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Ozone and Childhood Respiratory Health: a primer for US pediatric providers and a call for a more protective standard

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Abstract

Ground level ozone is a potent respiratory toxicant with decades of accumulated data demonstrating respiratory harms to children. Despite the ubiquity of ozone in the United States (US), impacting both urban and rural communities, the associated harms of exposure to this important air pollutant are often infrequently or inadequately covered during medical training including pulmonary specialization. Thus, many providers caring for children's respiratory health may have limited knowledge of the harms which may result in reduced discussion of ozone pollution during clinical encounters. Further, the current US air quality standard for ozone does not adequately protect children. In this non-systematic review, we present basic background information for healthcare providers caring for children's respiratory health, review the US process for setting air quality standards, discuss the respiratory harms of ozone for healthy children and those with underlying respiratory disease, highlight the urgent need for a more protective ozone standard to adequately protect children's respiratory health, review impacts of climate change on ozone levels, and provide information for discussion in clinical encounters.

Keywords

ozone; childhood asthma; air pollution

Introduction

Ground level ozone (O_3) is a widely prevalent outdoor air pollutant responsible for >1 million annual deaths worldwide[1] that contribute to the global burden of chronic respiratory disease[2]. In the United States (US), ozone is a criteria air pollutant and therefore regulated by the Environmental Protection Agency (EPA) under the Clean Air Act (CAA)[3]. Despite ozone having many adverse respiratory effects in children, exposures to ozone and other outdoor air pollutants are infrequently or inadequately addressed during medical training,

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which may lead to reduced healthcare provider discussion with patients who may benefit from such knowledge[4–7].

Despite the reduction in ozone concentrations over the last several decades as a result of the CAA, notably while the gross domestic product also increased[8], 1/3 of the US population remains exposed to levels exceeding the current EPA national ambient air quality standard (NAAQS)[9]. Climate change has already impacted ozone concentrations and will lead to further ozone increases for most of the US, reducing the benefits of current regulatory policies[9]. As such, ozone exposure remains of significant concern for millions of US children and will remain so for the foreseeable future.

It is incumbent upon those who care for children's respiratory health to have knowledge of the harmful impacts of ozone on their patients. Further, a considerable body of evidence demonstrates that the current NAAQS does not adequately protect children from adverse effects. The goal of this critical review is to summarize salient information for healthcare providers on the harms of ozone exposure on causing and exacerbating childhood respiratory disease, the implications of climate change on ozone levels, and the need for a more protective NAAQS. Discussion of non-respiratory impacts of ozone exposure, such as metabolic and cardiovascular, are outside the scope of this review.

Basics of ozone pollution and regulation in the United States

Ground level ozone is a colorless and odorless gaseous pollutant for which a threshold of safe exposure has not yet been identified[10,11] although a recent review suggests that levels greater than 33–42 parts per billion (ppb) are harmful to human health[8]. Compared to stratospheric ozone (a.k.a. ozone layer, "good" ozone) which is naturally formed and reduces ultraviolet radiation, there is substantial evidence demonstrating the harmful effects of both short and long-term ground-level ozone exposure on human health[10].

Ground-level ozone, hereafter referred to as "ozone", is not directly emitted but is formed by a photochemical reaction involving precursor agents such as oxides of nitrogen (NOx), volatile organic compounds (VOC), carbon monoxide, and methane in the presence of sunlight and heat[3,10]. Ozone is typically higher in the afternoons during warmer months (e.g. summer), in urban environments, and tends to be higher in California, Texas, Denver, the Lake Michigan region, metropolitan Atlanta, and the Northeast[3] (Figure 1). However, high levels of ozone can occur in rural locations[12], at nighttime[13], and during cold months[14,15] due to transport of urban O_3, natural topography (e.g. Western US basins), and oil and gas development release of high precursor agents[3]. Ozone precursor agents arise from both anthropogenic (man-made) and natural sources. The majority of ozone in the US originates from man-made NOx and VOC[13]. Contributors in the US include fuel combustion and evaporation associated with motor vehicles; large stationary sources such as power plants, oil refineries, and factories; small stationary sources such as gas stations and print shops; off-road engines in aircraft, trains, construction equipment, agricultural operations, and lawn and garden equipment. In addition, organic compound evaporation from consumer products such as paints, cleaners, and solvents also contribute to ozone generation[13]. Ozone and

ozone precursor agents can disperse over large distances contributing to elevated O_3 levels in other regions. Indeed, non-US emissions contribute to US background levels of ozone[13].

In the US, the EPA regulates outdoor ozone concentrations as directed by the CAA of 1970[3]. Ozone is one of six criteria pollutants for which levels are set by a NAAQS. NAAQS are supposed to be re-evaluated every 5 years by a panel of external experts (a.k.a. Clean Air Science Advisory Committee (CASAC)) to assess the scientific evidence of harm to public health[16]. The current primary NAAQS for ozone is 70 ppb for the annual fourth-highest daily maximum 8 hour-concentration averaged over 3 years (Table 1)[3]. NAAQSs have primary and secondary levels, set by the impacts of the criteria pollutant on human health (primary) and the environment (secondary). Per the CAA, the NAAQS must be set to protect public health with an adequate margin of safety to protect vulnerable populations. Ultimately, it is the EPA administrator, a political appointee, who issues a final rule to retain or revise the current NAAQS based on information from the Integrated Science Assessment (ISA), Risk/Exposure Assessment, Policy Assessment, CASAC advice, and public comment[17]. Thus, presidential elections have direct impact on the ozone NAAQS[18].

Children are more susceptible to the harmful effects of ozone

An individual's ozone exposure is dependent upon the: 1) ambient ozone concentration, 2) duration of exposure, and 3) amount breathed during the exposure time (i.e. minute ventilation). This explains why someone sitting outside will have less exposure than someone vigorously exercising. Compared to adults, children have increased minute ventilation rates relative to body size, increased mouth breathing, increased physical activity levels, and spend increased time outdoors, which serve to increase exposure[19–22].

Additionally, children's respiratory and immune systems are still developing and although inadequately understood, there are 'critical windows' during which insults can have lasting impacts on development[23–25]. Indeed, the origins of many adult respiratory diseases are likely to be found during childhood, including gestation[26,27]. Further, children's airways are narrower than adults, such that bronchoconstriction and inflammation can produce earlier and more severe symptoms.

Respiratory harms of ozone exposure

Ozone is a potent oxidant gas that causes oxidative stress in the respiratory tract. The EPA concludes O_3 is the "most prevalent photochemical oxidant present in the atmosphere and the one for which there is a very large, well-established evidence base of its health and welfare effects"[3]. The recent ISA concludes that short-term ozone exposure is causally associated with respiratory health effects, with long-term exposures likely to be causal (Table 2)[10]. Mechanistically, ozone is inhaled into the lower respiratory tract where it dissolves in the thin layer of epithelial lining fluid. There it reacts with epithelial cells, immune cells, and neural receptors to cause injury, inflammation, and oxidative stress[13].

Numerous epidemiological and controlled human exposure studies have documented respiratory harms of ozone exposure, including airway inflammation, decreased forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV1), airway hyperresponsiveness,

obstruction, lung injury, enhanced allergic sensitization and responses, impaired host defenses including impaired mucociliary clearance[28], and respiratory symptoms such as cough, throat irritation, pain on inspiration, chest tightness, and shortness of breath[10,13,29]. Notably, although children have similar lung function responses to ozone, they report fewer symptoms compared to adults[10]. Population level effects of short-term ozone exposure include increased risk of emergency department visits, hospital admissions, asthma exacerbations, and respiratory infections[10].

While much of our understanding of the human physiologic responses to ozone comes from experimental controlled-exposure or chamber studies, such studies, for ethical reasons, do not include children. Therefore, we lack data on controlled exposure outcomes for one of the most susceptible populations, namely children with underlying respiratory disease. Controlled-exposure studies are also limited by lack of accounting for real-world exposures[30]. For example, during activities of daily living children are exposed to ozone in conjunction with other air pollutants (e.g. NOx, fine particle pollution), aeroallergens (e.g. pollens, molds), heat, and/or bacteria and viruses[31]. In adults, there is experimental evidence of ozone-induced enhancement of bronchoconstrictor responses to inhaled aeroallergen in specifically-sensitized individuals[32,33]. Additionally, exposures to higher levels of ozone are frequently repeated, over days to months[22]. Therefore, although epidemiological studies are often limited by exposure uncertainties (e.g. pollutant mixtures are heterogenous making it difficult to disentangle single pollutant effects), such studies are critical for our understanding of the health harms of ozone exposure in children and particularly children with respiratory disease.

Long-term exposure to ozone has been found to reduce lung function[34] and increase morbidity[35] and mortality[2,36,37]. Notably, a landmark study of the entire US Medicare population, almost 61 million persons, found an increased risk of death for every 10 ppb increase in average warm season ozone (hazard ratio (HR) 1.011 (95% CI 1.010–1.012)), even in locations with ozone < 50 ppb (HR 1.010 (95% CI 1.009–1.011))[37]. The association was stronger in persons eligible for Medicaid[37].

There is individual variability in responses to ozone exposure, although persons with asthma and underlying lung disease[38,39], elderly persons[40], under-resourced persons and communities[38,41], and children are at enhanced risk[3]. As the respiratory tract epithelial lining fluid is rich in antioxidants[10], persons with diminished ability to metabolize reactive oxygen species are at increased risk for adverse outcomes. Several studies have demonstrated ozone modifying effects such as diet (including antioxidants)[42–44], birth weight[45], neighborhood and individual low income[37,38,46,47], genetics[48,49], and co-exposures[45,50]. Further studies evaluating the mitigating role of antioxidants for clinical management are needed before recommending such therapy[31,51–53].

Healthy children

Numerous epidemiological studies of healthy children attending summer camps have demonstrated short-term ozone exposure and reductions in FEV1[10]. A longitudinal study of the effects of childhood exposure to relatively high levels of ozone in Mexico showed a reduced rate of growth of lung function[54]. In addition, a cross-sectional study of

University of California, Berkeley freshmen students showed reduced lung function in students who had grown up in Southern California with relatively high lifetime cumulative ozone exposure as compared to those who had grown up in Northern California with lower cumulative exposure[55].

Several studies have noted an association with gestational exposures to ozone and preterm birth or low birth weight, however not all[56]. As preterm birth is a well described risk factor for development of asthma in childhood[57], such an association could impact asthma development.

In a nationwide study of children and adults, ozone exposure was associated with aeroallergen sensitization supporting a link with allergic disease[58]. Mechanistically, this finding is supported by several studies demonstrating increased IgE, Th2 cytokines, thymic stromal lymphopoietin, eosinophilic inflammation, goblet cell metaplasia, and mucin expression in response to ozone exposure[10,59–63].

Several epidemiological studies have demonstrated short-term ozone exposure and associations with illness-related school absentism[64,65] and with emergency department visits for pneumonia[66], respiratory infections[66,67], and respiratory-related visits[68]. For example, in a time-series analysis of emergency department visits for respiratory infections in children aged 0–4 years, ozone exposure increased estimated risk for pneumonia and upper respiratory infections even at levels as low as 30 ppb[67]. Notably, the rate ratios were stronger during the cold season when ozone levels were generally lower, supporting that ozone exposure is a concern year-round and not just during warm seasons.

Incident respiratory disease

Several recent studies have supported an association between long-term ozone exposure and the development of childhood asthma[69,70], although not all[71]. A workshop published in 2018 concluded that several mechanistic studies support ozone exposure and incident asthma, although the epidemiologic data are less clear[72]. In a large study of Black and Hispanic children, ozone exposure in the first year of life or first 3 years of life was not associated with asthma[71]. Notably, that study did demonstrate a significant association between NO_2, an ozone precursor, and incident asthma. A study of >3,000 children from 12 different communities found increased risk of incident asthma in children with heavy exercise (≥3 or more sports) vs. no sport participation in communities with high ozone (relative risk (RR) 3.3, (95% CI 1.9–5.8), median 4-year 8-hour ozone in high communities 57 ppb (IQR 56, 69ppb))[70]. More recently, a large longitudinal study of school-aged children in Canada found exposure to total oxidants (NO_2 + O_3) at birth increased risk of developing asthma by 17% and eczema by 7%. Notably, NO_2 and O_3 were significantly negatively correlated. The reported median (IQR) ozone exposure for children with asthma was 43.3 ppb (42.4, 44.3), and although difficult to compare to current NAAQS, this supports that even low average levels of ozone exposure are associated with new-onset asthma[69].

Existing respiratory disease

There is robust literature demonstrating the effects of ozone exposure on childhood asthma outcomes[10], however there are scant studies evaluating the association between ozone exposure and other childhood respiratory outcomes such as cystic fibrosis (CF)[73–76], primary ciliary dyskinesia, sickle-cell disease[77–80], interstitial lung disease, post-prematurity respiratory disease[81], or non-CF bronchiectasis. For example, a recent systematic review of outdoor air pollution in cystic fibrosis identified only 5 studies evaluating air pollution and cystic fibrosis, of which 4 evaluated the effects of ozone[82]. Most studies identified an association with short-term exposure to ozone and CF-pulmonary exacerbations[74–76], although not all[73]. For sickle cell disease, most studies have demonstrated an association with ozone exposure and emergency department visits[79] or hospitalizations[77,78], although not all[80], with variability in outcomes measures used (e.g. pain, respiratory infection, acute chest syndrome). Further research evaluating the effects of short- and long-term ozone exposure on non-asthma chronic childhood respiratory outcomes is urgently needed.

Numerous studies have demonstrated associations with short-term ozone exposure and increased risk of asthma exacerbations requiring emergency department visits[46,58,66,83,84] and hospitalizations[85–87]. Additionally, short-term ozone exposure has been associated with increased asthma symptoms[45,88,89], increased rescue medication usage[89], and decreased lung function[45,90,91]. Some studies evaluating the modification of inhaled corticosteroids (ICS) have demonstrated non-protective effects[88,90,91], although not all[45,92]. For example, Lewis, et. al. found children with asthma receiving ICS reported more shortness of breath, chest tightness, and wheeze following ozone exposure as compared to no ICS[88]. Hernandez, et. al. found asthma medications did not protect against short-term ozone-induced lung function decreases[90]. Altman et. al. found that 30% of all non-virus triggered asthma exacerbations were associated with ozone, despite all children receiving ICS +/− long-acting beta agonists (LABA)[93].

Long-term ozone exposures are also associated with increased risk of adverse asthma outcomes. For example, a study of children in New York found every 1 pbb increase in average ozone was associated with increased asthma hospitalizations[35].

Current ozone NAAQS is not adequate

A recent systematic review and meta-analysis of the effects of ozone on lung function reviewed epidemiological studies from 2013–2020[34]. Most of the studies in children demonstrated a relationship between reduced lung function and ozone exposure at levels below current NAAQS, especially for longer exposures[34]. As such, the current ozone NAAQS is not adequately protective for children’s lung function.

While results from controlled-exposure studies in children are unavailable, results from young adults support this finding. A study of exercising healthy young adults exposed to 60 ppb ozone for 6.6 hours demonstrated reduced lung function and increased inflammation[94]. In another study of healthy young adults, ages 18–25, exposure to mean ozone concentrations of 60, 70, 80, and 87 ppb increased total symptom score (throat tickle, cough, shortness of breath, and pain on deep inspiration) and decreased FEV1 by

−2.72, −5.34, −7.02, and −11.42%, respectively, although at 60 ppb the decrease was not significant[95]. By exposure group, the number (%) of participants with FEV1 decreases of 10% or more at 6.6 hours was 5 (16%), 6 (19%), 9 (29%) and 13 (32%) for 60, 70, 80, and 87 ppb, respectively[95]. Thus, even at levels <70 ppb, 16% of participants had reductions in lung function greater than expected for test variation.

For children with asthma, a recent study of Black adolescents with persistent asthma found short-term ozone exposures (8-hour maximum averages <70 ppb) were associated with reductions in FVC despite receiving ICS +/− LABA[90]. Although limited by small size, the study supports that asthma controller medications may not protect against harms of ozone exposure, even at levels below the current NAAQS.

A nationwide study of adults and children receiving Medicaid found every 1 ppb increase in short term warm-season O_3 was associated with a 10% increased risk of asthma hospitalizations[47]. In subgroup analysis by age, the association with O_3 was greatest for teens aged 13–18 years old (43%, 95%CI 21–65%) but not seen for children 12 years and younger. In a cohort sub-analysis, the association between O_3 exposure and risk was observed at 8-hour maximum mean levels <70 ppb (12% increased risk, 95 CI 7–17%) and <60 ppb (10% increased risk, 95% CI 4–16%), and was higher among persons residing in zip codes with higher neighborhood disadvantage and lower population density[47]. Another study found associations between ozone and childhood asthma emergency department visits, even at cold season 8-hour maximum average ozone levels between 39–51 ppb[84].

For infections, associations between short-term ozone and emergency department visits for pneumonia and upper respiratory infections in young children were found for ozone levels as low as 30 ppb, well below the current NAAQS[67]. As a study found early life pneumonia was associated with decreased lung function and asthma later in life, reducing pneumonia episodes may also reduce adult respiratory disease[96].

Taken together, these studies provide evidence that the current EPA standard does not provide an adequate margin of protection for children and in particular, children with asthma. Indeed, since 2007 the American Thoracic Society (ATS) has endorsed a primary NAAQS of 60 ppb[97,98], which ~80% of monitored US counties would exceed if instituted[11,99] (Figure 1).

Benefits of adopting a lower standard

An EPA analysis concluded that reducing the NAAQS to 60 ppb would result in 15% reductions in hospital admissions and mortality[16]. The most recent ATS and Marron Institute Report estimated the health impacts attributable to exceeding the ATS ozone standard as > 29 million adversely impacted days (restricted activity days, work loss days, and school days), almost 15,000 major morbidity events, and greater than 3,600 deaths, albeit these are neither specific to children nor respiratory outcomes.

For children, the gains of adopting the ATS standard are likely even greater. For example, lung function peaks during early adulthood and slowly declines with age[100], thus insults to optimal lung growth during childhood are likely to confer increased risk of respiratory

disease later in life[96,101–103]. Additionally, asthma is the most common chronic respiratory disease of childhood affecting over 5 million US children[104]. Emergency departments costs for childhood asthma exacerbations are not insignificant, estimated in 2010 to cost $272 million for Medicaid recipients alone[105]. A study of transportation changes made in Atlanta, GA during the 1996 Olympics demonstrated decreases in regional ozone levels, which were associated with decreased childhood asthma emergency department visits and hospitalizations (42% reduction)[106]. Further, when using 3-day cumulative ozone levels during the study period and values <60 ppb as reference, the relative risk for acute asthma events increased stepwise for increasing ozone levels: RR 1.61 (95% CI 1.13–2.30) for values 60–89 ppb to RR 1.88 (95%CI 1.24–2.83) for values ≥90 ppb. Such findings augment mechanistic, controlled-exposure and epidemiological data in demonstrating the real-world benefits for children in adopting a lower ozone standard.

Climate change and ozone

The Fourth National Climate Assessment concluded that without further reduction in precursor emissions (e.g. VOC, NOx), ozone levels will increase over most of the US as a result of climate change, both from warmer temperatures and increases in natural emissions (e.g. wildfires[107])[9]. Such an increase has been termed ‘climate penalty’, meaning even with reductions in precursor agents, ozone levels will rise given increased temperatures[108]. Indeed, without climate change mitigation or reduction in ozone precursor agents, days with ozone levels >75 ppb are predicted to increase for much of the US by 2050[109]. Further, US wildland fire frequency, duration, and intensity have markedly increased over the last 4 decades[110], thus contributing to emissions of ozone precursor agents. Moreover, there is growing evidence of a likely synergistic effect of heat and air pollution in worsening health outcomes[111,112]. Thus, with regards to ozone pollution and childhood respiratory health, mitigating climate change is imperative to protect against harm[113].

Policies which support reduction of fossil-fuel combustion are necessary for climate change mitigation and will also serve to reduce ozone pollution. For example, methane (‘natural gas’) is a potent greenhouse gas[9,114], therefore policies that require reduced extraction, distribution, fugitive emissions, and combustion of methane are also beneficial for reducing ozone[9,115,116].

Healthcare providers can provide important insights for policy makers at institutional, local, regional, and national levels regarding the adverse health effects of air pollution and increasing temperatures on their patients[20]. Healthcare providers are uniquely poised to advocate on behalf of children’s respiratory health, especially children from groups who, as a result of exclusionary and/or racist policies, have been inequitably burdened with respiratory disease and adverse outcomes[117], increased exposure to air pollution[117–120], and have reduced access to resources for climate adaptation[113,121,122].

Addressing ozone during clinical encounters

Data informing what, how, and to whom healthcare providers should discuss the harms of ozone exposure during clinical encounters are lacking. The National Asthma Education

and Prevention Program guidelines, along with the American Academy of Pediatrics policy statement[20] endorse discussion of the Air Quality Index (AQI) with patients with asthma and children, respectively. In the US, the EPA provides an hourly ozone AQI (as a forecast 'NowCast') via the AirNow website[123] or app. The AQI is a single pollutant concentration index that provides behavioral recommendations by category (Table 3)[124].

Advising patients of the AQI is prudent, however much remains unknown about this behavioral health intervention. For an air quality index to be effective at preventing adverse health outcomes, several tenets are required: the index, derived from pollutant concentrations, should be associated with the health outcomes it seeks to prevent; the index must be easily understood and widely accessible to people; persons must be aware of the index including how and when to use and respond; persons must be motivated and able to implement the response; and the response should result in reduced exposure and therefore reduction of adverse health outcomes[125–127]. Few studies have been conducted in children with respiratory disease for any of these components[126,128–136].

Until such time as high-quality clinical algorithms, based on evidence, are available, it remains appropriate to educate families and children with respiratory disease of the use of AirNow as a method to reduce short-term outdoor ozone exposure (Table 4). Most studies support provider discussion is associated with increased usage of the AQI[136–138].

As a recent study demonstrated an association with non-viral triggered asthma exacerbations and levels of ozone below which AQI alerts would be issued[93], using the AQI as a way to learn personal susceptibilities in conjunction with responding to alerts may be a preferable strategy. Based on a small randomized clinical trial of adding the AQI to childhood asthma action plans[135] and from the known benefits of physical activity, we recommend clinicians monitor physical activity closely in children with respiratory disease using the AQI to learn personal ozone susceptibilities. Importantly, clinicians can advise patients and families that ozone tends to be greater on hot, stagnant, summer days in the late afternoon and evenings. Changing outdoor physical activity to the mornings on such days preserves activity yet reduces exposure.

Notably, the most equitable air pollution interventions are those at policy levels, which provide the most benefit and least individual burden[126,133] and for which personal interventions should never be a substitute. Indeed, as many childhood respiratory conditions inequitably burden non-White and/or economically excluded persons and communities[117,121], individual level interventions such as modifying behavior according to the AQI have the potential to exacerbate inequities and should be monitored closely[126,133].

Indoor ozone levels are often substantially lower (30–70%) compared to outside[126], particularly in tightly sealed buildings[139], with most indoor ozone originating from outdoors as opposed to being emitted[140]. However, indoor ozone emission sources can include ozone generators, electrostatic precipitators, or ionizers marketed to consumers to improve air quality, for which there has been no federal consumer regulatory oversight[141]. This information is pertinent for childhood healthcare providers as caregivers often inquire about methods to improve indoor air quality. The EPA advises avoidance of indoor air cleaners that

intentionally produce ozone[142] and recommends usage of proven reduction methods[141]. The EPA's online 'Guide to Air Cleaners in the Home' is available for patients and families[142].

Conclusion:

Ozone exposure causes adverse respiratory effects in children, particularly in children with asthma. Climate change will increase ozone levels, which will impact the respiratory health of children. The current ozone NAAQS does not sufficiently protect children with an adequate margin of safety and must be revised by the EPA. We recommend adoption of the ATS ozone standard of 60 ppb to protect children. Healthcare providers caring for children's respiratory health should be aware of the harms of ozone for their patients and discuss using the AQI via AirNow as part of clinical management.

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Abbreviations:

AQI	Air Quality Index
ATS	American Thoracic Society
CAA	Clean Air Act
CASAC	Clean Air Science Advisory Committee
CI	confidence interval
EPA	Environmental Protection Agency
FEV1	forced expiratory volume in 1 second
FVC	forced vital capacity
HR	hazard ratio
ICS	inhaled corticosteroid
IQR	interquartile range
ISA	Integrated Science Assessment
NAAQS	National Ambient Air Quality Standard
NO_2	nitrogen dioxide
NOx	oxides of nitrogen
O_3	ozone
OR	odds ratio
ppb	parts per billion

RR	relative risk
US	United States
VOC	volatile organic compounds

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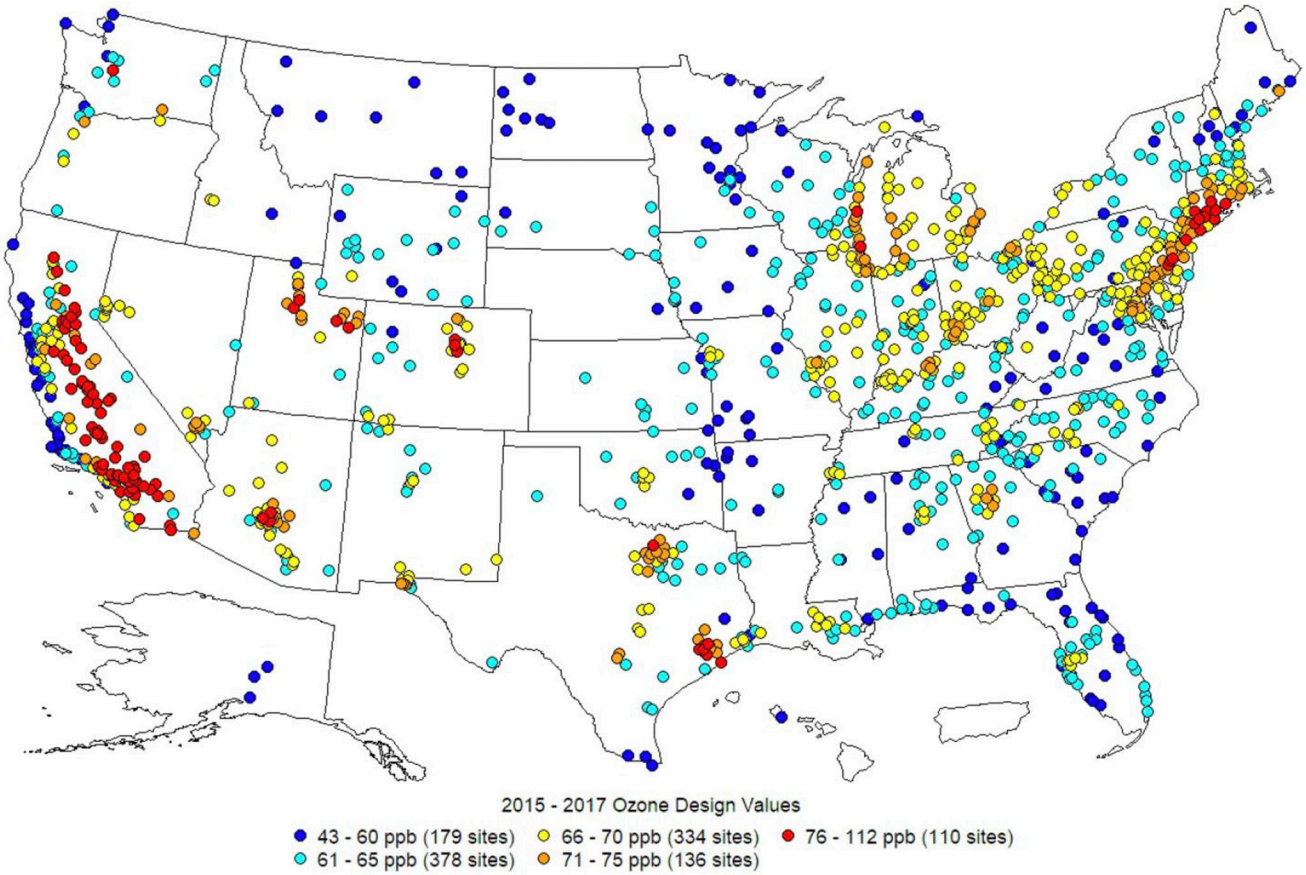

Figure 1:

Ozone design values (3-year average of annual 4th highest maximum daily 8-hour average ozone concentration) for individual monitors for 2015–2017. ppb= parts per billion. Source: Figure 1–8 from ISA[10]

Table 1:

Historical National Ambient Air Quality Standards (NAAQS) for ozone

Year	1° NAAQS	Calculation
1979	120 ppb	1 hour averaging time; expected number of days per year with maximum hourly average concentration > than 120 equaled one or less.
1997	80 ppb	8 hour averaging times; Annual fourth-highest daily maximum, averaged across three consecutive years.
2008	75 ppb	8 hour averaging times; Annual fourth-highest daily maximum, averaged across three consecutive years.
2015	70 ppb	8 hour averaging times; Annual fourth-highest daily maximum, averaged across three consecutive years.

Limits are set in parts per million, displayed here as parts per billion (ppb). Information obtained from: https://www.epa.gov/ground-level-ozone-pollution/timeline-ozone-national-ambient-air-quality-standards-naaqs.

Table 2:

Ozone exposures and respiratory health effects

Exposure	EPA 2020 Causal Determination	Health effects
Short-term	Causal	Healthy: decreased lung function; airway inflammation, injury and oxidative stress; increased airway responsiveness (involvement of parasympathetic pathways); respiratory infections including pneumonia; increased symptoms: cough, pain on deep inspiration, shortness of breath; Type 2 immune responses. Asthma: exacerbations, emergency department visits; hospitalizations; decreased lung function; symptoms; inflammation and oxidative stress; enhanced allergic responses and bronchoconstriction (involvement of vagal C-fibers).
Long-term	Likely to be causal	Healthy: compromised airway growth and development; development of childhood asthma; allergic response (allergic sensitization and enhanced allergic responses); Asthma: emergency department visits; hospitalizations; symptoms.

EPA causal determination obtained from ISA[10] and represents impacts of ozone exposure on respiratory health effects, all ages. Long term refers to exposures over months to years. Effects of COPD and mortality not included in table.

Table 3:

US Air Quality Index for Ozone for Children and Persons with Respiratory Disease

AQI Category	Index Values	At Risk	O_3 Breakpoints, 8-hour avg	Behavioral Recommendations
Good	0 – 50	-	0 – 54 ppb	It's a great day to be active outside
Moderate	51 – 100	Some people who may be unusually sensitive to ozone	55 – 70 ppb	Unusually sensitive people: *Consider reducing* prolonged or heavy outdoor exertion. Watch for symptoms such as coughing or shortness of breath. These are signs to take it easy.
Unhealthy for sensitive groups	101 – 150	Sensitive groups include people with lung disease such as asthma, older adults, children and teenagers, and people who are more active outdoors	71 – 85 ppb	***Reduce* prolonged or heavy outdoor exertion.** Take more breaks, do less intense activities. Watch for symptoms such as coughing or shortness of breath. Schedule outdoor activities in the morning when ozone is lower. People with asthma should follow their asthma action plans and keep quick-relief medicine handy.
Unhealthy	151 – 200	Everyone	86 – 105 ppb	***Avoid* prolonged or heavy outdoor exertion.** Schedule outdoor activities in the morning when ozone is lower. Consider moving activity indoors. People with asthma, keep quick-relief medicine handy.
Very Unhealthy	201 – 300	Everyone	106 – 200 ppb	***Avoid all* physical activity outdoors.** Move activities indoors or reschedule to a time when air quality is better. People with asthma, keep quick-relief medicine handy.
Hazardous	301 – 500	Everyone	201ppb to significant harm level	***Avoid all* physical activity outdoors**

Information obtained from EPA https://www.airnow.gov/sites/default/files/2021-03/air-quality-guide_ozone_2015.pdf (accessed 09/17/2022) and https://www.epa.gov/sites/default/files/2015-10/documents/20151001_air_quality_index_updates.pdf (accessed 9/20/2022). At risk is defined by EPA AQI categories.

Table 4:

Considerations for healthcare providers to address ozone pollution

Individual actions	• Reduce generating ozone precursors – Transportation: drive less (e.g. carpool, trip-chain, telecommute, bike or walk where possible), don't idle vehicle(s); refuel after dusk on hotter days – Home: use zero-VOC paints and solvents; use electric powered lawn equipment (e.g. mower, edger, leaf-blowers); purchase energy efficient appliances; conserve electricity (e.g. set air conditioners to no lower than 78 °F); reduce usage of pesticides and if necessary, opt for low-emission products. • Increase knowledge about ozone and health harms to share with patients, colleagues, healthcare organizations, and communities. – Learn more about ozone: Ozone and Your Patients' Health Training Course[13] – Learn about your region's spatiotemporal ozone distribution – Learn about additional alert systems within your region (i.e. local health departments may have resident alert systems) – Serve as an expert consultant for schools, daycare facilities, public health organizations, policy makers – Serve on committees within healthcare organizations to promote adoption of clean air operations • Appreciate that the burden of ozone exposure cannot be solely placed upon an individual and that the most equitable interventions are sound policies which reduce ozone air pollution for everyone. Advocate for such policies. • Appreciate ozone pollution is linked with climate change. Policies which support climate change mitigation will also improve air quality. Advocate for such policies. • Vote for candidates (local, regional, national) who support sound air quality policies
Clinical actions *	Outdoor ozone exposure: • Provide education regarding harms of ozone exposure on respiratory health. Example discussions could include: – Ozone is a known respiratory irritant and causes worsening respiratory symptoms – Ozone is generally higher on hot, stagnant summer days in the afternoon and early evening. Recommend changing physical activity to in the morning on such days. • Provide information about AirNow, which is widely available as a smartphone app & on the AirNow website. – Encourage parents/patients to sign-up for air alerts and to check the AQI prior to going outside to be active. Follow the recommendations of the AQI for each category. Review the importance of physical activity and that most AQI recommendations are to reduce the duration or intensity of an outdoor activity and not to stop physical activity completely (see Table 3). – For children with respiratory disease, consider discussing usage of the AQI as a way to learn individual sensitivities to ozone as such children may be at higher risk to experience symptoms in the moderate AQI range. If using this approach, particularly in regions with a high prevalence of moderate days, monitor physical activity closely. – Establish a good rapport for patients to communicate difficulties with ozone exposure. For example, if a patient with asthma reports they have increased symptoms on or following ozone yellow days, consider reviewing asthma control and/or options for indoor physical activity. Indoor ozone exposure • Recommend against the usage of any marketed 'air cleaner' or other device(s) which generate ozone • Provide families/patients the EPA "Guide to Air Cleaners in the Home"[142] • Recommend closing windows on days with ozone alerts or at levels (if lower than alerts) which induce symptoms. When recommending closing windows, screen for and address indoor air pollutants. For example, if there is active combustion and/or aerosolization inside the home, closing windows may worsen air pollution exposure.

* Note: this table is specific to ozone pollution and clinical conversations regarding air quality should include discussion of other common outdoor air pollutants such as fine particle pollution ($PM_{2.5}$) and nitrogen dioxide (NO_2) for which additional recommendations would be applicable (e.g. avoid exercise/activity near major roadways). As the AQI via AirNow is standardized, we recommend usage of AirNow as opposed to using an AQI available on many smartphone apps or other sources, which may or may not be the standardized EPA AQI.