



# Lowering the Ozone Standard Will Not Measurably Improve PUBLIC HEALTH

by Bryan Shaw, Sabine Lange, and Michael Honeycutt

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The Texas Commission on Environmental Quality argues that the thoughtful integration of scientific data does not support the assumption that tightening the ozone standard will result in measurable health benefits.

**T**he Texas Commission on Environmental Quality (TCEQ) strives to protect our state's public health and natural resources consistent with sustainable economic development. In accordance with this mission, the State of Texas alone has spent >\$1 billion since 2001 striving to achieve the 1997 0.08 parts per million (ppm) ozone standard. Most of Texas' air quality areas recorded their lowest ozone values ever in 2014. The Houston and Dallas/Fort Worth areas, for example, have seen ozone levels reduced 29% and 21%, respectively, during the past 15 years, while the population has increased

34% and 29%, respectively. We will continue to expend resources to achieve the 2008 75 parts per billion (ppb) ozone standard, which has yet to be fully implemented by the U.S. Environmental Protection Agency (EPA). However, as the concentration of ambient ozone decreases, it becomes exponentially more difficult, and expensive, to attain further reductions. EPA is poised to lower the standard further. While cost cannot be considered in setting the standard, the high cost of further lowering the standard necessitates that this be a sound policy decision and will result in measurable health benefits.



ological associations between short-term ozone exposure and mortality is regional heterogeneity. This heterogeneity means that different cities have different associations between short-term exposure to ozone and mortality, and very few of those associations are positive.<sup>1-4</sup>

For example, Smith et al.<sup>1</sup> found that only 7 of the 98 cities investigated showed a statistically significant positive association between 8-hr ozone concentrations and mortality (this is very close to the 5% that would be expected purely by chance). Additionally, there was no association between the estimated effect of ozone on mortality for a city and the concentration of ozone in that city (see Figure 1 on page 28). EPA<sup>5</sup> estimates short-term mortality impacts based on Zanobetti and Schwartz<sup>4</sup> and the Smith et al. study.<sup>1</sup> However, the concentration response functions (CRFs) vary from negative to positive for the same city, depending on study selection, ozone averaging time, model specifications, and ozone season. In fact, most of these estimates are indistinguishable from zero. EPA uses a pooled nationwide estimate for their risk calculations, but the substantial heterogeneity between cities that ranges from positive to null or even negative (i.e., higher ozone concentrations correlated with reduced mortality) makes this nationwide estimate misleading and overestimates ozone risk.

The relationship between long-term ozone exposure and mortality has been investigated in at least 12 epidemiology studies.<sup>6-17</sup> When considering other potential causes of mortality, such as other air pollutants, only one of those studies<sup>15</sup> showed a statistically significant (but very small) effect of ozone on respiratory mortality. Interestingly, the effect only occurred at temperatures above 82 °F. It is known that very warm or very cold temperatures are associated with increased mortality.<sup>18</sup> Paradoxically, the increased mortality was not observed in U.S. regions with the highest ozone concentrations (e.g., Southern California) nor in areas with the highest number of respiratory deaths (e.g., the Northeast and industrial Midwest). Therefore, long-term mortality studies also demonstrate unexplained regional heterogeneity and mostly don't show associations between ozone and long-term mortality.

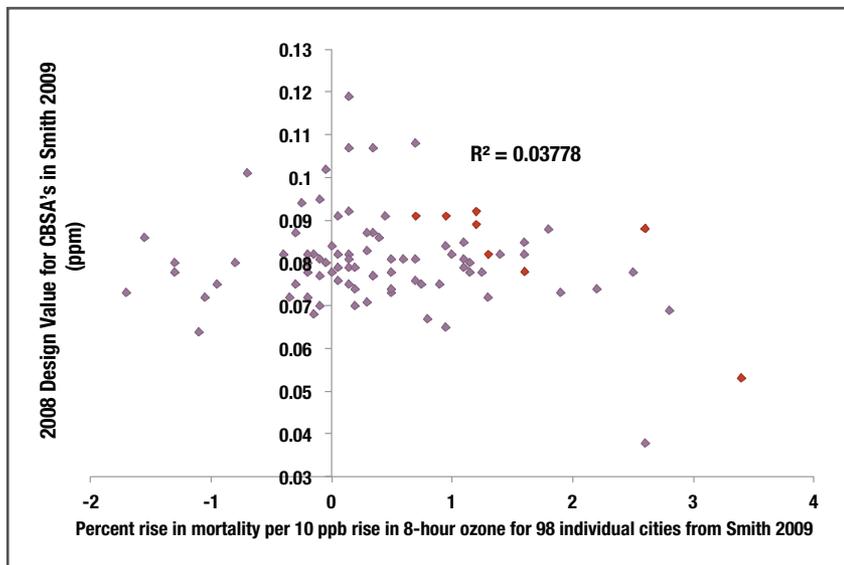
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Ozone ecological epidemiology studies suffer from severe exposure measurement error.

EPA bases its proposal to lower the ozone standard on three key health-related endpoints: premature mortality, respiratory morbidity (i.e., asthma exacerbation, emergency department visits, and hospital admissions), and lung function (i.e., primarily FEV<sub>1</sub> [Forced Expiratory Volume in 1 second, a measure of lung function] decrements). We agree that respiratory effects can occur at the high ozone concentrations that were measured in the 1980s and 1990s. The pertinent question is whether lowering the ozone standard from 75 ppb to 70 or 65 ppb will result in a measurable reduction in these effects. In this short review, we consider some important concerns with EPA's conclusions about the health effects of ambient ozone concentrations. We conclude that EPA has not demonstrated that public health will measurably improve by decreasing the level of the ozone standard.

### **Ecological Epidemiology Studies, Not Adequate for Setting Standard**

EPA relies heavily on ecological epidemiology studies for its assessment of premature mortality and respiratory morbidity. These studies have been very inconsistent in their findings, and flaws, biases, and unusual characteristics of the data have made them difficult to interpret. One unusual and as-yet unexplained characteristic of the epidemi-



**Figure 1. Association between 2008 Ozone Design Values and 8-hr Effect Estimates of Cities.<sup>1</sup>**

*Notes:* Approximate mortality effect estimates (in percent rise per 10-ppb increase in 8-hr ozone) from different cities in Smith et al. (2009)<sup>1</sup> are plotted against the 2008 ozone design values (the 4th highest ambient ozone concentration, averaged over the years 2006–2008) for the matched core-based statistical area (CBSA). Purple points represent cities where mortality was not statistically associated with ambient ozone concentration and red points represent cities where mortality was statistically associated with ambient ozone concentration. The correlation coefficient for the relationship between the mortality effect estimates and the ozone design values ( $R^2$ ) is given. If ozone and mortality were associated, one would expect an increase in mortality as ozone concentrations (design values) increase.

Ecological epidemiology studies suffer from severe exposure measurement error, because they assume that people are continuously exposed (i.e., 24 hours a day, 7 days a week) to the pollutant concentrations measured at the ambient monitors. In the case of ozone, this error is even more egregious because of the nature of ozone as a pollutant. Ozone is primarily an outdoor pollutant, with ventilation and indoor structures scavenging it and removing it from indoor air. The average American adult, senior citizen, and child will spend only 5.3%, 5.8%, and 7.9% of their time outdoors, respectively,<sup>19</sup> and so they will often not be exposed to ozone.

Studies<sup>20,21</sup> that have investigated ozone personal exposure and compared it to ambient concentrations have found that personal exposure is much lower than ambient exposure (i.e., approximately 10% of the measured ambient level), and that there may not even be a correlation between personal and ambient concentrations.<sup>22,23</sup> Even outdoor workers—whom EPA considers to be an at-risk population—experienced personal ozone concentrations that were only 60% of ambient concentrations.<sup>24</sup> Because of this personal exposure issue, the use of ambient ozone concentrations as a proxy for ozone exposure concentrations grossly overestimates their exposure, and therefore risk. This is particularly true of the short-term mortality data, where the subjects of the study (who are mostly elderly) are within days of death when the ambient concentrations are measured, and so are even less likely to be outdoors.

Altogether, this means that it is highly unlikely that the measured associations between ozone and respiratory mortality/morbidity are plausible, because the ozone exposures of the people in the population are so low. Were *all* of the hundreds of thousands of people in the epidemiology studies outside for 8 hours the day immediately before their deaths? In fact, this concern was raised by the Clean Air Scientific Advisory Committee (CASAC) ozone review panel, EPA’s scientific advisors, in a June 5, 2006 letter<sup>25</sup> to EPA: “The Ozone Staff Paper should consider the problem of exposure measurement error in ozone mortality time-series studies. It is known that personal exposure to ozone is not reflected adequately, and sometimes not at all, by ozone concentrations measured at central monitoring sites...Therefore, it seems unlikely that the observed associations between short-term ozone concentrations and daily mortality are due solely to ozone itself.” This difference between ambient ozone concentrations and personal exposures is critical for interpreting both epidemiological studies as well as clinical exposure studies.

### **Lung Function Decrements Unlikely to Be Adverse Below Current Standard**

The TCEQ agrees with EPA that the ozone clinical data are best for setting the ozone standard. The American Thoracic Society (ATS) defines adversity as a significant decrease in FEV<sub>1</sub> with a significant increase in symptoms.<sup>26</sup> The ATS notes that FEV<sub>1</sub> decrements can vary by as much as 5% in healthy adults within a single day and by 15% or more from year to year. EPA defines a 10% FEV<sub>1</sub> decrement in a sensitive population as an appropriate adverse effect to protect against because it is mild and reversible. EPA asserts that two clinical studies, by Kim et al.<sup>27</sup> and Schelegle et al.,<sup>28</sup> justify lowering the current 75-ppb standard.

The Kim study reported statistically significant FEV<sub>1</sub> decrements (1.71%) in healthy young adults after 6.6 hours of 60-ppb ozone exposure while exercising heavily for 50 minutes out of every hour. However, these decrements are within normal variation and are not adverse by either the ATS criteria (i.e., because they were not statistically

associated with symptoms), or by EPA's criteria (i.e., because they were less than 10%).

The Schelegle study reported statistically significant FEV<sub>1</sub> decrements—5.34%, 7.23%, and 11.42%, respectively—associated with symptoms in healthy young adults after 6.6 hours exposure to 72-, 81-, and 88-ppb ozone, but not 63-ppb ozone, while exercising heavily for 50 minutes out of every hour. For 72-, 81-, and 88-ppb ozone, this exposure meets the ATS criteria for adversity, but at 72- and 81-ppb, it does not meet EPA's criteria of adversity until 88-ppb, which is above the current standard.

To claim that the lung effects at 60- and 72-ppb from the Kim study and the Schelegle study are adverse, even though the group mean FEV<sub>1</sub> decrements were not adverse, EPA notes that at 60-ppb, 3 of 59 study subjects had FEV<sub>1</sub> decrements greater than 10%, and at 72-ppb 5 of 31 individual participants had FEV<sub>1</sub> decrements greater than 10%. EPA is essentially basing its assertion of adverse effects occurring at concentrations lower than the current standard on these eight individual measurements.

On the other hand, 5 of 31 individual participants had *increases* in FEV<sub>1</sub> after 72-ppb exposure. The remaining participants showed little, if any, change in FEV<sub>1</sub>, altogether confirming the known large inter-individual variability in lung function responses. Lung function returned to baseline for all of the participants within 1–4 hours after cessation of exposure.<sup>28</sup> As noted by Folinsbee et al.<sup>29</sup> and McDonnell et al.,<sup>30</sup> the exposure regimens used in the Kim and Schelegle studies simulate work performed during a day of heavy manual labor in outdoor workers. This is an unrealistic exposure scenario for sensitive subpopulations, such as asthmatic children and elderly chronic obstructive pulmonary disease patients. In addition, these lung function decrements would be transient, reversible, would not interfere with normal activity, and would not result in permanent injury or respiratory dysfunction.<sup>31</sup>

Further, EPA evaluated these effects based on exposure concentration, not *dose* (i.e., a function of exposure concentration, time, and ventilation rate). The healthy young study participants exercised vigorously for the majority of their 6.6 hour



EPA has not demonstrated that lowering the ozone standard from 75-ppb to 70–65-ppb will result in a decrease in adverse lung function effects in the population.

## References

- Smith, R.L.; Xu, B.; Switzer, P. Reassessing the relationship between ozone and short-term mortality in U.S. urban communities; *Inhal. Toxicol.* **2009**, *21* (Suppl. 2), 37-61.
- Bell, M.L.; McDermott, A.; Zeger, S.L.; Samet, J.M.; Dominici, F. Ozone and short-term mortality in 95 U.S. urban communities, 1987–2000; *J. Am. Medical Assn.* **2004**, *292* (19), 2372-2378.
- Bell, M.L.; Dominici, F.L.; Samet, J.M. A meta-analysis of time-series studies of ozone and mortality with comparison to the National Morbidity, Mortality, and Air Pollution Study; *Epidemiol.* **2005**, *16*, 436-445.
- Zanobetti, A.; Schwartz, J. Is there adaptation in the ozone mortality relationship: A multi-city case-crossover analysis; *Environ. Health.* **2008**, *7*, 22.
- Health Risk and Exposure Assessment for Ozone: Final Report*; EPA-452/R-14-004a; Office of Air and Radiation, U.S. Environmental Protection Agency, 2014.
- Dockery, D.W.; Pope, C.A.; Xu, X.; Spengler, J.D.; Ware, J.H.; Fay, M.E.; Ferris, B.G. Jr.; Speizer, F.E. An association between air pollution and mortality in six U.S. cities; *N. Engl. J. Med.* **1993**, *329* (24), 1753-1759.
- Abbey, D.E.; Nishino, N.; McDonnell, W.F.; Burchette, R.J.; Knutsen, S.F.; Lawrence Beeson, W.; Yang, J.X. Long-term inhalable particles and other air pollutants related to mortality in nonsmokers; *Am. J. Respir. Crit. Care Med.* **1999**, *159* (2), 373-382.
- Lipfert, F.W.; Perry, H.M.; Miller, J.P.; Baty, J.D.; Wyzga, R.E.; Carmody, S.E. The Washington University–EPRI veterans' cohort mortality study: Preliminary results; *Inhal. Toxicol.* **2000**, *12* (Suppl. 4), 41-73.
- Pope, C.A.; Burnett, R.T.; Thun, M.J.; Calle, E.E.; Krewski, D.; Ito, K.; Thurston, G.D. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution; *J. of the Am. Med. Assn.* **2002**, *287*, 1132-1141.
- Chen, L.H.; Knutsen, S.F.; Shavlik, D.; Beeson, W.L.; Petersen, F.; Ghamsary, M.; Abbey, D. The association between fatal coronary heart disease and ambient particulate air pollution: Are females at greater risk? *Environ. Health Perspect.* **2005**, *113*, 1723-1729.
- Jerrett, M.; Burnett, R.T.; Ma, R.; Pope, C.A.; Krewski, D.; Newbold, K.B.; Thurston, G.; Shi, Y.; Finkelstein, N.; Calle, E.E.; Thun, M.J. Spatial analysis of air pollution and mortality in Los Angeles; *Epidemiol.* **2005**, *16* (6), 727-736.
- Lipfert, F.W.; Baty, J.D.; Miller, J.P.; Wyzga, R.E. PM<sub>2.5</sub> constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans; *Inhal. Toxicol.* **2006**, *18*, 645-657.
- Lipfert, F.W.; Wyzga, R.E.; Baty, J.D.; Miller, J.P. Traffic density as a surrogate of environmental exposures in studies of air pollution health effects: Long-term mortality in a cohort of U.S. veterans; *Atmos. Environ.* **2006**, *40*, 154-169.
- Krewski, D.; Jerrett, M.; Burnett, R.T.; Ma, R.; Hughes, E.; Shi, Y.; Turner, M.C.; Pope, C.A.; Thurston, G.; Calle, E.E.; Thun, M.J. *Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality*; Research Report No. 140; Health Effects Institute, 2009.
- Jerrett, M.; Burnett, R.T.; Pope, C.A.; Ito, K.; Thurston, G.; Krewski, D.; Shi, Y.; Calle, E.; Thun, M. Long-term ozone exposure and mortality; *N. Engl. J. Med.* **2009**, *360* (11), 1085-1095.
- Wang, X.Y.; Hu, W.; Tong, S. Long-term exposure to gaseous air pollutants and cardio-respiratory mortality in Brisbane, Australia; *Geospat. Health.* **2009**, *3*, 257-263.
- Smith, K.R.; Jerrett, M.; Anderson, H.R.; Burnett, R.T.; Stone, V.; Derwent, R.; Atkinson, R.W.; Cohen, A.; Shonkoff, S.B.; Krewski, D.; Pope, C.A.; Thun, M.J.; Thurston, G. Public health benefits of strategies to reduce greenhouse-gas emissions: health implications of short-lived greenhouse pollutants; *Lancet* **2009**, *374*, 2091-2103.
- Ye, X.; Wolff, R.; Yu, W.; Vaneckova, P.; Pan, X.; Tong, S. Ambient temperature and morbidity: A review of epidemiological evidence; *Environ. Health Perspect.* **2012**, *120*, 19-28.

exposure, dramatically increasing their dose, and therefore response, as compared to a resting or moderate exercise ventilation rate for the same exposure concentration. Given these facts, EPA has not demonstrated that lowering the ozone standard from 75-ppb to 70–65-ppb will result in a decrease in *adverse* lung function effects in the population.

## Evidence for Ozone Exacerbation of Asthma Is Insufficient

EPA investigated the epidemiology studies that show effects of ambient ozone concentrations on asthma health outcomes. Keeping in mind that these studies suffer from the same exposure measurement errors as the mortality studies, EPA showed that 21 of the 33 reported associations between ozone and asthma symptoms were not statistically significant, and those that were significant were not consistent with one another.<sup>19</sup> This result is quantified in the regulatory impact analysis,<sup>32</sup> where EPA shows that there is no statistically significant decrease in asthma exacerbations with a decreasing level of the ozone standard. EPA also states that emergency department visits and hospital admissions are robust to co-pollutant con-

founders, but does not mention investigation of confounding by pollen, which is a known, strong inducer of asthma.<sup>33,34</sup> Also, confounding by race, ethnicity, and household poverty are important considerations, as was shown in a recent study demonstrating that asthma incidence and morbidity is not more associated with urban (more polluted) areas, but rather with ethnicity and poverty.<sup>35</sup> Therefore, EPA should not have drawn the conclusion that ozone enhances asthma morbidity at ambient concentrations based on these data.

In conclusion, the TCEQ thinks the thoughtful integration of the scientific data does not support the assumption that lowering the ozone standard from 75 ppb to 70–65 ppb will result in measurable health benefits. The ecological epidemiology studies are critically flawed due to severe exposure misclassification because personal exposure to ozone is approximately 10% of ambient levels, dramatically reducing the ozone dose people actually receive. The clinical studies do not indicate anything beyond mild, reversible effects below 75 ppb. It is biologically implausible that 8-hr ambient ozone concentrations below 75 ppb would cause mortality when they do not cause mild effects. **em**

19. *Integrated Science Assessment for Ozone and Related Photochemical Oxidants*; EPA 600/R-10/076F; Office of Air and Radiation, U.S. Environmental Protection Agency, 2013.
20. Lee, K.; Parkhurst, W.J.; Xue, J.; Ozkaynak, A.H.; Neuberger, D.; Spengler, J.D. Outdoor/indoor/personal ozone exposures of children in Nashville, Tennessee; *J. Air & Waste Manage. Assoc.* **2004**, *54* (3), 352-9.
21. Xue, J.; McCurdy, T.; Spengler, J.; Ozkaynak, H. Understanding variability in time spent in selected locations for 7–12-year-old children; *J. Expo. Anal. Environ. Epidemiol.* **2004**, *14*, 222-233.
22. Sarnat, J.A.; Schwartz, J.; Catalano, P.J.; Suh, H.H. Gaseous pollutants in particulate matter epidemiology: Confounders or surrogates? *Environ. Health Perspect.* **2001**, *109*, 1053-1061.
23. Sarnat, J.A.; Brown, K.W.; Schwartz, J.; Coull, B.A.; Koutrakis, P. Ambient gas concentrations and personal particulate matter exposures: Implications for studying the health effects of particles; *Epidemiol.* **2005**, *16*, 385-395.
24. O'Neill, M.S.; Ramirez-Aguilar, M.; Meneses-Gonzalez, F.; Hernandez-Avila, M.; Geyh, A.S.; Sienra-Monge, J.J.; Romieu, I. Ozone exposure among Mexico City outdoor workers; *J. Air & Waste Manage. Assoc.* **2003**, *53*, 339-346.
25. Clean Air Scientific Advisory Committee. See [http://yosemite.epa.gov/sab/sabproduct.nsf/0202D7053AC6E2AC852571870075C1D2/\\$File/casac-06-007.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/0202D7053AC6E2AC852571870075C1D2/$File/casac-06-007.pdf) (accessed Feb. 16, 2015).
26. Pellegrino, R.; Viegi, G.; Brusasco, V.; Crapo, R.O.; Burgos, F.; Casaburi, R.; Coates, A.; van der Grinten, C.P.; Gustafsson, P.; Hankinson, J.; Jensen, R.; Johnson, D.C.; MacIntyre, N.; McKay, R.; Miller, M.R.; Navajas, D.; Pedersen, O.F.; Wanger, J. Interpretative strategies for lung function tests; *Eur. Respir. J.* **2005**, *26* (5), 948-968.
27. Kim, C.S.; Alexis, N.E.; Rappold, A.G.; Kehrl, H.; Hazucha, M.J.; Lay, J.C.; Schmitt, M.T.; Case, M.; Devlin, R.B.; Peden, D.B.; Diaz-Sanchez, D. Lung function and inflammatory responses in healthy young adults exposed to 0.06-ppm ozone for 6.6 hours; *Am. J. Respir. Crit. Care Med.* **2011**, *183*, 1215-1221.
28. Schelegle, E.S.; Morales, C.A.; Walby, W.F.; Marion, S.; Allen, R.P. 6.6-Hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans; *Am. J. Respir. Crit. Care Med.* **2009**, *180* (3), 265-272.
29. Folinsbee, L.J.; McDonnell, W.F.; Horstman, D.H. Pulmonary function and symptom responses after 6.6-hour exposure to 0.12-ppm ozone with moderate exercise; *J. Air Poll. Control Assoc.* **1988**, *38* (1), 28-35.
30. McDonnell, W.F.; Kehrl, H.R.; Abdul-Salaam, S.; Ives, P.J.; Folinsbee, L.J.; Devlin, R.B.; O'Neil, J.J.; Horstman, D.H. Respiratory response of humans exposed to low levels of ozone for 6.6 hours; *Arch. Environ. Occup Health.* **1991**, *46*, 145-150.
31. Goodman, J.E.; Prueitt, R.L.; Chandalia, J.; Sax, S.N. Evaluation of adverse human lung function effects in controlled ozone exposure studies; *J. Appl. Toxicol.* **2014**, *34* (5), 516-524.
32. *Regulatory Impact Analysis of the Proposed Revisions to the National Ambient Air Quality Standards for Ground-Level Ozone*; EPA-452/P-14-006; Office of Air and Radiation, U.S. Environmental Protection Agency, 2014.
33. D'Amato, G.; Liccardi, G.; D'Amato, M.; Holgate, S. Environmental risk factors and allergic bronchial asthma; *Clin. Exp. Allergy.* **2005**, *35*, 1113-1124.
34. Babin, S.M.; Burkorn H.S.; Holtry R.S.; Taberner N.R.; Stokes L.D.; Davies-Cole J.O.; DeHaan K.; Lee D.H. Pediatric patient asthma-related emergency department visits and admissions in Washington, DC, from 2001–2004, and associations with air quality, socio-economic status and age group; *Environ. Health.* **2007**; doi: 10.1186/1476-069X-6-92007.
35. Keet, C.A.; McCormack, M.C.; Pollack, C.E.; Peng, R.D.; McGowan, E.; Matsui, E.C. Neighborhood poverty, urban residence, race/ethnicity, and asthma: Rethinking the inner-city asthma epidemic; *J. Allergy Clin. Immunol.* **2015**; PMID=25617226 (accessed Feb 13, 2015).