estimate population-level exposures. For these reasons, we recommend relying upon this study to provide the ACS-based PM mortality estimates in EPA RIA's.

Key science policy questions

1. Krewski et al. reports the strongest association between IHD mortality and long-term $PM_{2.5}$ exposure, while Jerrett finds a positive relationship between long-term ozone exposure and respiratory mortality. Krewski also reconfirms previous findings regarding long-term PM exposure and lung cancer. Based on the strength of this evidence, does the SAB agree that EPA:
    a. should begin to report IHD- and Lung cancer-related PM mortality and
    b. respiratory-related ozone mortality?
2. When estimating the monetary value of avoided PM-related mortalities based on long-term PM mortality risk coefficients, EPA discounts the stream of mortality benefits according to an SAB-recommended cessation lag. Should EPA apply such a lag to ozone-related premature mortality based on the risk estimate reported in Jerrett? If so, how should it specify this lag?
3. While the results are not presented here, the Jerrett et al. study finds limited evidence for a population threshold. The authors apply a threshold model, finding that a threshold value of 56 ppb best fits the data. However, this result fails a test of statistical significance (p= 0.06) and the authors conclude that the threshold model is "not clearly a better fit." Does the SAB recommend:
    a. performing a quantitative sensitivity analysis based on this limited evidence, or instead
    b. providing a qualitative characterization of uncertainty around this parameter?
4. Does the SAB agree that EPA should present:
    a. the Krewski et al. estimates as a substitute for the Pope et al. (2002)?
    b. the Jerrett et al. estimates as a complement to the existing array of short-term mortality estimates?

Background information

Key findings of Krewski et al. (2009) include:

- *Mortality due to ischemic heart disease was most strongly related to $PM_{2.5}$ exposure.* The authors find that the inclusion of ecological co-variates had the greatest effect on this endpoint. This finding appears to reinforce the conclusions of previous studies, including Pope et al. (2004). The study also reconfirms associations between long-term $PM_{2.5}$ exposure and other causes of death, including Lung Cancer.

- *Certain co-variates modify the PM-mortality relationship significantly.* In particular, the authors found that educational attainment strongly affected the PM mortality relationship—especially so for IHD. Table 8 (page 25) summarizes the risk estimates according to education attainment, showing that the all-cause mortality risk is greater among populations with less than a high

school education; conversely, the all-cause risk is lower for those with greater than a high school education. These risk estimates may be useful for Environmental Justice and distributional analyses.

- *The city-specific analyses indicate that risk can be spatially heterogeneous.* The authors predicted mortality risk for L.A. and New York City using a land-use regression and krieging technique, finding that risk was more uniform in New York and highly spatially variable in L.A. These findings suggest the importance of considering finer-scale health impacts and considering city-specific effect mortality risk estimators.

- *The authors were unable to find a specific exposure window significantly associated with PM mortality.* The analysis did not identify any specific window of exposure as being most closely associated with PM mortality.

- *The analysis is silent with respect to PM mortality thresholds.* The authors do not provide any additional information regarding the presence or absence of population or individual-level thresholds. However, in a letter to EPA, the authors state "As noted above, the HEI Health Review Committee commented on the lack of evidence for a threshold exposure level in Pope et al. (2002) with follow-up through the year 1998. The present report, which included follow-up through the year 2000, also does not appear to demonstrate the existence of a threshold in the exposure-response function within the range of observed $PM_{2.5}$ concentrations."

- *The authors find that neither CO nor NO2 are strongly associated with mortality.*

Key findings of Jerrett et al. (2009) include:

- *Ozone and $PM_{2.5}$ contribute independently to mortality in the ACS cohort.* The authors find that *long-term* exposure to ozone is linked to respiratory premature mortality in a two-pollutant model that controls for $PM_{2.5}$. This is the first long-term cohort study to have observed such a relationship.

- *The authors find the most robust evidence for respiratory mortality.* Using a two-pollutant model, Jerrett and colleagues estimate a relative risk (RR) of 1.04 (95th CI: 1.013—1.067) for respiratory mortality and a RR <1 for all other causes.

- *This analysis finds limited evidence for a population threshold.* The authors apply a threshold model, finding that a threshold value of 56 ppb best fits the data. However, this result fails a test of statistical significance (p= 0.06) and the authors conclude that the threshold model is "not clearly a better fit."

- *The authors were unable to find a critical exposure window.* Jerrett and colleagues did not find that considering a longer exposure period of 10 years affected the risk estimates.

- *Certain effect modifiers strongly influence the results*. The authors find that the ozone-mortality effect is to a significant degree modified by both region of the U.S. and external temperature. In contrast to Krewski et al. (2009) this analysis does not find education to be an important effect modifier.

References

Bell, M L, Dominici F, Samet J M. 2005. A meta-analysis of time-series studies of ozone and mortality with comparison to the national morbidity, mortality, and air pollution study. Epidemiology. 16(4): 436-45.

Bell, M L, McDermott A, Zeger S L, Domenici F. 2004. Ozone and short-term mortality in 95 U.S. urban communities, 1987-2000. JAMA 292 (19): 2372-2378

Huang Y, Dominici F, Bell M. 2005. Bayesian hierarchical distributed lag models for summer ozone exposure and cardio-respiratory mortality. Environmetrics 16 (5): 547-562

Ito, K, De Leon S F, Lippmann M. 2005. Associations between ozone and daily mortality: analysis and meta-analysis. Epidemiology 16(4): 446-57.

Jerrett M, Burnett R, Pope A C, Ito K, Thurston G. 2009. Long-Term Ozone Exposure and Mortality. JAMA 360 (11) 1085-1095.

Krewski D, Jerrett M, Burnett R T, Ma R, Hughes E, et al. 2009 Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. HEI Research Report, 140, Health Effects Institute, Boston, MA.

Laden F J, Schwartz J, Speizer FE, Dockery DW 2006. Reduction in Fine Particulate Air Pollution and Mortality. Am J Respir Crit Care Med 173 667-672

Levy, J I, Chemerynski S M, Sarnat J A. 2005. Ozone exposure and mortality: an empiric bayes metaregression analysis. Epidemiology. 16(4): 458-68.

Pope, C A, Burnett R T, Thun M J, Calle E E, Krewski D, Ito K,Thurston G D 2002 Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA. 287(9):1132-1141

Roman, H, Walker K, Walsh T, Conner L, Richmond H, Hubbell B, Kinney P. 2008. Expert Judgment Assessment of the Mortality Impact of Changes in Ambient Fine Particulate Matter in the U.S. Environ. Sci. Technol.,42(7):2268 2274.

Schwartz J. 2005. How sensitive is the association between ozone and daily deaths to control for temperature? Am J Respir Crit Care Med 171 (6): 627-631