

**American Academy of Pediatrics • American College of Preventative Medicine
American Heart Association • American Lung Association
American Medical Association • American Public Health Association •
American Thoracic Society • Asthma and Allergy Foundation of America
Children's Environmental Health Network
National Association of County and City Health Officials
National Association for Medical Direction of Respiratory Care
Health Care Without Harm • Trust for America's Health**

March 17, 2015

The Honorable Gina McCarthy
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue
Washington, DC 20460
Sent via A-and-R-Docket@EPA.Gov

Re: EPA Docket I.D. No: EPA-HQ-OAR-2008-0699

Dear Administrator McCarthy:

As national organizations representing medical societies, public health and patient advocacy organizations, we write to provide comments to the U. S. Environmental Protection Agency on the proposed Ozone National Ambient Air Quality Standards. Our organizations appreciate and would like to express our support to the EPA for moving forward to update the current ozone standard, and welcome this opportunity to provide input to this process, which we hope will result in a standard that is better protective of public health. Our organizations urge you to select a level for the primary health standard that will meet the Clean Air Act requirement to protect the health of the public with an adequate margin of safety: 60 parts per billion (ppb).

[EPA Must Protect the Health of the Public, including Sensitive Populations](#)

The Clean Air Act establishes the primary National Ambient Air Quality Standard to protect public health from the nation's most widespread air pollutants. The Clean Air Act directs the Administrator to set standards that are "requisite to protect public health" with "an adequate margin of safety" (42 U.S.C. § 7409 (b) (1)).

The list of populations who risk demonstrated harm from ozone pollution has grown significantly from the previous review. Children, people with asthma and other lung diseases, seniors, outdoor workers and people who have low socioeconomic status have long been shown to be vulnerable to ozone. Newer evidence shows some otherwise healthy adults are especially sensitive to ozone exposure because of limitations in some nutrients and certain genetic variants. In addition to these groups, the

EPA's *Integrated Science Assessment* has documented evidence that suggests increased risk to fetal development and to cardiovascular harm (EPA, Integrated Science Assessment, 2013). Health-based standards must be set at levels that will protect all people, but particularly these sensitive groups.

[Ozone poses a grave threat to public health at levels well below the current standard](#)

The current standard of 75 ppb fails to meet the requirements of the Clean Air Act. Clinical and epidemiological studies have repeatedly shown that breathing ozone can threaten life and health at concentrations far lower than the 75 ppb 8-hour average standard.

Extensive, public reviews of the large body of evidence by EPA's independent science advisors, the Clean Air Scientific Advisory Committee (CASAC), and by EPA staff scientists have confirmed that the 2008 primary ozone standard is set at a level that is too weak to protect public health. In fact, three successive CASAC panels -- each under different leadership -- have reached the same conclusion: the 2008 standard should not be retained.

- As part of the advice to the EPA during the previous review that ended in 2008, CASAC sent letters repeatedly supporting a standard between 60 and 70 ppb (Henderson, 2006; Henderson, 2007). After EPA published its final decision in 2008, CASAC sent a rare letter to the Administrator commenting on the decision. The CASAC stated unequivocally that they disagreed with the decision to set the standard at 75 ppb. These scientists notified the Administrator that they *"do not endorse the new primary ozone standard as being sufficiently protective of public health."* (Emphasis in the original.) They urged that the Administrator or his successor "select a more health-protective" standard in the next review cycle (Henderson, 2008). It is important to note that their decision was based on the scientific evidence as it stood in 2006, the close of that review period.
- When asked to reevaluate the evidence during EPA's ill-fated reconsideration of the 2008 standard in February 2010, CASAC again was explicit: "EPA has recognized the large body of data and risk analyses demonstrating that retention of the current standard would leave large numbers of individuals at risk for respiratory effects and/or other significant health consequences including asthma exacerbations, emergency room visits, hospital admissions and mortality" (Samet, 2010).
- Now, the current CASAC has echoed this consensus again. In their letter to EPA on June 14, 2014, they stated it simply: "The CASAC finds scientific justification that current evidence and the results of the exposure and risk assessment call into question the adequacy of the current standard" (Frey, 2014).

We share the conclusion repeatedly presented to EPA by the CASAC: EPA cannot justify retention of the current standard based on the health evidence.

Multiple CASAC reviews have recommended a standard between 60 and 70 ppb.

Not only have the three separate CASAC committees, under three different Chairs, unanimously confirmed that the current ozone standard is not protective of public health, but each recommended that the standard should be set in the range of 60 to 70 ppb.

In each of the three comment letters the CASAC wrote to EPA Administrator Stephen L. Johnson, the independent experts charged with advising EPA unanimously recommended selection of an 8-hour average ozone NAAQS within the range of 60 to 70 ppb (Henderson 2006; Henderson 2007; Henderson 2008).

During the reconsideration of the 2008 Ozone NAAQS, CASAC reaffirmed its support for the selection of an 8-hour average ozone NAAQS within the 60 – 70 ppb range (Samet, 2010). Again, that recommendation came based solely on the studies that had been available during the prior review, a period that closed in 2006.

Now able to fully consider the additional studies available in the 2007 to 2012 period, the most recent CASAC summarized extensive scientific evidence in their recommendations to EPA for a range from 70 to 60 ppb:

“The CASAC further concludes that there is adequate scientific evidence to recommend a range of levels for a revised primary ozone standard from 70 ppb to 60 ppb. The CASAC reached this conclusion based on the scientific evidence from clinical studies, epidemiologic studies, and animal toxicology studies, as summarized in the Integrated Science Assessment (ISA), the findings from the exposure and risk assessments as summarized in the HREA, and the interpretation of the implications of these sources of information as given in the Second Draft PA” (Frey, 2014).

However, the CASAC concluded that new evidence showed that even that range is too broad, noting that “based on the scientific evidence, a level of 70 ppb provides little margin of safety for the protection of public health particularly for sensitive subpopulations” (Frey, 2014).

“At 70 ppb, there is substantial scientific evidence of adverse effects as detailed in the charge question responses, including decrease in lung function, increase in respiratory symptoms, and increase in airway inflammation. Although a level of 70 ppb is more protective of public health than the current standard, it may not meet the statutory requirement to protect public health with an adequate margin of safety” (Frey, 2014).

CASAC concluded the evidence showed that a level of “60 ppb would certainly provide more public health protection than a standard of 65 or 70 ppb and would provide an adequate margin of safety” (Frey, 2014).

The significantly stronger scientific and medical evidence available in this current review led CASAC to provide even more explicit comments than during the 2008 review and the subsequent reconsideration process. Their explicit conclusion that 60 ppb meets the requirement to provide more protection and an adequate margin of safety raises questions about EPA’s decision to exclude 60 ppb from the proposal.

Our organizations offer evidence that demonstrates why 60 ppb should be adopted as the level of the health-based standard.

[The evidence for a standard of 60 ppb has grown.](#)

The scientific and medical understanding of the mechanisms by which exposure to ambient ozone pollution harms human health has grown considerably stronger since 2007. The EPA evaluated 1,000 new studies in the current review, studies that have been published since the completion of the 2006 Criteria Document. These studies inform our understanding of the health impacts of ozone at low concentrations.

Multiple chamber studies provide robust evidence of harm to healthy adults down to 60 ppb. Adding to previous research by Adams (2002) and Adams (2006), both Brown et al (2008) and Kim et al (2011) provide still more evidence that exposures down to 60 ppb can reduce lung function and cause inflammation that meets the American Thoracic Society's criteria for judging adversity. The subjects in these chamber studies were healthy young adults -- not children, the elderly, or people with asthma who are more susceptible to ozone. The chamber studies establish solid evidence that concentrations above 60 ppb would provide significant risk not only to many healthy adults, but most critically, to susceptible populations, including children, seniors and people with asthma and other chronic lung diseases.

Epidemiological studies provide real-world evidence for the need for 60 ppb. The analysis presented in the *Policy Assessment* digs deeper into six epidemiological studies in the U.S. and Canada and provides further real-world evidence that a standard of either 70 ppb or 65 ppb fails to provide adequate protection. These studies (Bell et al., 2006; Cakmak et al., 2006b; Dales et al., 2006; Katsouyanni et al., 2009, Mar and Koenig, 2009; Stieb et al, 2009) examined the positive and statistically significant associations from the most serious health threat—premature death—as well as from hospital admissions and emergency department visits. In most locations where increased risk was found, the ozone levels would have met the weaker standards of either 70 or 65 ppb, but would have failed to meet a standard set at 60 ppb. (*Policy Assessment*, pp. 4-13 to 4-15).

A standard of 60 ppb would result in a far greater reduction in premature morbidity and mortality.

The EPA's estimates show that compared to meeting a standard of 65 ppb or 70 ppb, meeting a standard of 60 ppb would prevent many more premature deaths and hospital admissions, asthma attacks and days missed at work and school. Looking just at the parts of the nation expected to meet a standard of 60 ppb by 2025 (not including California), EPA provides a table of these estimates based on established modeling projections.

Nationwide Benefits of Attaining Standard in 2025 Throughout the United States (except California)			
Measure	60 ppb	65 ppb	70 ppb
Premature Deaths Avoided in 2025	7,900	4,300	1,440
Asthma Attacks Avoided in Children in 2025	1,800,000	960,000	320,000
Respiratory Hospital Admissions Avoided in 2025	2,900	1,500	510
Asthma Emergency Department Visits Avoided in 2025	4,100	2,300	1,400
Missed School Days Avoided in 2025	1,900,000	1,000,000	330,000

Taken from Table ES -11 of the U.S. EPA, Regulatory Impact Analysis of the Proposed Revision to the National Ambient Air Quality Standards for Ground-level Ozone, November 2014. EPA -452/P-14-006. Estimates based on modeling and assumptions explained in detail in the document. California was excluded because it is not expected to meet these standards in 2025.

In 2025, the reduction in premature deaths expected with a standard of 60 ppb is projected to be nearly *double* that of a standard set at 65 ppb and *more than five times* the benefit of a standard set at 70 ppb.

Growing evidence expands health effects of ozone exposure

Your decision must be founded in the strongest requirement of the Clean Air Act: that the NAAQS not only protect public health, but include an adequate margin of safety. In both the prior review ending in 2008 and in the 2010 reconsideration, our organizations recommended strongly that the primary 8-hour standard should be 60 ppb based on the available evidence. In addition to the strong evidence of increased morbidity from ozone down to 60 ppb, multiple well-reviewed studies had identified a new, strong association with premature death, with no discernable threshold, that made the risks to the large, vulnerable groups even graver. Even during the prior reviews, the evidence demonstrated that standards between 65 and 70 ppb would not be effective in protecting public health with an adequate margin of safety.

Since the 2008 standard, new research has added weight to the evidence showing the extensive impact of ozone. Research not only confirms the previous conclusions about ozone's impact on human health, but adds to and clarifies the impact on multiple physiologic systems, including respiratory and cardiovascular. Examination of long-term exposure has identified outcomes beyond the traditional concerns to include the central nervous system and reproductive and developmental effects. The growing evidence of effects associated with breathing ozone for longer periods adds to the urgency to set the most protective standard now to reduce those exposures.

Respiratory Health Effects, including Premature Mortality

The largest body of research documents the impact of ozone on respiratory symptoms, lung function changes, emergency department visits for respiratory disease, and hospital admissions. Since the previous review large studies examining exposures in multiple cities and continents have shown the consistent and pervasive threats to respiratory health.

New studies confirm the impact on children with asthma. Multiple studies demonstrated increased pulmonary inflammation (Berhane et al., 2011; Khatri et al., 2009; Barraza-Villerreal et al, 2008), and increased risk of hospital admissions (Silverman and Ito, 2010; Strickland et al., 2010).

Several large studies looking at single cities and multiple cities confirm that breathing ozone increases the risk of hospital admission and emergency department visits for respiratory conditions (Katsouyanni et al, 2009; Lin et al., 2008a; Wong et al., 2009; Darrow et al., 2011); Stieb et al., 2009). Multiple- and single-city studies showed increased risk of respiratory hospital admissions and emergency department visits in cities that met the current ozone standard of 75 ppb (Cakmak et al., 2006; Dales et al., 2006; Katsouyanni et al., 2009; Stieb et al., 2009) or where most cities would have met standards set at either 65ppb or 70 ppb (Cakmak et al., 2006; Katsouyanni et al., 2009; Stieb et al. 2009).

The American Thoracic Society summarized some of the new studies in the attached editorial in the *American Journal of Respiratory and Critical Care Medicine* advocating EPA adoption of a standard of 60 ppb (Rice, et al., 2015).

“Highlights of this new body of evidence include a study of emergency department visits among children aged 0 to 4 in Atlanta, which found that each 30 ppb increase in the 3-day average of ozone was associated with an 8% higher risk of pneumonia and a 4% higher risk for upper respiratory infection(5)[Darrow et al 2014]. Several studies have demonstrated dose-response relationships between ozone exposure and childhood asthma admissions at exposure levels in the 60 to 80 ppb range (6–9)[Strickland et al 2014, Strickland et al 2010, Gleason et al 2014, Silverman et al 2010]. Similar associations have been found for adult admissions for asthma(9–11) [Silverman and Ito 2010, Glad et al 2012, Meg et al 2010] and COPD(12, 13)[Ko and Hui 2012, Media-Ramon et al 20076]. A population-based cohort study of generally healthy adults found that FEV1 was 56 mL lower after days when ambient ozone ranged from 59 to 75 ppb compared to days with levels under 59 ppb(14) [Rice et al 2013]. Controlled human exposure studies have re-affirmed lung function decrements in healthy adults after exposure to 60 to 70 ppb of ozone (15,16) [Schelegle et al 2009, Kim et al 2011]. Perhaps of greatest concern, there is now stronger evidence of increased mortality in association with ozone (17–19)[Peng et al 2013, Romieu et al 2012,Zanobetti and Schwartz 2008], particularly among the elderly and those with chronic disease(20, 21)[Medina-Ramon and Schwartz 2008, Zanobetti and Schwartz 2011]”.

Cardiovascular Health Effects, including Premature Mortality

Evidence is accumulating about the cardiovascular effects of ozone, with the strongest evidence for increased risk of premature death. Previous studies have shown adverse associations between ozone exposure and various cardiovascular health endpoints, including alterations in heart rate variability in older adults (Park et al., 2005), cardiac arrhythmias (Rich et al., 2006), strokes, (Henrotin et al., 2007)

heart attacks (Ruidavets et al., 2005), and hospital admissions or cardiovascular diseases (Koken et al., 2003). Newer large epidemiologic studies from the U.S. (Zanobetti and Schwartz, 2008b), Europe (Samoli et al., 2009) and Asia (Wong et al 2010) have provided evidence of premature death from cardiovascular effects, including two large studies that confirmed the effect after controlling for particulate matter exposure (Katsouyanni et al 2009; Stafoggia, 2010).

Reproduction and Development Effects

A growing body of research raises concerns about longer-term exposure to ozone, particularly during pregnancy. Some toxicological studies warn that ozone may affect development of the pulmonary system and central nervous system. Several large studies in California and Australia point to association of prenatal ozone exposure with low birth weight and impaired fetal growth (Salem et al., 2005; Morello-Frosch, et al. 2010; Hansen et al 2007, Hansen et al 2008; Mannes et al 2005). Low birth weight is linked to increased risk of chronic disease as adults (Rogers et al., 2012; Berends et al., 2012).

Central Nervous System Effects

Increased research since the last review has expanded evidence of the potential effects on the central nervous system. Toxicological studies provide evidence that short- or long-term exposure to ozone may affect cognitive abilities, such as memory (Rivas-Arancibia et al., 1998), and may produce changes similar to those seen in human neurodegenerative disorders (Rivas-Arancibia et al., 2010; Santiago-López et al., 2010; Guevara-Guzman et al., 2009). The only human epidemiological study found an association for long-term ozone exposure with reduced performance on specific tests (Chen and Schwartz 2009). While more research is clearly needed, these studies provide added weight for selecting the most protective level.

Mortality Effects

Breathing ozone can kill. Short-term increases in ozone were found to increase deaths from cardiovascular and respiratory causes in a large 14-year study in 95 U.S. cities. The relationship between mortality and ozone was evident even on days when pollution levels above 60 ppb were excluded from the analysis. (Bell, et al., 2004). A series of meta-analyses and multi-city studies has documented an increase in premature death following ozone exposures below 75 ppb, particularly among the elderly (Bell, et al., 2005; Levy et al., 2005; Ito et al., 2005). Furthermore, research has focused on controlling for weather variables in assessing the effect of ozone on mortality. A case crossover study (Schwartz, 2005) of more than one million deaths in 14 U.S. cities found that “the association between ozone and mortality risk is unlikely to be confounded by temperature.”

Multiple new studies have confirmed that ozone causes premature deaths (Zanobetti and Schwartz, 2008b; Samoli et al., 2009; Wong et al 2010) and provided evidence that these deaths occur even after controlling for other pollutants, including particulate matter (Stafoggia, 2010; Katsouyanni et al., 2009). Of special concern the risk of premature death from ozone showed up more frequently in communities with higher unemployment or that had a higher percentage of Black/African-American population, as well as in individuals who were Black/African-American or who had lower socioeconomic status. (Median-Ramón and Schwartz, 2008). EPA needs to ensure the strongest, most protective standards are in place to prevent this deadly pollutant from threatening the lives of thousands of Americans.

Millions of Americans face greater risk from breathing ozone pollution

Research has shown that many groups face greater risk from breathing ozone pollution or are more vulnerable to the harm because of their activities or residence. Their greater risk may come from age, preexisting diseases or genetics, as well as income. Greater vulnerability may stem from outdoor occupations or activities or from living in areas with higher ozone exposures.

Children and adolescents

Children are acutely vulnerable to the hazardous effects of air pollution(AAP, 2004). Relative to adults, children tend to spend more time out of doors, they are often more physically active, they breathe more rapidly, their airways are narrower and they inhale relatively more pollutants in proportion to their body weight (AAP, 2003). Additionally, lung growth continues long after birth, with as much as 80 percent of the alveoli developing during childhood and adolescence (Diertert et al., 2000). Epidemiologic evidence indicates that children face additional health risks beyond the adverse effects observed in the general population. Children experience acute effects such as difficulty breathing (Triche et al., 2006), increased hospitalizations (Burnett et al., 2001), and emergency room visits (Tolbert et al., 2000) from ozone exposure at concentrations below the current standard and may suffer long-lasting effects such as stunted lung function in young adulthood (Tager et al., 2005).

A national standard of 60 ppb would reduce children's exposures of concern from ozone by 95 to 100 percent. A standard of 60 ppb would provide critical protection for children from the dangers from ozone compared to the current standard, according to EPA's *Risk and Exposure Assessment*. The strength of that protection draws a stark comparison to the far weaker options of 65 ppb to 70 ppb. By contrast, a standard of 70 ppb would reduce such exposures by only 15 to 35 percent, while a standard of 65 would reduce such exposures by 30 to 65 percent (EPA, *Risk and Exposure Analysis*, 2014).

Older Adults

Multiple factors place older adults at greater risk from ozone and other air pollutants, including greater time spent outdoors after age 65, the gradual decline in the functioning of the body's systems that accompany aging and an increase in the responsiveness to ozone (EPA, ISA 2013). Recent studies also added to the existing evidence that older adults face greater risk of premature death from ozone (Medina-Ramón and Schwartz 2008; Zanobetti and Schwartz, 2008a; Cakmak et al 2011).

Chronic Disease

Individuals with preexisting lung disease face substantial risks. People with asthma, particularly children but also adults, have shown exacerbated respiratory symptoms in multi-city studies (Mortimer et al., 2002, Romieu et al., 1996 and 1997; O'Connor et al., 2008). Studies have tracked increases in hospitalization among adults suffering from chronic obstructive pulmonary disease (Peel et al., 2007; Median-Ramón, et al., 2006). Newer research, in a large, multi-continent study, also shows increased risk of premature death from cardiovascular disease triggered by ozone pollution (Katsouyanni et al., 2009).

Outdoor workers and exercisers

Outdoor workers as well as active adults who exercise outdoors (Brauer et al., 1996; Korrick et al., 1998) are particularly vulnerable to ozone exposure due to greater exposure because of time spent outdoors and activity levels. A recent study of lifeguards in Galveston, Texas, provided evidence of the impact of even short-term exposure to ozone on healthy, active adults. Testing the breathing capacity of these outdoor workers several times a day, researchers found that many lifeguards suffered increased obstruction in their airways when ozone levels were higher (Thaller et al., 2008).

Socioeconomic Status

Several large studies have identified that individuals who have low socioeconomic status or who live in communities with low socioeconomic status face higher risk of hospital admissions and emergency department visits associated with ozone pollution (Lin et al., 2008; Cakmak et al., 2006b; Burra et al., 2009). As noted earlier, additional studies have identified people who live in communities with high unemployment or other markers of low socioeconomic status as having greater risk of premature death from ozone pollution (Bell and Dominici, 2008; Katsouyanni et al., 2009). Meeting a standard of 60 ppb would provide greater protection to groups already facing substantial challenges.

We call on EPA to adopt a standard of 60 ppb

The Clean Air Act requires that the EPA set the standard based on the need to protect public health “with an adequate margin of safety.” In 2001, the Supreme Court unanimously ruled that protecting health was the only legal basis for the standard. The existing standard fails to protect public health with a margin of safety. EPA must strengthen it.

Given the weight of evidence, we urge you to set the eight-hour ozone standard at 60 ppb to protect against known and anticipated adverse health effects and to provide a margin of safety as required by the Clean Air Act.

Sincerely,

American Academy of Pediatrics

American College of Preventive Medicine

American Heart Association

American Lung Association

American Medical Association

American Public Health Association

American Thoracic Society

Asthma and Allergy Foundation of America

Children's Environmental Health Network

Health Care Without Harm

**National Association of County and City
Health Officials**

**National Association for Medical Direction
of Respiratory Care**

Trust for America's Health

References

Adams, WC. (2000). Ozone dose-response effects of varied equivalent minute ventilation rates. *J Expo Sci Environ Epidemiol* 10: 217-226.

Adams, WC. (2002). Comparison of chamber and face-mask 6.6-hour exposures to ozone on pulmonary function and symptoms responses. *Inhal Toxicol* 14: 745-764.

American Academy of Pediatrics (2004). *Pediatric Environmental Health, 2nd Ed.* Elk Grove Village, IL: American Academy of Pediatrics; 2003; 74-75.

American Academy of Pediatrics, Committee on Environmental Health. Ambient air pollution: health hazards to children. *Pediatrics* 2004; 114: 1699-1707. Statement was reaffirmed in 2010.

Barraza-Villarreal, A; Sunyer, J; Hernandez-Cadena, L; Escamilla-Nunez, MC; Sienna-Monge, JJ; Ramirez-Aguilar, M; Cortez-Lugo, M; Holguin, F; Diaz-Sanchez, D; Olin, AC; Romieu, I. (2008). Air pollution, airway inflammation, and lung function in a cohort study of Mexico City schoolchildren. *Environ Health Perspect* 116: 832-838.

Bell ML, Dominici F, Samet JM. (2005). A meta-analysis of time-series ozone and mortality with comparison to the national morbidity, mortality, and air pollution study. *Epidemiology* 2005; 16: 436-445.

Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. (2004). Ozone and short-term mortality in 95 US urban communities, 1987-2000. *J Am Med Assn* 2004; 292:2372-2378.

Bell, ML; Dominici, F. (2008). Effect modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. *Am J Epidemiol* 167: 986-997.

Bell, ML; Peng, RD; Dominici, F. (2006). The exposure-response curve for ozone and risk of mortality and the adequacy of current ozone regulations. *Environ Health Perspect* 114: 532-536.

Berends LM, Ozane SC. (2012). Early determinants of type-2 diabetes. Best practice & research. *Clinical endocrinology & metabolism*. 26(5):569-80

Berhane K; Zhang Y; Linn WS; Rappaport EB; Bastain TM; Salam MT; Islam T; Lurmann F; Gilliland FD. (2011). The effect of ambient air pollution on exhaled nitric oxide in the Children's Health Study. *Eur Respir J* 37: 1029-1036.

Brauer M, Brumm J, Vedal S, Petkau AJ. Effect of ambient ozone exposure on lung function in farm workers. *Am J Respir Crit Care Med* 1996; 154: 981-987.

Brown JS; Bateson TF; McDonnell WF. (2008). Effects of exposure to 0.06 ppm ozone on FEV1 in humans: A secondary analysis of existing data. *Environ Health Perspect* 116: 1023-1026.

Burnett RT, Smith-Doiron M, Stieb D, Raizenne ME, Brook JR, Dales RE, Leech JA, Cakmak S, Krewski D. (2001). Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. *Am J Epidemiol* 153: 444-452.

Burra, TA; Moineddin, R; Agha, MM; Glazier, RH. (2009). Social disadvantage, air pollution, and asthma physician visits in Toronto, Canada. *Environ Res* 109: 567-574.

Cakmak S; Dales, RE; Angelica Rubio, M; Blanco Vidal, C. (2011). The risk of dying on days of higher air pollution among the socially disadvantaged elderly. *Environ Res* 111: 388-393.

Cakmak, S; Dales, RE; Judek, S. (2006a). Do gender, education, and income modify the effect of air pollution gases on cardiac disease? *J Occup Environ Med* 48: 89-94.

Cakmak, S; Dales, RE; Judek, S. (2006b). Respiratory health effects of air pollution gases: Modification by education and income. *Arch Environ Occup Health* 61: 5-10.

Dales, RE; Cakmak, S; Doiron, MS. (2006). Gaseous air pollutants and hospitalization for respiratory disease in the neonatal period. *Environ Health Perspect* 114: 1751-1754.

Diertert RR, Etzel RA, Chen D, Halonen M, Holladay SD, Jarabek AM, Landreth K, Peden DC, Pinkerton K, Smialowicz RJ, Zoetis T. (2000). Workshop to identify critical window of exposure for children's health: immune and respiratory systems work group summary. *Environ Health Perspect Suppl* 108(3): 483-490.

Frey, Dr. H. Christopher, Chair, Clean Air Scientific Advisory Committee, letter (Frey, 2014) to Gina McCarthy, Administrator, U.S. Environmental Protection Agency, re Clean Air Scientific Advisory Committee Recommendations Concerning the *Second Draft Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards*, June 14, 2014.

Hansen C, Neller A, Williams G, Simpson R. (2007). Low levels of ambient air pollution during pregnancy and fetal growth among term neonates in Brisbane, Australia. *Environ Res.* 103: 383-389.

Hansen CA, Barnett AG, Pritchard G (2008). The effect of ambient air pollution during early pregnancy on fetal ultrasound measurements during mid-pregnancy. *Environ Health Perspect.* 116:362-369.

Henderson, Dr. Rogene, Chair Clean Air Scientific Advisory Committee letter (Henderson, 2006) to Stephen L. Johnson, Administrator U.S. Environmental Protection Agency, on Clean Air Scientific Advisory Committee's (CASAC) Peer Review of the Agency's Final Ozone Staff Paper, EPA-CASAC-07-001, October 24, 2006.

Henderson, Dr. Rogene, Chair, Clean Air Scientific Advisory Committee letter (Henderson, 2007) to Stephen L. Johnson, Administrator U.S. Environmental Protection Agency, on Clean Air Scientific Advisory Committee's (CASAC) Peer Review of the Agency's 2nd Draft Ozone Staff Paper, EPA-CASAC-07-002, March 26, 2007.

Henderson, Dr. Rogene, Chair, Clean Air Scientific Advisory Committee letter (Henderson, 2008) to Stephen L. Johnson, Administrator, U.S. Environmental Protection Agency, re Clean Air Scientific Advisory Committee Recommendations Concerning the Final Rule for the National Ambient Air Quality Standards for Ozone, EPA – CASAC 08-009, April 7, 2008.

Henrotin JB, Besancenot JP, Bejot Y, Giroud M. (2007). Short-term effects of ozone air pollution on ischaemic stroke occurrence: a case-crossover analysis from a 10-year population-based study in Dijon, France. *Occup Environ Med* 64: 4439-445.

Ito K, DeLeon SF, Lippmann M. (2005). Associations between ozone and daily mortality: analysis and meta-analysis. *Epidemiology.* 16: 446-457.

Katsouyanni, K; Samet, JM; Anderson, HR; Atkinson, R; Le Tertre, A; Medina, S; Samoli, E; Touloumi, G; Burnett, RT; Krewski, D; Ramsay, T; Dominici, F; Peng, RD; Schwartz, J; Zanobetti, A. (2009). Air pollution and health: A European and North American approach (APHENA). (Research Report 142). Boston, MA: Health Effects Institute.

Khatri, SB; Holguin, FC; Ryan, PB; Mannino, D; Erzurum, SC; Teague, WG. (2009). Association of ambient ozone exposure with airway inflammation and allergy in adults with asthma. *J Asthma* 46: 777-785.

Kim, CS; Alexis, NE; Rappold, AG; Kehrl, H; Hazucha, MJ; Lay, JC; Schmitt, MT; Case, M; Devlin, RB; Peden, DB; Diaz-Sanchez, D. (2011). 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* 183: 1215-1221.

Koken PJ, Piver WT, Ye F, Elixhauser A, Olsen LM, Portier CJ. (2003). Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. *Environ Health Perspec* 111: 1312-1317

Korrick SA, Neas LM, Dockery DW, Gold DR, Allen GA, Hill LB, Kimball KD, Rosner BA, Speizer FE. (1998) Effects of ozone and other pollutants on the pulmonary function of adult hikers. *Environ Health Perspect.* 106: 93-99.

Levy JL, Chermerynski SM, Sarnat JA (2005). Ozone Exposure and Mortality: An Empiric Bayes Metaregression Analysis, *Epidemiology*, 16: 458-468.

Mannes T, Jalaludin B, Morgan D, et al. (2005). Impact of ambient air pollution on birth weight in Sydney, Australia. *Occup Environ Med.* 62: 524-530.

Medina-Ramon M, Zanobetti A, Schwartz J. (2006). The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multi-city study. *Am J of Epidemiol.* 163: 579-588.

Morello-Frosch R., Jesdale BM, Sadd JL, Pastor M. (2010). Ambient air pollution exposure and full-term birth weight in California, *Environ. Health*, 9(44)

Mortimer KM, Neas LM, Dockery DW, Redline S, Tager IB. (2002). The effect of air pollution on inner-city children with asthma. *Eur Respir J* 19: 699-705;

Park SK, O'Neill MS, Vokonas PS, Sparrow D, and Schwartz J. (2005). Effects of Air Pollution on Heart Rate Variability: The VA Normative Aging Study. *Environ Health Perspec.* 113: 304-309.

Rice MB, Guidotti TL, Cromar KR, on behalf of the ATS Environmental Health Policy Committee. (2015) Scientific Evidence Supports Stronger Limits on Ozone. *Am J Res Crit Care Med.* 191(5): 501-503 DOI: 10.1164/rccm.201411-1976ED

Rich DQ, Mittleman MA, Link MS, Schwartz J, Luttmann-Gibson H, Catalano PJ, Speizer FE, Gold DR, Dockery DW. (2006). Increased Risk of Paroxysmal Atrial Fibrillation Episodes Associated with Acute Increases in Ambient Air Pollution. *Environ Health Perspec.* 114: 120-123.

Rogers LK, Velten M. (2011). Maternal inflammation, growth retardation, and preterm birth: insights into adult cardiovascular disease. *Life Sciences.* 89(13-14):417-21;

Ruidavets J-B, Cournot M, Cassadou S, Giroux M, Meybeck M, Ferrières J. (2005) Ozone Air Pollution is Associated with Acute Myocardial Infarction. *Circulation.* 111: 563-569.

Salam MT, Millstein J, Li Y-F, Lurmann FW, Margolis HG, Gilliland FD. (2005). Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the children's health study. *Environ Health Perspec.* 113: 1638-1644.

Samet, Dr. Jonathan M., Chair, Clean Air Scientific Advisory Committee letter (Samet, 2010) to The Honorable Lisa P. Jackson. Review of EPA's proposed Ozone National Ambient Air Quality Standard (*Federal Register*, Vol. 75, No. 11, January 19, 2010), EPA-CASAC-10-007, February 19, 2010.

Samoli E, Zanobetti A, Schwartz J, et al. (2009). The temporal pattern of mortality responses to ambient ozone in the APHEA project, *J. Epidemiol. Community Health*; 63(12): 960-966.

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

Stafoggia M. (2010). Susceptibility factors to ozone-related mortality: a population-based case-crossover analysis, *Am. J. Respir. Crit. Care Med.*, 182(3): 376-84

Tager IB, Balmes J, Lurmann F, Ngo L, Alcorn S, Kunzli N. (2005). Chronic exposure to ambient ozone and lung function in young adults. *Epidemiology.* 16: 751-759.

Tolbert PE, Mulholland JA, MacIntosh DL, Xu F, Daniels D, Devine OJ, Carlin BP, Klein M, Dorley J, Butler AJ, Nordenberg DF, Frumkin H, Ryan PB, White MC. (2000). Air quality and pediatric emergency room visits for asthma in Atlanta, Georgia, USA. *Am J Epidemiol* .151: 798-810.

Triche EW, Gent JF, Holford TR, Belanger K, Bracken MB, Beckett WS, Laeher L, McSharry J-E, Leaderer BP. (2006)/ Low-Level Ozone Exposure and Respiratory Symptoms in Infants. *Environ Health Perspect*, 114:911–916.

U.S. Environmental Protection Agency, *Health Risk and Exposure Assessment for Ozone Final Report*, EPA-452/R-14-004f, August 2014.

U.S. Environmental Protection Agency, *Integrated Science Assessment for Ozone and Related Photochemical Oxidants*, 2013. EPA/600/R-10/076F.

Wong CM, Vichit-Vadakan N, Vakanapoom N, Ostro B, et al. (2010). Part 5. Public health and air pollution in Asia (PAPA): a combined analysis of four studies of air pollution and mortality. *Res. Rep, Health Eff. Inst.*, (154): 377-418.

Zanobetti A., Schwartz J. (2008a). Air Pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health* 60: 890-895.

Zanobetti A., Schwartz J. (2008b). Mortality displacement in the association of ozone with mortality: an analysis of 48 cities in the United States, *Am. J. Respir. Crit. Care Med.*, 177 (2): 184-9.

8. Naidoo RN. Occupational exposures and chronic obstructive pulmonary disease: incontrovertible evidence for causality? *Am J Respir Crit Care Med* 2012;185:1252–1254.
9. Darby AC, Waterhouse JC, Stevens V, Billings CG, Billings CG, Burton CM, Young C, Wight J, Blanc PD, Fishwick D. Chronic obstructive pulmonary disease among residents of an historically industrialised area. *Thorax* 2012;67:901–907.
10. Messing K, Punnett L, Bond M, Alexanderson K, Pyle J, Zahm S, Wegman D, Stock SR, de Grosbois S. Be the fairest of them all: challenges and recommendations for the treatment of gender in occupational health research. *Am J Ind Med* 2003;43: 618–629.
11. Couper D, LaVange LM, Han M, Barr RG, Bleecker E, Hoffman EA, Kanner R, Kleerup E, Martinez FJ, Woodruff PG, *et al.*; SPIROMICS Research Group. Design of the Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS). *Thorax* 2014;69:491–494.
12. Regan EA, Hokanson JE, Murphy JR, Make B, Lynch DA, Beaty TH, Curran-Everett D, Silverman EK, Crapo JD. Genetic epidemiology of COPD (COPDGene) study design. *COPD* 2010;7: 32–43.
13. Marchetti N, Garshick E, Kinney GL, McKenzie A, Stinson D, Lutz SM, Lynch DA, Criner GJ, Silverman EK, Crapo JD; COPDGene Investigators. Association between occupational exposure and lung function, respiratory symptoms, and high-resolution computed tomography imaging in COPDGene. *Am J Respir Crit Care Med* 2014;190:756–762.
14. Martinez CH, Kim V, Chen Y, Kazerooni EA, Murray S, Criner GJ, Curtis JL, Regan EA, Wan E, Hersh CP, *et al.*; COPDGene Investigators. The clinical impact of non-obstructive chronic bronchitis in current and former smokers. *Respir Med* 2014;108:491–499.
15. Han MK, Agusti A, Calverley PM, Celli BR, Criner G, Curtis JL, Fabbri LM, Goldin JG, Jones PW, Macnee W, *et al.* Chronic obstructive pulmonary disease phenotypes: the future of COPD. *Am J Respir Crit Care Med* 2010;182:598–604.
16. de Jong K, Boezen HM, Kromhout H, Vermeulen R, Vonk JM, Postma DS; LifeLines Cohort Study. Occupational exposure to vapors, gases, dusts, and fumes is associated with small airways obstruction. *Am J Respir Crit Care Med* 2014;189: 487–490.
17. Dijkstra AE, de Jong K, Boezen HM, Kromhout H, Vermeulen R, Groen HJ, Postma DS, Vonk JM. Risk factors for chronic mucus hypersecretion in individuals with and without COPD: influence of smoking and job exposure on CMH. *Occup Environ Med* 2014;71: 346–352.
18. Doney B, Hnizdo E, Graziani M, Kullman G, Burchfiel C, Baron S, Fujishiro K, Enright P, Hankinson JL, Stukovsky KH, *et al.* Occupational risk factors for COPD phenotypes in the Multi-Ethnic Study of Atherosclerosis (MESA) Lung Study. *COPD* 2014;11: 368–380.
19. Caillaud D, Lemoigne F, Carré P, Escamilla R, Chanez P, Burgel PR, Court-Fortune I, Jebrak G, Pinet C, Perez T, *et al.*; initiative BPCO Scientific Committee. Association between occupational exposure and the clinical characteristics of COPD. *BMC Public Health* 2012; 12:302.
20. Kuschner WG, Hegde S, Agrawal M. Occupational history quality in patients with newly documented, clinician-diagnosed chronic bronchitis. *Chest* 2009;135:378–383.
21. Lam KB, Yin P, Jiang CQ, Zhang WS, Adab P, Miller MR, Thomas GN, Ayres JG, Lam TH, Cheng KK. Past dust and GAS/FUME exposure and COPD in Chinese: the Guangzhou Biobank Cohort Study. *Respir Med* 2012;106:1421–1428.

Copyright © 2015 by the American Thoracic Society

Scientific Evidence Supports Stronger Limits on Ozone

In 2007, 2010, and now again in 2015, the American Thoracic Society has recommended that the U.S. Environmental Protection Agency (EPA) adopt an 8-hour ozone national ambient air quality standard of 60 ppb to adequately protect public health (1, 2). Although the recommended standard endorsed by the American Thoracic Society has not changed during this time, the scientific evidence supporting this recommendation has significantly strengthened. The scientific evidence available 7 years ago justifying this recommendation has been supplemented by an even greater understanding of the health effects of ozone exposures, including infant respiratory problems, worse childhood asthma control, reduced lung function, and increased mortality in adults.

On November 25, 2014, the EPA proposed a standard in the range of 65–70 ppb, which is lower than the current standard of 75 ppb (the standard is defined as the annual fourth highest maximum daily 8-hour ozone average averaged over 3 years). Although we applaud the EPA for proposing a stricter standard, we believe the scientific evidence clearly calls for a standard of 60 ppb to protect human health. We are currently in the public comment period for the proposed ozone rule and urge the EPA to issue a more protective standard of 60 ppb. This is the second time the Obama Administration has reviewed the current ozone standard of 75 ppb. The previous administration established the current standard outside the range recommended by the Clean Air Science Advisory

Committee of 60–70 ppb (3). In 2010, the Clean Air Science Advisory Committee reaffirmed its initial recommendation as part of an early reassessment of the ozone standard, an effort that was ultimately abandoned in 2011 (4). Because a new science assessment was not conducted as part of that review, the current review of the ozone standard is the first to consider new scientific evidence since 2006.

Since 2006, much more evidence has accumulated that ozone exposures in the range of 60–75 ppb have adverse physiologic effects across the entire age spectrum, from infants to older adults. Although there is also some evidence of health effects of ozone exposure below 60 ppb, the strongest evidence supports the conclusion that serious adverse health effects occur across all ages at levels above 60 ppb.

Highlights of this new body of evidence include a study of emergency department visits among children aged 0 to 4 years in Atlanta, Georgia, which found that each 30-ppb increase in the 3-day average of ozone was associated with an 8% higher risk of pneumonia and a 4% higher risk for upper respiratory infection (5). Several studies have demonstrated dose–response relationships between ozone exposure and childhood asthma admissions at exposure levels in the 60–80 ppb range (6–9). Similar associations have been found for adult admissions for asthma (9–11) and chronic obstructive pulmonary disease (12, 13). A population-based cohort study of generally healthy adults found that FEV₁ was 56 ml lower after days

when ambient ozone ranged from 59 to 75 ppb compared with days with levels lower than 59 ppb (14). Controlled human exposure studies have reaffirmed lung function decrements in healthy adults after exposure to 60–70 ppb of ozone (15, 16). Perhaps of greatest concern, there is now stronger evidence of increased mortality in association with ozone (17–19), particularly among the elderly and those with chronic disease (20, 21).

In making this recommendation, we acknowledge that challenges exist in reducing ambient ozone concentrations. Unlike other pollutants regulated by the Clean Air Act, ozone is a secondary pollutant formed from precursor pollutants through photochemical reactions in the atmosphere. This presents challenges in designing successful abatement plans. For example, the natural presence of precursor chemicals and long-range transport of ozone from beyond U.S. jurisdictional boundaries can each contribute to background ozone levels (22). However, the adverse health effects of ozone do not discriminate on the basis of the source of precursor pollutants, nor do these complexities change the reality that serious adverse health effects occur at concentrations higher than 60 ppb. Although the science surrounding background ozone is still emerging, the evidence of adverse health risks of ozone is clear.

Another challenge for ozone management is that the secondary formation of ozone can result in higher concentrations downwind from the primary sources of precursor pollutants, cutting across jurisdictions. As a result, integrated planning across jurisdictional boundaries and compliance with the “good neighbor” provision of the Clean Air Act will be necessary to reduce regional ozone to levels that adequately protect public health (23).

Although controlling ambient ozone will be a challenge, it will also present opportunities for innovation and leadership. State Implementation Plans will vary in how counties across the United States plan to remediate unhealthy levels of ozone. Although all plans will take time to achieve the needed results, the best approaches will be identified and serve as a model that other regions can follow to protect public health.

The timing is excellent for revision of the ozone standard to 60 ppb, as the new standard can build on substantial recent progress. In March 2014, the EPA finalized new standards for motor vehicle emissions and cleaner fuels that are expected to reduce ozone levels significantly (24). Already-adopted revisions to standards for particulate matter and air toxics are also likely to further reduce ozone formation (25). Above all, however, we are entering an era of technological innovation, infrastructure reconstruction, and commitment to sustainability in which obsolete technologies are being replaced by more efficient and less-polluting innovations. This is exactly the right time to lay down the correct performance criteria and design specifications for the new technology before we commit to a new energy and transportation regime that could limit our choices in the future.

The U.S. EPA has taken significant actions in the past when justified by scientific evidence, most notably by reducing the permissible concentrations of airborne lead by 90% in 2008 and reducing the permissible annual concentrations of fine particle pollution by 20% in 2013 (26). We encourage

the EPA administrator, with the full support of the president, to acknowledge the large body of scientific evidence documenting the harms caused by ozone pollution and set a standard of 60 ppb to protect the health of the American public. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

Mary B. Rice, M.D.
Division of Pulmonary, Critical Care and Sleep Medicine
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Tee L. Guidotti, M.D., M.P.H.
Institute for Science, Society and Policy
University of Ottawa
Ottawa, Ontario, Canada

Kevin R. Cromar, Ph.D.
Department of Environmental Medicine
New York University School of Medicine
New York, New York

On behalf of the ATS Environmental Health Policy Committee

References

1. Dey R, Van Winkle L, Ewart G, Balmes J, Pinkerton K; ATS Environmental Health Policy Committee. A second chance: setting a protective ozone standard. *Am J Respir Crit Care Med* 2010;181:297–299.
2. Pinkerton KE, Balmes JR, Fanucchi MV, Rom WN. Ozone, a malady for all ages. *Am J Respir Crit Care Med* 2007;176:107–108.
3. US Environmental Protection Agency. Clean Air Scientific Advisory Committee recommendations concerning the final rule for the national ambient air quality standards for ozone. Washington, DC: U.S. Environmental Protection Agency; 2008 [accessed 2015 Feb 6]. Available from: <http://nepis.epa.gov/Exe/ZyPDF.cgi/P1000JY2.PDF?Dockey=P1000JY2.PDF>
4. US Environmental Protection Agency. Review of EPA's proposed ozone national ambient air quality standard. Washington, DC: US Environmental Protection Agency; 2010 [accessed 2015 Feb 6]. Available from: [http://yosemite.epa.gov/sab/sabproduct.nsf/610BB57CFAC8A41C852576CF007076BD/\\$File/EPA-CASAC-10-007-unsigned.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/610BB57CFAC8A41C852576CF007076BD/$File/EPA-CASAC-10-007-unsigned.pdf)
5. Darrow LA, Klein M, Flanders WD, Mulholland JA, Tolbert PE, Strickland MJ. Air pollution and acute respiratory infections among children 0–4 years of age: an 18-year time-series study. *Am J Epidemiol* 2014;180:968–977.
6. Strickland MJ, Klein M, Flanders WD, Chang HH, Mulholland JA, Tolbert PE, Darrow LA. Modification of the effect of ambient air pollution on pediatric asthma emergency visits: susceptible subpopulations. *Epidemiology* 2014;25:843–850.
7. Strickland MJ, Darrow LA, Klein M, Flanders WD, Sarnat JA, Waller LA, Sarnat SE, Mulholland JA, Tolbert PE. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med* 2010;182:307–316.
8. Gleason JA, Bielory L, Fagiano JA. Associations between ozone, PM_{2.5}, and four pollen types on emergency department pediatric asthma events during the warm season in New Jersey: a case-crossover study. *Environ Res* 2014;132:421–429.
9. Silverman RA, Ito K. Age-related association of fine particles and ozone with severe acute asthma in New York City. *J Allergy Clin Immunol* 2010;125:367–373.
10. Glad JA, Brink LL, Talbott EO, Lee PC, Xu X, Saul M, Rager J. The relationship of ambient ozone and PM_{2.5} levels and asthma

- emergency department visits: possible influence of gender and ethnicity. *Arch Environ Occup Health* 2012;67:103–108.
11. Meng YY, Rull RP, Wilhelm M, Lombardi C, Balmes J, Ritz B. Outdoor air pollution and uncontrolled asthma in the San Joaquin Valley, California. *J Epidemiol Community Health* 2010;64:142–147.
 12. Ko FWS, Hui DSC. Air pollution and chronic obstructive pulmonary disease. *Respirology* 2012;17:395–401.
 13. Medina-Ramón M, Zanobetti A, Schwartz J. The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multicity study. *Am J Epidemiol* 2006;163:579–588.
 14. Rice MB, Ljungman PL, Wilker EH, Gold DR, Schwartz JD, Koutrakis P, Washko GR, O'Connor GT, Mittleman MA. Short-term exposure to air pollution and lung function in the Framingham Heart Study. *Am J Respir Crit Care Med* 2013;188:1351–1357.
 15. Schelegle ES, Morales CA, Walby WF, Marion S, Allen RP. 6.6-hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans. *Am J Respir Crit Care Med* 2009;180:265–272.
 16. Kim CS, Alexis NE, Rappold AG, Kehrl H, Hazucha MJ, Lay JC, Schmitt MT, Case M, Devlin RB, Peden DB, et al. 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.
 17. Peng RD, Samoli E, Pham L, Dominici F, Touloumi G, Ramsay T, Burnett RT, Krewski D, Le Tertre A, Cohen A, et al. Acute effects of ambient ozone on mortality in Europe and North America: results from the APHENA study. *Air Qual Atmos Health* 2013;6:445–453.
 18. Romieu I, Gouveia N, Cifuentes LA, de Leon AP, Junger W, Vera J, Strappa V, Hurtado-Díaz M, Miranda-Soberanis V, Rojas-Bracho L, et al.; HEI Health Review Committee. Multicity study of air pollution and mortality in Latin America (the ESCALA study). *Res Rep Health Eff Inst* 2012;5–86.
 19. Zanobetti A, Schwartz J. Mortality displacement in the association of ozone with mortality: an analysis of 48 cities in the United States. *Am J Respir Crit Care Med* 2008;177:184–189.
 20. Medina-Ramón M, Schwartz J. Who is more vulnerable to die from ozone air pollution? *Epidemiology* 2008;19:672–679.
 21. Zanobetti A, Schwartz J. Ozone and survival in four cohorts with potentially predisposing diseases. *Am J Respir Crit Care Med* 2011;184:836–841.
 22. US Environmental Protection Agency. Policy assessment for the review of the ozone national ambient air quality standards. Washington, DC: U.S. Environmental Protection Agency; 2014 [accessed 2015 Feb 6]. Available from: <http://www.epa.gov/ttn/naaqs/standards/ozone/data/20140829pa.pdf>
 23. Supreme Court of the United States. Environmental Protection Agency et al. v. Eme Homer City Generation, L.P., et al. 2013 [accessed 2015 Feb 6]. Available from: http://www.supremecourt.gov/opinions/13pdf/12-1182_553a.pdf
 24. U.S. Environmental Protection Agency. Control of air pollution from motor vehicles: tier 3 motor vehicle emission and fuel standards; final rule. *Federal Register* Vol. 79, No. 81. 2014 [accessed 2015 Feb 6]. Available from: <http://www.gpo.gov/fdsys/pkg/FR-2014-04-28/pdf/2014-06954.pdf>
 25. U.S. Environmental Protection Agency. Reconsideration of certain new source issues: national emission standards for hazardous air pollutants from coal- and oil-fired electric utility steam generating units and standards of performance for fossil-fuel-fired electric utility, industrial-commercial-institutional, and small industrial-commercial-institutional steam generating units. 2013 [accessed 2015 Feb 6]. Available from: <http://www.gpo.gov/fdsys/pkg/FR-2013-04-24/pdf/2013-07859.pdf>
 26. US Environmental Protection Agency. National ambient air quality standards for lead. *Federal Register* Vol. 73, No. 219. 2008 [accessed 2015 Feb 6]. Available from: <http://www.gpo.gov/fdsys/pkg/FR-2008-11-12/pdf/E8-25654.pdf>

Copyright © 2015 by the American Thoracic Society