Title

Ambient ozone effects on respiratory outcomes among smokers modified by neighborhood poverty: An analysis of SPIROMICS AIR

Authors

Belz, Daniel C
Woo, Han
Putcha, Nirupama
et al.

Publication Date

2022-07-01

DOI

10.1016/j.scitotenv.2022.154694

Peer reviewed

HHS Public Access

Author manuscript

Sci Total Environ. Author manuscript; available in PMC 2023 July 10.

Published in final edited form as:

Sci Total Environ. 2022 July 10; 829: 154694. doi:10.1016/j.scitotenv.2022.154694.

Ambient ozone effects on respiratory outcomes among smokers modified by neighborhood poverty: an analysis of SPIROMICS AIR

Daniel C Belz, MD MPH[a], **Han Woo, PhD**[a], **Nirupama Putcha, MD MHS**[a], **Laura M Paulin, MD MHS**[b], **Kirsten Koehler, PhD**[c], **Ashraf Fawzy, MD MPH**[a], **Neil E Alexis, PhD**[d], **R. Graham Barr, MD PhD**[e], **Alejandro P Comellas, MD**[f], **Christopher B Cooper, MD**[g], **David Couper, PhD**[d], **Mark Dransfield, MD**[h], **Amanda J Gassett, PhD**[i], **MeiLan Han, MD MS**[j], **Eric A Hoffman, PhD**[f], **Richard E Kanner, MD**[k], **Jerry A Krishnan, MD PhD**[l], **Fernando J Martinez, MD MS**[m], **Robert Paine III, MD**[k], **Roger D Peng, PhD**[c], **Stephen Peters, MD PhD**[n], **Cheryl S Pirozzi, MD MS**[k], **Prescott G Woodruff, MD MPH**[o], **Joel D Kaufman, MD MPH**[i], **Nadia N Hansel, MD MPH**[a]

SPIROMICS Investigators

[a.]Department of Medicine, Johns Hopkins University, 1830 E. Monument, 5th Floor, Baltimore, MD 21205, USA

[b.]Dartmouth-Hitchcock Medical Center/Geisel School of Medicine at Dartmouth, 1 Medical Center Dr, Pulmonary 5C Ste, Lebanon, NH 03756, USA

[c.]Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA

[d.]University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

[e.]Columbia University Medical Center, 630 W. 168th St., New York, NY 10032, USA

Corresponding author – 1830 E. Monument, 5th Floor, Baltimore, MD 21205, USA, DC Belz: Dbelz2@jhmi.edu.

CRediT authorship contribution statement

Daniel C Belz: Writing - Original Draft, Formal analysis, Visualization, Conceptualization; **Han Woo**: Formal analysis, Writing - Review & Editing, Visualization; **Nirupama Putcha**: Writing - Review & Editing, Visualization; **Laura M Paulin**: Formal analysis, Writing - Review & Editing; **Kirsten Koehler**: Writing - Review & Editing; **Ashraf Fawzy**: Writing - Review & Editing; **Neil E Alexis**: Supervision, Writing – Review & Editing; **R. Graham Barr**: Supervision, Methodology, Writing – Review & Editing; **Alejandro P Comellas**: Supervision, Writing – Review & Editing; **Christopher B Cooper**: Supervision, Writing – Review & Editing; **David Couper**: Supervision, Writing – Review & Editing; **Mark Dransfield**: Supervision, Writing – Review & Editing; **Amanda J Gassett**: Methodology, Formal analysis; **MeiLan Han**: Supervision, Writing – Review & Editing; **Eric A Hoffman**: Methodology; **Richard E Kanner**: Supervision, Writing – Review & Editing; **Jerry A Krishnan**: Supervision, Writing – Review & Editing; **Fernando J Martinez**: Supervision, Methodology, Writing – Review & Editing; **Robert Paine III**: Supervision, Writing – Review & Editing; **Roger D Peng**: Methodology, Formal analysis, Writing – Review & Editing; **Stephen Peters**: Supervision, Writing – Review & Editing; **Cheryl S Pirozzi**: Writing – Review & Editing; **Prescott G Woodruff**: Supervision, Writing – Review & Editing; **Joel D Kaufman**: Conceptualization, Methodology, Supervision, Writing - Review & Editing; **Nadia N Hansel**: Conceptualization, Methodology, Supervision, Writing - Review & Editing

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

[f.]University of Iowa Department of Internal Medicine, 200 Hawkins Drive, Iowa City, IA 52242, USA

[g.]University of California, Los Angeles, 10833 Le Conte Ave, Los Angeles, CA 90095, USA

[h.]University of Alabama, Birmingham, 1720 2nd Ave South, Birmingham, AL 35294, USA

[i.]University of Washington, 1959 NE Pacific St, Seattle, WA 98195, USA

[j.]University of Michigan, 1500 E Medical Center Dr, Ann Arbor, MI 48109, USA

[k.]University of Utah, 50 North Medical Drive, Salt Lake City, Utah 84132, USA

[l.]University of Illinois at Chicago, 1853 West Polk Street, Chicago, IL 60612

[m.]Weill Cornell Medicine, 300 York Ave, New York, NY 10065, USA

[n.]Wake Forest University, 475 Vine St, Winston-Salem, NC 27101, USA

[o.]University of California, San Francisco, 513 Parnassus Ave, HSE, San Francisco CA 94143, USA

Abstract

Background: Neighborhood poverty has been associated with poor health outcomes. Previous studies have also identified adverse respiratory effects of long-term ambient ozone. Factors associated with neighborhood poverty may accentuate the adverse impact of ozone on respiratory health.

Objectives: To evaluate whether neighborhood poverty modifies the association between ambient ozone exposure and respiratory morbidity including symptoms, exacerbation risk, and radiologic parameters, among participants of the SPIROMICS AIR cohort study.

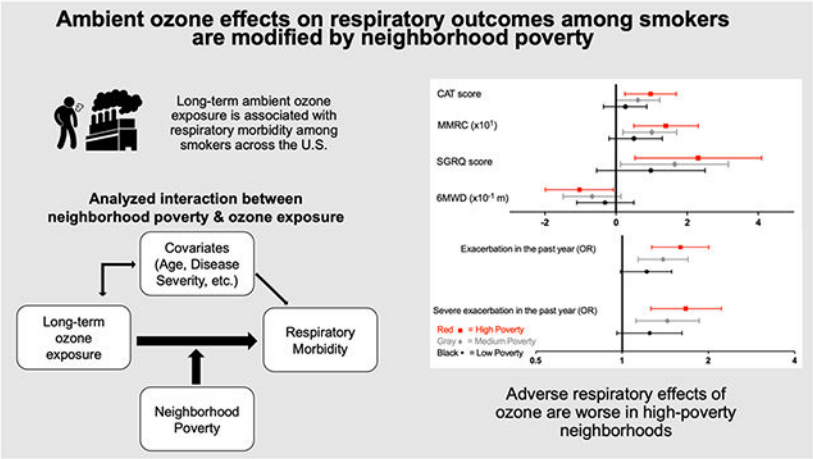
Methods: Spatiotemporal models incorporating cohort-specific monitoring estimated 10-year average outdoor ozone concentrations at participants' homes. Adjusted regression models were used to determine the association of ozone exposure with respiratory outcomes, accounting for demographic factors, education, individual income, body mass index (BMI), and study site. Neighborhood poverty rate was defined by percentage of families living below federal poverty level per census tract. Interaction terms for neighborhood poverty rate with ozone were included in covariate-adjusted models to evaluate for effect modification.

Results: 1874 participants were included in the analysis, with mean (± SD) age 64 (± 8.8) years and FEV_1 (forced expiratory volume in one second) 74.7% (± 25.8) predicted. Participants resided in neighborhoods with mean poverty rate of 9.9% (± 10.3) of families below the federal poverty level and mean 10-year ambient ozone concentration of 24.7 (± 5.2) ppb. There was an interaction between neighborhood poverty rate and ozone concentration for numerous respiratory outcomes, including COPD Assessment Test score, modified Medical Research Council Dyspnea Scale, six-minute walk test, and odds of COPD exacerbation in the year prior to enrollment, such that adverse effects of ozone were greater among participants in higher poverty neighborhoods.

Conclusion: Individuals with COPD in high poverty neighborhoods have higher susceptibility to adverse respiratory effects of ambient ozone exposure, after adjusting for individual factors. These

findings highlight the interaction between exposures associated with poverty and their effect on respiratory health.

Graphical abstract



Keywords

Air pollution; Chronic obstructive pulmonary disease; Socioeconomic factors; Ozone; Poverty areas

1. Introduction

Lower individual and neighborhood socioeconomic status (SES) has been associated with chronic disease morbidity, and respiratory morbidity specifically, including higher prevalence of chronic obstructive pulmonary disease (COPD) and worse COPD outcomes.[1,2] Existing literature has focused primarily on the impact of short-duration, high-concentration exposures to ozone on acute respiratory outcomes.[3] However, recent evidence shows long-term exposure to ambient ozone is associated with worse respiratory morbidity among individuals with and without COPD.[4,5] Because regulatory standards do not exist in the United States for ozone concentrations on time scales longer than 8 hours, the impacts of chronic ozone exposure on vulnerable populations is understudied. In addition, some studies suggest that long-term pollutant exposures may be more harmful in the context of poverty.[6–8] To our knowledge, no studies have evaluated the interaction between neighborhood poverty rate and long-term ambient ozone exposure with regards to respiratory outcomes among individuals with and at risk for COPD. The proposed mechanisms by which ozone exposure can negatively impact respiratory health – direct cell toxicity, promotion of inflammation and oxidative stress, altered innate immune responses, and sensitization to environmental allergens – are all potentially amplified by socioeconomic stressors.[9–13] Understanding the possible interaction between neighborhood poverty and long-term ambient air pollution has the potential to further the understanding of the complex mechanisms by which SES impacts respiratory health.

The purpose of this analysis was to evaluate the interaction between neighborhood poverty rate and 10-year average historical ozone levels on respiratory morbidity of current and former smokers with or without airway obstruction. These individuals were enrolled in the Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS), a multicenter prospective cohort study that aimed to identify new COPD subgroups and intermediate markers of disease progression. The current analysis specifically utilized data from the SPIROMICS Air Pollution Study (SPIROMICS AIR), an ancillary study that sought to examine respiratory effects of exposure to several air pollutants among individuals with heavy smoking histories – a group at increased risk for respiratory morbidity. We hypothesized that the adverse effects of long-term ambient ozone exposure would be heightened for individuals living in neighborhoods with high poverty rates.

2. Methods:

2.1 Study Population and Participant Characterization

The current study is a cross-sectional analysis of data collected at the SPIROMICS enrollment baseline visit as part of SPIROMICS AIR, an ancillary study with baseline visits conducted from 2010 to 2015 that included 2382 participants enrolled at 7 of the 12 SPIROMICS clinical sites.[14] A total of 1874 SPIROMICS AIR participants were current or former smokers and had available 10-year historical ambient ozone exposure and neighborhood poverty data. SPIROMICS was approved by the institutional review board at each clinical center. All study participants provided written informed consent. Participants in SPIROMICS were 40 to 80 years of age at baseline, were current or former smokers (≥ 20 pack-years) and included individuals with spirometry confirmed COPD (postbronchodilator forced expiratory volume in the first second of expiration/forced vital capacity [FEV_1/FVC] < 70%), as well as current or former smokers without airways obstruction. Healthy controls with ≤1 pack-year smoking history were excluded from the analysis. Smoking history was defined as lifetime cumulative pack-years and as a binary indication for current smoking status (yes or no) of smoking within the past month. Trained staff at the clinical sites collected demographic, smoking and occupational exposure, and clinical data.[15]

2.2 Ambient Ozone Exposure Assessment

We determined 10-year average outdoor concentrations of pollutants at each participant's home as previously described.[4] Briefly, two-week mean outdoor concentrations of ozone and particulate matter with a diameter of less than 2.5 μm ($PM_{2.5}$) were estimated at each participant's precise geocoded home location using validated spatiotemporal modeling methods and, linking to the residential history of each individual reported for the 10 years prior to the baseline visit, averaged to obtain the long-term pollutant exposure estimate. The spatiotemporal modeling approach used benefits from incorporation of regulatory monitoring, cohort-focused monitoring, and hundreds of geographic covariates incorporated via partial least squares regression. This approach, developed and validated for the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air),[16] performs well in terms of both prediction accuracy and precision and allows for finer-scale predictions than prior models based on chemical transport modeling. This allows for better understanding of spatial variation in ozone concentration and improved exposure predictions for analysis

of long-term exposure for individuals. A detailed description of pollutant monitoring and spatiotemporal models has been previously published.[4,14,16,17]

2.3 Neighborhood Poverty

Addresses of participants at baseline were linked to the census tract-level data from the 2006-10 American Community Survey from the US Census Bureau.[18] Neighborhood poverty rate was measured as the percentage of all families in a census-tract with annual income below the 2010 federal poverty level. Neighborhood poverty rate was analyzed as a continuous variable, but for ease of interpretability in comparing neighborhoods with different poverty rates, some results are displayed comparing participants residing in low, medium, and high poverty areas – defined as neighborhoods with poverty rates less than 5%, between 5% and 20%, and greater than 20%, respectively. These rates were chosen based on definitions commonly used in the respiratory and public policy literature.[19–22]

2.4 Respiratory Outcomes

Respiratory-specific quality of life was ascertained using the St. George's Respiratory Questionnaire (SGRQ), and health status was identified with the COPD Assessment Test (CAT). Dyspnea was assessed with the modified Medical Research Council (mMRC) Dyspnea Scale, and functional exercise capacity was evaluated with the 6-minute walk test (6MWT).[23–26] Exacerbations were based on report of antibiotic and/or steroid use, unscheduled physician visits, emergency department (ED) visits and hospitalizations for COPD, and frequency of these instances over the past year. Severe exacerbations were defined as events requiring an ED visit or hospitalization. Participants underwent whole-lung multidetector helical computed tomography (CT) scans. Percentage of emphysema was defined as percent of total voxels in the field less than −950 Hounsfield units (HU) at total lung capacity, and percentage of air trapping was defined as percent of total voxels in the field less than −856 HU at residual volume. Pi10 (the square root of the wall area of a theoretical airway with a lumen perimeter of 10 mm) was used as a measure of airway wall thickness.[27]

2.5 Statistical Analysis

Descriptive analyses were used to compare means and proportions between participants residing in low, medium, and high poverty areas. Using multivariable linear regression for continuous outcomes and logistic regression for discrete outcomes, we assessed whether the association between ozone and COPD outcomes was modified by neighborhood poverty rates. We considered both ozone and neighborhood poverty rate as continuous variables on the natural scale and included them as predictors along with the interaction term (ozone x poverty rate) in 2-way interaction model. Models were adjusted for age, sex, race (white vs. non-white), educational attainment (high school graduate or less vs. above high school), annual household income, body mass index (BMI), current smoking status (former vs current), smoking pack-years, occupational exposure to vapors, gases, dusts, or fumes (VGDF), and study site. The effect estimate of the two-way interaction between ozone and neighborhood poverty rate represented the change in ozone's association with COPD outcome by neighborhood poverty rate. The ozone effect at each poverty rate (low, medium, high) was assessed by estimating ozone's association with COPD outcome measures while

holding constant the neighborhood poverty rate at the appropriate level: 5%, 12.5%, and 20% for “low”, “medium”, and “high” poverty rate, respectively. Given that $PM_{2.5}$ levels, NO_2 levels, and chronic disease prevalence may be higher among low-SES individuals and associated with COPD respiratory outcomes, models were run as sensitivity analyses adjusting for additional covariates, including 10-year historical concentration of $PM_{2.5}$, model-predicted indoor NO_2,[28] outdoor NO_2, and comorbidities.[29] Additional sensitivity analyses included 1- and 5-year mean ambient ozone concentration as the main exposure variable. A three-way interaction model between ozone concentration, neighborhood poverty rate, and smoking status was run to assess for additional effect modification by smoking status.

All analyses were performed with StataMP software, version 15.1 (StataCorp LLC). The threshold of statistical significance for the main associations and interaction terms was a 2-sided $P < 0.05$.

3. Results

3.1 Participant characteristics

This cross-sectional analysis included 1874 participants. The mean (SD) neighborhood poverty rate at baseline was 10% (9.9%); the national mean neighborhood poverty rate was 11.8% in 2010.[30] Compared to participants living in low (< 5%) poverty neighborhoods, those living in medium (5% to 20%), and high (> 20%) poverty neighborhoods were younger (mean age 60-64 years in medium and high areas compared to 60 years in low areas), more likely to be female (48-49% in medium and high areas vs 42% in low areas), less likely to be white (43% in high areas vs 80% and 91% in medium and low areas), and less likely to have an educational attainment level above high school (48% in high poverty areas vs 59% and 75% in medium and low areas) (Table 1). They were also more likely to have an annual household income below $35,000 (53% in high poverty areas vs 38% and 24% in medium and low areas), more likely to report occupational exposure to VGDF (55% in high areas vs 50% and 45% in medium and low areas), and were more likely to be current smokers (55% in high areas vs 38% and 30% in medium and low areas). Participants in high poverty areas had lower lifetime tobacco smoke exposure compared to those in medium and low poverty areas (45 pack-years in high poverty areas vs 50-51 pack-years in medium and low areas). Mean historical ambient ozone concentrations were lower in high poverty areas (20.4 ppb in high poverty areas vs 25.2-25.8 ppb in medium and low poverty areas); however, $PM_{2.5}$ levels were higher in high poverty areas (12.8 $\mu g/m^3$ in high vs 11.3 $\mu g/m^3$ and 10.4 $\mu g/m^3$ in medium and low poverty areas, respectively).

3.2 Multivariable Regression

Adjusting for covariates, there was an interaction between neighborhood poverty rate and ambient ozone concentration such that adverse effects of ozone were greater among participants in higher poverty neighborhoods for several outcomes including CAT, mMRC, 6MWT, percent air trapping on CT scan, and odds of COPD exacerbation in the 12 months prior to baseline visit (Table 2, Figure 1 and E2). For example, the adverse effect of a 5 ppb increase in 10-year average historical ozone concentration on CAT score was

magnified by 0.49 points (95% CI, 0.12–0.85) for every one standard deviation increase in neighborhood poverty (10.3% increase in poverty rate). A 5 ppb increase in 10 year average ozone concentration was associated with a 0.97 point worse CAT score in high poverty areas (95% CI, 0.25-1.69) and a 0.61 point worse CAT score in medium poverty areas (95% CI, 0.004-1.23) but was not associated with CAT score in low poverty areas (β=0.26, 95% CI, −0.35-0.87). Similarly, for every 1 SD increase in neighborhood poverty rate, the odds of any exacerbation and of severe exacerbation per 5 ppb increase in ozone increased by 21% (OR=1.21; 95% CI, 1.07-1.36) and 22% (OR=1.22, 95%CI, 1.06-1.42), respectively. For every 5 ppb increase in ozone, the odds of any exacerbation and severe exacerbations increased by 60% (OR=1.60; 95%CI, 1.27-2.01) and 67% (OR=1.67, 95%CI, 1.26-2.22), respectively, in high poverty areas and by 39% (OR=1.39; 95%CI, 1.14-1.70) and 44% (OR=1.44; 95%CI, 1.12-1.86) in medium poverty areas, while the ozone association was more modest in low poverty areas (OR=1.22, 95%CI, 0.99-1.49 for any exacerbation; OR=1.25, 95%CI, 0.96-1.62 for severe exacerbation). No significant interaction between neighborhood poverty rate and ozone concentration was observed for FEV_1 percent predicted, airway wall thickness (pi10), and percent emphysema. A modest interaction was observed for SGRQ (β=0.92, 95% CI, −0.004-1.84, P_{intx}=0.051) (Table 2).

3.3 Sensitivity and Three-way Analyses

When additionally adjusting for either outdoor $PM_{2.5}$ or outdoor NO_2, collinearity was introduced; however, the association of ozone with respiratory outcomes remained robust in terms of magnitude and direction in both cases. Importantly, the interaction between ozone and neighborhood poverty was unaffected by co-pollutant adjustment (Figure E1). Modeled indoor NO_2 levels were available for only a subset of participants (n = 992); however, within this subset results remained similar both for the overall ozone x neighborhood poverty interaction (Table E1) and the ozone x neighborhood poverty interaction additionally adjusted by modeled indoor NO_2 (Table E2). When additionally adjusting for cardiovascular comorbidities or all comorbidities, modest changes in the effect modification by neighborhood poverty rate were noted for SGRQ and 6MWT. The results held similar for all other outcomes (Table E3 and E4). A three-way interaction model between ozone concentration, neighborhood poverty rate, and smoking status found no evidence of effect modification by smoking status (all $P_{3\text{-way interaction}}$ >0.10), such that the effects of ozone remained worse in higher poverty areas regardless of smoking status (Table E5). When considering alternate mean times of ozone exposure, the interaction between neighborhood poverty and ozone exposure was similar to the 10-year ozone concentration when using 1- and 5-year historical ozone concentrations (Table E6).

4. Discussion

This study of smokers with and at risk for COPD demonstrates that the adverse respiratory effects of long-term ambient ozone exposure are heightened in high poverty neighborhoods. Specifically, the association of ozone exposure with dyspnea, respiratory-related quality of life, exacerbation risk, and degree of air trapping on CT scan was increased among individuals living in neighborhoods with moderate to high poverty rates compared to those living in neighborhoods with low poverty rates.

The long-term effect of exposure to ambient ozone pollution on several measures of respiratory health was previously published in this cohort.[4] While the observed mean ozone concentrations were significantly lower than the 70 ppb 8-hour maximum concentrations regulated by the NAAQS (National Ambient Air Quality Standards), long-term exposure to similar levels of ambient ozone have been associated with decreased lung function among the general population as well as high-risk individuals with alpha-1 antitrypsin deficiency.[5,31] Evidence from exposure and field studies have shown considerable variability in an individual's response to ozone concentration with no evidence of a lower threshold of effect,[3] and associations with outcomes such as mortality persisting at levels as low as 15 ppb.[32] Further, some evidence suggests that exposure risk to changes in pollutant concentration are greater at lower levels of pollutant, further highlighting that increases at relatively low concentrations can have harmful effects.[4,33] Therefore, it is possible that longer term mean levels of exposure should be considered for regulation in addition to 8-hour maximum concentrations. Whether additional measures of exposure, such as area under the curve or peak exposures, could have additional risk is unclear. The current analysis furthers this understanding by identifying neighborhood poverty as an important modifier of the association between ambient ozone and respiratory health, even when adjusting for an individual's socioeconomic status (household income, education, and occupation), suggesting that the mechanisms by which ozone impacts respiratory health may be enhanced by community-level risk factors. These results represent clinically important changes in exacerbation rates, dyspnea, and quality of life for individuals living in the poorest neighborhoods. The 10 year average ozone concentration in our study ranged from 11.1 to 44.6 ppb and poverty rates ranged from 0 to 100%, suggesting that residing in a high poverty and high ozone area has potential for large clinical impact. For example, a 5 ppb increase in 10 year average ozone concentration was not associated with CAT score in low poverty areas (β=0.26, 95% CI, −0.35-0.87), but the same increase for an individual living in a 35% poverty area was associated with a 2 point worse CAT score, corresponding to the minimal clinically important difference (MCID) for CAT. These findings add to the literature documenting the effect of neighborhood SES on respiratory health and further highlight how deleterious factors may coalesce in disadvantaged neighborhoods.

These findings are consistent with previous evidence demonstrating accentuated harmful effects of pollutants on general and respiratory health in low income environments. Low neighborhood SES has been found to heighten the impact of short-term ozone exposure on ED visits and mortality in the US.[20,34] Short- and long-term exposure to other ambient pollutants, such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and total suspended particles (TSP) have shown increased effects on among low-SES individuals in international cohorts.[7,35] In a large French cohort, neighborhood SES demonstrated an effect on the association between short-term exposure to ambient NO_2 and all-cause mortality, with this effect modified by increased long-term exposure.[7] Similarly, a Canadian study found that long-term exposures to SO_2 and TSP were associated with an increased risk of cardiopulmonary as well as all-cause mortality, and that this risk was increased for individuals in low-SES neighborhoods.[35]

There are several mechanisms by which ozone's effects on respiratory health could be enhanced by neighborhood poverty. Neighborhood poverty is associated with increased

adverse indoor and outdoor environmental exposures,[36] higher concentration of tobacco stores,[37] lower access to healthy food choices,[38,39] decreased access to health care, and lack of social cohesion to support community members;[36,40,41] and residents of high poverty neighborhoods may have high stress, prevalence of comorbidities, tobacco and occupational exposures, and poor quality dietary intake.[40,41] Many of these factors have been shown to lead to increased oxidative stress and heightened inflammation,[9–11] which are key mechanistic pathways for the development of COPD and triggers for exacerbations.[42,43] Similarly, exposure to ozone increases inflammation and oxidative stress both systemically and in airways specifically,[44,45] and thus can act synergistically with other sources of oxidative stress and inflammation that are prevalent in high-poverty areas. As an example, pro-inflammatory diets have been associated with COPD,[46,47] and diet supplementation with antioxidant vitamins (C and E) may decrease inflammatory effects of ozone.[48] In addition, high indoor allergen exposure is common among low-SES households,[49] and ozone may act on respiratory epithelium to increase sensitization and hyperresponsiveness to allergens.[50,51] Given that the prevalence of atopy among individuals with COPD is estimated to be as high as 35-36%, increased allergen sensitization via ozone exposure may affect a substantial number of individuals with COPD.[52] Finally, despite overall lower ambient levels, personal exposure to ozone may be higher in high-poverty neighborhoods because of lower access to central air conditioning and increased reliance on open windows and window air conditioning units,[53] increasing outdoor pollutant penetrance into homes during warm months when ambient ozone concentrations are highest.[54]

Through the clinical and exposure phenotyping in SPIROMICS AIR, this analysis was able to examine several of these potential mechanisms. In the current model, the interaction between neighborhood poverty rate and ozone persisted even when accounting for tobacco smoke and occupational VGDF exposures, as well as comorbidity burden in sensitivity analysis.[29] Additionally, other ambient pollutants are known to negatively impact respiratory health, and particulate matter and ozone can interact synergistically to increase airway inflammation.[55] In this analysis, while levels of outdoor air pollution from $PM_{2.5}$ were higher in high-poverty neighborhoods, the interaction between neighborhood poverty rate and ozone was robust to adjustment by $PM_{2.5}$.

Ambient ozone levels in this cohort were lower in high-poverty neighborhoods, consistent with previous studies.[56,57] As a secondary pollutant arising from reactions of ultraviolet sunlight with byproducts of hydrocarbon combustion, ozone exists in an equilibrium with these primary pollutants (namely, NO_2, NO, and volatile organic compounds).[58] Thus, ambient ozone concentrations are often found to be lower near large sources of hydrocarbon combustion where emissions of NO are highest, such as highways and industrial areas, which could be more common in high-poverty areas. The current finding of an association of ozone exposure with respiratory morbidity, even in areas of relatively low historical ozone concentrations, is in line with epidemiologic as well as ozone chamber studies which support deleterious effects of ozone even at concentrations below National Ambient Air Quality Standards.[12,59,60] This finding may have important implications with regards to the “double jeopardy” hypothesis that low-SES individuals often face both higher exposure to air pollution while possessing more co-occurring risk factors for the deleterious effects of pollution.[61,62] In the case of the current analysis, individuals in low-SES neighborhoods had

higher susceptibility to adverse respiratory effects of ambient ozone exposure in spite of lower average exposure to ozone.

The current analysis has some limitations. We were unable to explore several mechanisms by which residing in high poverty neighborhoods may accentuate harmful effects of ozone, including time spent outdoors, building characteristics, access to healthy foods, and indoor pollution. In particular, indoor air pollution including indoor PM and NO_x and exposure to allergens may be higher in poor neighborhoods.[63–65] While these exposures may act synergistically with ambient ozone, they were not captured in the current analysis. Additionally, while our definition of neighborhood poverty is commonly used throughout the literature, it may not capture other important measures of neighborhood disorder and deprivation that could impact respiratory health. Furthermore, the spatial resolution of neighborhood poverty at the census tract level may not account for differing exposures to "neighborhood-level" exposures such as access to greenspace, exposures to violence, and others which may vary widely within a census tract.[62] Challenges of assessing the effect of ambient pollutant exposure on human health, as referenced by LaKind et al., including appropriate duration of exposure, monitoring stations as a proxy for personal exposure, and challenges of addressing copollutants exist in the current study. [66] However, we present fine spatiotemporal models with inclusion of cohort-specific monitoring and sensitivity analyses adjusting for $PM_{2.5}$ and NO_2, to minimize these limitations. This study also has several strengths. In clarifying the extent to which certain exposures may explain the neighborhood poverty-ozone interaction, the current analysis benefits from the extensive clinical and exposure phenotyping conducted in SPIROMICS AIR, including geocoding and fine-scale pollution monitoring. These data allowed for exploration of the influence of factors such as individual SES, comorbidities, and co-exposure to other pollutants in the interaction between neighborhood poverty and ambient ozone. Additionally, participants were recruited from cities across the United States, increasing its generalizability to neighborhoods throughout the country.

5. Conclusion

This secondary analysis of SPIROMICS AIR found a significant interaction between neighborhood poverty rate and increasing historical ambient ozone concentration for numerous respiratory outcomes among current and former smokers, such that adverse effects of chronic ozone exposure were greater among participants in higher poverty neighborhoods. This interaction persisted even when accounting for individual SES and the relatively lower ozone levels in high poverty neighborhoods. These findings suggest that neighborhood poverty may accentuate the mechanisms by which ozone impacts respiratory health. In the setting of poverty, individuals are vulnerable to even relatively low levels of ozone, and these findings speak to the complex interaction between numerous exposures associated with poverty and their effect on respiratory health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank the SPIROMICS participants and participating physicians, investigators, and staff for making this research possible. More information about the study and how to access SPIROMICS data is available at www.spiromics.org. The authors would like to acknowledge the University of North Carolina at Chapel Hill BioSpecimen Processing Facility for sample processing, storage, and sample disbursements (http://bsp.web.unc.edu/). We would like to acknowledge the following current and former investigators of the SPIROMICS sites and reading centers: Neil E Alexis, MD; Wayne H Anderson, PhD; Mehrdad Arjomandi, MD; Igor Barjaktarevic, MD, PhD; R Graham Barr, MD, DrPH; Patricia Basta, PhD; Lori A Bateman, MSc; Surya P Bhatt, MD; Eugene R Bleecker, MD; Richard C Boucher, MD; Russell P Bowler, MD, PhD; Stephanie A Christenson, MD; Alejandro P Comellas, MD; Christopher B Cooper, MD, PhD; David J Couper, PhD; Gerard J Criner, MD; Ronald G Crystal, MD; Jeffrey L Curtis, MD; Claire M Doerschuk, MD; Mark T Dransfield, MD; Brad Drummond, MD; Christine M Freeman, PhD; Craig Galban, PhD; MeiLan K Han, MD, MS; Nadia N Hansel, MD, MPH; Annette T Hastie, PhD; Eric A Hoffman, PhD; Yvonne Huang, MD; Robert J Kaner, MD; Richard E Kanner, MD; Eric C Kleerup, MD; Jerry A Krishnan, MD, PhD; Lisa M LaVange, PhD; Stephen C Lazarus, MD; Fernando J Martinez, MD, MS; Deborah A Meyers, PhD; Wendy C Moore, MD; John D Newell Jr, MD; Robert Paine, III, MD; Laura Paulin, MD, MHS; Stephen P Peters, MD, PhD; Cheryl Pirozzi, MD; Nirupama Putcha, MD, MHS; Elizabeth C Oelsner, MD, MPH; Wanda K O'Neal, PhD; Victor E Ortega, MD, PhD; Sanjeev Raman, MBBS, MD; Stephen I. Rennard, MD; Donald P Tashkin, MD; J Michael Wells, MD; Robert A Wise, MD; and Prescott G Woodruff, MD, MPH. The project officers from the Lung Division of the National Heart, Lung, and Blood Institute were Lisa Postow, PhD, and Lisa Viviano, BSN;

SPIROMICS was supported by contracts from the NIH/NHLBI (HHSN268200900013C, HHSN268200900014C, HHSN268200900015C, HHSN268200900016C, HHSN268200900017C, HHSN268200900018C, HHSN268200900019C, HHSN268200900020C), grants from the NIH/NHLBI (U01 HL137880 and U24 HL141762), the NIEHS (R01ES023500, K23ES025781, P30ES07033), the EPA (RD831697, RD83830001) and supplemented by contributions made through the Foundation for the NIH and the COPD Foundation from AstraZeneca/MedImmune; Bayer; Bellerophon Therapeutics; Boehringer-Ingelheim Pharmaceuticals, Inc.; Chiesi Farmaceutici S.p.A.; Forest Research Institute, Inc.; GlaxoSmithKline; Grifols Therapeutics, Inc.; Ikaria, Inc.; Novartis Pharmaceuticals Corporation; Nycomed GmbH; ProterixBio; Regeneron Pharmaceuticals, Inc.; Sanofi; Sunovion; Takeda Pharmaceutical Company; and Theravance Biopharma and Mylan.

Daniel Belz reports grant support from NIH/NHLBI.

Mark Dransfield reports grant support from NIH, DOD, and the American Lung Association; consulting from AstraZeneca, GlaxoSmithKline, Pulmonx, Teva; and contracted clinical trials through Boerhinger Ingelheim, Gala, and Pulmonx

MeiLan Han reports consulting for Novartis, Sunovion, Cipla, Chiesi, Teva, Verona, Merck, Mylan, Sanofi, GlaxoSmithKline, Boehringer Ingelheim and AstraZeneca as well as research support from Novartis and Sunovion.

Jerry Krishnan reports research grants from NIH, PCORI, and Sergey Brin Family Foundation as well as consulting fees from GlaxoSmithKline for monoclonal antibody against SARS-CoV-2.

Nadia Hansel reports grants from NIH, grants from COPD Foundation, grants and personal fees from AstraZeneca, grants and personal fees from GSK, grants from Boehringer Ingelheim, personal fees from Mylan during the conduct of the study.

Abbreviations:

6MWT	Six Minute Walk Test
CAT	COPD Assessment Test
COPD	chronic obstructive pulmonary disease
FEV_1	forced expiratory volume in the first second of expiration
FVC	forced vital capacity
mMRC	Modified Medical Research Council Dyspnea Scale

NAAQS	National Ambient Air Quality Standards
$PM_{2.5}$	particulate matter with a diameter of less than 2.5 μm
SPIROMICS	Subpopulations and Intermediate Outcome Measures in COPD Study
SPIROMICS AIR	SPIROMICS Air Pollution Study
VGDF	vapors, gases, dusts, or fumes

References

1. Woo H, Brigham EP, Allbright K, et al. Racial Segregation and Respiratory Outcomes among Urban Black Residents with and at Risk of COPD. Am J Respir Crit Care Med. 2021. doi:10.1164/rccm.202009-3721oc
2. Galiatsatos P, Woo H, Paulin LM, et al. The association between neighborhood socioeconomic disadvantage and chronic obstructive pulmonary disease. Int J COPD. 2020;15:981–993. doi:10.2147/COPD.S238933
3. Filippidou E, Koukouliata A. Ozone effects on the respiratory system. Prog Heal Sci. 2011 ;1 (2):144–155.
4. Paulin LM, Gassett AJ, Alexis NE, et al. Association of Long-term Ambient Ozone Exposure With Respiratory Morbidity in Smokers. JAMA Intern Med. 2019;21205. doi:10.1001/jamainternmed.2019.5498
5. Wang M, Aaron CP, Madrigano J, et al. Association Between Long-term Exposure to Ambient Air Pollution and Change in Quantitatively Assessed Emphysema and Lung Function. JAMA. 2019;322(6):546. doi: 10.1001/jama.2019.10255 [PubMed: 31408135]
6. Chi GC, Hajat A, Bird CE, et al. Individual and Neighborhood Socioeconomic Status and the Association between Air Pollution and Cardiovascular Disease. Environ Health Perspect. 2016;124(12): 1840–1847. doi:10.1289/EHP199 [PubMed: 27138533]
7. Deguen S, Petit C, Delbarre A, et al. Neighbourhood characteristics and long-term air pollution levels modify the association between the short-term nitrogen dioxide concentrations and allcause mortality in Paris. PLoS One. 2015; 10(7):1–14. doi:10.1371/journal.pone.0131463
8. Clougherty JE, Kubzansky LD. A framework for examining social stress and susceptibility to air pollution in respiratory health. Environ Health Perspect. 2009;117(9):1351–1358. doi:10.1289/ehp.0900612 [PubMed: 19750097]
9. Tawakol A, Osborne MT, Wang Y, et al. Stress-Associated Neurobiological Pathway Linking Socioeconomic Disparities to Cardiovascular Disease. J Am Coll Cardiol. 2019;73(25):3243–3255. doi: 10.1016/j.jacc.2019.04.042 [PubMed: 31248544]
10. Epel ES, Blackburn EH, Lin J, et al. Accelerated telomere shortening in response to life stress. 2004. www.pnas.orgcgidoi10.1073pnas.0407162101. Accessed March 4, 2021.
11. Zannas AS, Jia M, Hafner K, et al. Epigenetic upregulation of FKBP5 by aging and stress contributes to NF-κB-driven inflammation and cardiovascular risk. Proc Natl Acad Sci U S A. 2019; 166(23): 11370–11379. doi: 10.1073/pnas.1816847116
12. Alexis NE, Lay JC, Hazucha M, et al. Low-level ozone exposure induces airways inflammation and modifies cell surface phenotypes in healthy humans. Inhal Toxicol. 2010;22(7):593–600. doi: 10.3109/08958371003596587 [PubMed: 20384440]
13. Alexis NE, Lay JC, Haczku A, et al. Fluticasone propionate protects against ozone-induced airway inflammation and modified immune cell activation markers in healthy volunteers. Environ Health Perspect. 2008;116(6):799–805. doi: 10.1289/ehp.10981 [PubMed: 18560537]
14. Hansel NN, Paulin LM, Gassett AJ, et al. Design of the subpopulations and intermediate outcome measures in COPD (SPIROMICS) AIR study. BMJ Open Respir Res. 2017. doi: 10.1136/bmjresp-2017-000186

15. Paulin LM, Diette GB, Blanc PD, et al. Occupational Exposures Are Associated with Worse Morbidity in Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2015; 191:557–565. doi: 10.1164/rccm.201408-1407OC [PubMed: 25562375]

16. Wang M, Keller JP, Adar SD, et al. Development of long-term spatiotemporal models for ambient ozone in six metropolitan regions of the United States: The MESA Air study. Atmos Environ. 2015;123:79–87. doi: 10.1016/j.atmosenv.2015.10.042

17. Keller JP, Olives C, Kim SY, et al. A unified spatiotemporal modeling approach for predicting concentrations of multiple air pollutants in the multi-ethnic study of atherosclerosis and air pollution. Environ Health Perspect. 2015;123(4):301–309. doi: 10.1289/ehp.1408145 [PubMed: 25398188]

18. U.S. Census Bureau. 2006-2010 American Community Survey 5-Year Public Use Microdata Sample.; 2011.

19. Zager S, Mendu ML, Chang D, et al. Neighborhood poverty rate and mortality in patients receiving critical care in the academic medical center setting. Chest. 2011 ;139(6): 1368–1379. doi:10.1378/chest.10-2594 [PubMed: 21454401]

20. O' Lenick CR, Chang HH, Kramer MR, et al. Ozone and childhood respiratory disease in three US cities: evaluation of effect measure modification by neighborhood socioeconomic status using a Bayesian hierarchical approach, doi: 10.1186/s12940-017-0244-2

21. Kneebone E, Holmes N. U.S. Concentrated Poverty in the Wake of the Great Recession. Vol 104.; 2016. https://www.brookings.edu/research/u-s-concentrated-poverty-in-the-wake-of-the-great-recession/. Accessed July 8, 2021.

22. Currier E Neighborhood Poverty and Household Financial Security.; 2016.

23. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis. 1992; 145(6): 1321–1327. doi: 10.1164/ajrccm/145.6.1321 [PubMed: 1595997]

24. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. Eur Respir J. 2009. doi: 10.1183/09031936.00102509

25. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54:581–586. doi: 10.1136/thx.54.7.581 [PubMed: 10377201]

26. Holland AE, Spruit MA, Troosters T, et al. An official European respiratory society/American thoracic society technical standard: Field walking tests in chronic respiratory disease. Eur Respir J. 2014;44(6): 1428–1446. doi: 10.1183/09031936.00150314 [PubMed: 25359355]

27. Kim WJ, Silverman EK, Hoffman E, et al. CT metrics of airway disease and emphysema in severe COPD. Chest. 2009;136(2):396–404. doi:10.1378/chest.08-2858 [PubMed: 19411295]

28. Zusman M, Gassett AJ, Kirwa K, et al. Modeling residential indoor concentrations of PM(2.5), NO(2), NO(x), and secondhand smoke in the Subpopulations and Intermediate Outcome Measures in COPD (SPIROMICS) Air study. Indoor Air. 2021 ;31 (3):702–716. doi: 10.1111/ina.12760 [PubMed: 33037695]

29. Laurent O, Bard D, Filleul L, Segala C. Effect of socioeconomic status on the relationship between atmospheric pollution and mortality. J Epidemiol Community Health. 2007;61 (8):665–675. doi: 10.1136/jech.2006.053611 [PubMed: 17630363]

30. U.S. Census Bureau. 2010 Census Summary; 2011. https://www.census.gov/programs-surveys/decennial-census/data/datasets.2010.html.

31. Wood AM, Harrison RM, Semple S, Ayres JG, Stockley RA. Outdoor air pollution is associated with disease severity in α1-antitrypsin deficiency. Eur Respir J. 2008;34(2):346–353. doi: 10.1183/09031936.00087908

32. Bell ML, Peng RD, Dominici F. The exposure-response curve for ozone and risk of mortality and the adequacy of current ozone regulations. Environ Health Perspect. 2006; 114(4):532–536. doi: 10.1289/ehp.8816 [PubMed: 16581541]

33. Bae S, Lim YH, Kashima S, et al. Non-linear concentration-response relationships between ambient ozone and daily mortality. PLoS One. 2015; 10(6): 1–11. doi: 10.1371/journal.pone.0129423

34. Bell ML, Dominici F. Effect modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. Am J Epidemiol. 2008;167(8):986–997. doi: 10.1093/aje/kwm396 [PubMed: 18303005]
35. Finkelstein MM, Jerrett M, DeLuca P, et al. Relation between income, air pollution and mortality: a cohort study. CMAJ. 2003;169(5):397–402. http://www.ncbi.nlm.nih.gov/pubmed/12952800. [PubMed: 12952800]
36. Bell ML, Ebisu K. Environmental inequality in exposures to airborne particulate matter components in the United States. Environ Health Perspect. 2012;120(12):1699–1704. doi:10.1289/ehp.1205201 [PubMed: 22889745]
37. Galiatsatos P, Kineza C, Hwang S, et al. Neighbourhood characteristics and health outcomes: Evaluating the association between socioeconomic status, tobacco store density and health outcomes in Baltimore City. Tob Control. November 2017. doi:10.1136/tobaccocontrol-2017-053945
38. Kuczmarski MF, Mason MA, Allegro D, Zonderman AB, Evans MK. Diet Quality Is Inversely Associated with C-Reactive Protein Levels in Urban, Low-Income African-American and White Adults. J Acad Nutr Diet. 2013;113(12): 1620–1631. doi:10.1016/j.jand.2013.07.004 [PubMed: 24035460]
39. Diez-Roux AV, Nieto FJ, Caulfield L, Tyroler HA, Watson RL, Szklo M. Neighbourhood differences in diet: The Atherosclerosis Risk in Communities (ARIC) study. J Epidemiol Community Health. 1999;53(1):55–63. doi:10.1136/jech.53.1.55 [PubMed: 10326055]
40. Freedman VA, Grafova IB, Rogowski J. Neighborhoods and chronic disease onset in later life. Am J Public Health. 2011;101 (1):79–86. doi:10.2105/AJPH.2009.178640 [PubMed: 20299643]
41. Wight RG, Cummings JR, Miller-Martinez D, Karlamangla AS, Seeman TE, Aneshensel CS. A multilevel analysis of urban neighborhood socioeconomic disadvantage and health in late life. Soc Sci Med. 2008;66(4):862–872. doi:10.1016/j.socscimed.2007.11.002 [PubMed: 18160194]
42. Wiegman CH, Michaeloudes C, Haji G, et al. Oxidative stress-induced mitochondrial dysfunction drives inflammation and airway smooth muscle remodeling in patients with chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2015;136(3):769–780. doi:10.1016/j.jaci.2015.01.046 [PubMed: 25828268]
43. Agustí A, Hogg JC. Update on the Pathogenesis of Chronic Obstructive Pulmonary Disease. Drazen JM, ed. N Engl J Med. 2019;381(13):1248–1256. doi:10.1056/NEJMra1900475 [PubMed: 31553836]
44. Liao D, Heiss G, Chinchilli VM, et al. Association of criteria pollutants with plasma hemostatic/inflammatory markers: A population-based study. J Expo Anal Environ Epidemiol. 2005;15(4):319–328. doi:10.1038/sj.jea.7500408 [PubMed: 15536489]
45. Wiegman CH, Li F, Ryffel B, Togbe D, Chung KF. Oxidative Stress in Ozone-Induced Chronic Lung Inflammation and Emphysema: A Facet of Chronic Obstructive Pulmonary Disease. Front Immunol. 2020;11. doi:10.3389/fimmu.2020.01957 [PubMed: 32082309]
46. Lemoine C, Brigham E, Woo H, et al. Relationship between omega-3 and omega-6 fatty acid intake and chronic obstructive pulmonary disease morbidity. Ann Am Thorac Soc. 2020;17(3):378–381. doi:10.1513/AnnalsATS.201910-740RL [PubMed: 31751155]
47. Brigham EP, Steffen LM, London SJ, et al. Diet pattern and respiratory morbidity in the atherosclerosis risk in communities study. Ann Am Thorac Soc. 2018;15(6):675–682. doi:10.1513/AnnalsATS.201707-571OC [PubMed: 29446981]
48. SIENRA-MONGE JJ, RAMIREZ-AGUILAR M, MORENO-MACIAS H, et al. Antioxidant supplementation and nasal inflammatory responses among young asthmatics exposed to high levels of ozone. Clin Exp Immunol. 2004;138(2):317–322. doi: 10.1111/j.1365-2249.2004.02606.x [PubMed: 15498043]
49. Jabre NA, Keet CA, McCormack M, Peng R, Balcer-Whaley S, Matsui EC. Material Hardship and Indoor Allergen Exposure among Low-Income, Urban, Minority Children with Persistent Asthma. J Community Health. 2020;45(5):1017–1026. doi:10.1007/s10900-020-00822-y [PubMed: 32377967]

50. Flayer CH, Ge MQ, Hwang JW, et al. Ozone Inhalation Attenuated the Effects of Budesonide on Aspergillus fumigatus-Induced Airway Inflammation and Hyperreactivity in Mice. Front Immunol. 2019;10:2173. doi:10.3389/fimmu.2019.02173 [PubMed: 31572383]
51. Kierstein S, Krytska K, Sharma S, et al. Ozone inhalation induces exacerbation of eosinophilic airway inflammation and hyperresponsiveness in allergen-sensitized mice. Allergy Eur J Allergy Clin Immunol. 2008;63(4):438–446. doi:10.1111/j.1398-9995.2007.01587.x
52. Putcha N, Fawzy A, Matsui EC, et al. Clinical Phenotypes of Atopy and Asthma in COPD: A Meta-analysis of SPIROMICS and COPDGene. In: Chest. Vol 158. Elsevier Inc.; 2020:2333–2345. doi: 10.1016/j.chest.2020.04.069 [PubMed: 32450244]
53. Residential Energy Consumption Survey. ASCII version. [Washington]: The Division : [U.S. Government Printing Office, Superintendent of Documents, distributor], 1990.; 2015. https://www.eia.gov/consumption/residential/index.php.
54. Meng QY, Spector D, Colome S, Turpin B. Determinants of Indoor and Personal Exposure to PM(2.5) of Indoor and Outdoor Origin during the RIOPA Study. Atmos Environ (1994). 2009;43(36):5750–5758. doi: 10.1016/j.atmosenv.2009.07.066 [PubMed: 20339526]
55. Valavanidis A, Loridas S, Vlahogianni T, Fiotakis K. Influence of ozone on traffic-related particulate matter on the generation of hydroxyl radicals through a heterogeneous synergistic effect. J Hazard Mater. 2009;162(2-3):886–892. doi:10.1016/j.jhazmat.2008.05.124 [PubMed: 18602214]
56. Marshall JD. Environmental inequality: Air pollution exposures in California's South Coast Air Basin. Atmos Environ. 2008;42(21):5499–5503. doi:10.1016/j.atmosenv.2008.02.005
57. Miranda ML, Edwards SE, Keating MH, Paul CJ. Making the environmental justice grade: The relative burden of air pollution exposure in the United States. Int J Environ Res Public Health. 2011 ;8(6): 1755–1771. doi: 10.3390/ijerph8061755 [PubMed: 21776200]
58. Lin X, Trainer M, Liu SC. On the nonlinearity of the tropospheric ozone production. J Geophys Res. 1988;93(D12):879–888. doi:10.1029/jd093id12p15879
59. Hernandez ML, Ivins S, Chason K, et al. Respiratory effects of sedentary ozone exposure at the 70-ppb national ambient air quality standard: A randomized clinical trial. Am J Respir Crit Care Med. 2021 ;203(7):910–913. doi: 10.1164/rccm.202006-2597LE [PubMed: 33400891]
60. Hů nová I, Maly M, ezáčová JR, Braniš M. Association between ambient ozone and health outcomes in Prague, doi: 10.1007/s00420-012-0751-y
61. Toward Environmental Justice: Research, Education, and Health Policy Needs. Washington, D.C.: National Academies Press; 1999. doi: 10.17226/6034
62. Hajat A, MacLehose RF, Rosofsky A, Walker KD, Clougherty JE. Confounding by Socioeconomic Status in Epidemiological Studies of Air Pollution and Health: Challenges and Opportunities. Environ Health Perspect. 2021;129(6):65001. doi:10.1289/EHP7980 [PubMed: 34124937]
63. Breysse PN, Buckley TJ, Williams D, et al. Indoor exposures to air pollutants and allergens in the homes of asthmatic children in inner-city Baltimore. Environ Res. 2005;98(2):167–176. doi:10.1016/j.envres.2004.07.018 [PubMed: 15820722]
64. Hansel NN, Breysse PN, McCormack MC, et al. A longitudinal study of indoor nitrogen dioxide levels and respiratory symptoms in inner-city children with asthma. Environ Health Perspect. 2008;116(10):1428–1432. doi:10.1289/ehp.11349 [PubMed: 18941590]
65. Levy JI, Quirós-Alcalá L, Fabian MP, Basra K, Hansel NN. Established and Emerging Environmental Contributors to Disparities in Asthma and Chronic Obstructive Pulmonary Disease. Curr Epidemiol Reports. 2018;5(2):114–124. doi:10.1007/s40471-018-0149-9
66. LaKind JS, Burns CJ, Pottenger LH, Naiman DQ, Goodman JE, Marchitti SA. Does ozone inhalation cause adverse metabolic effects in humans? A systematic review. Crit Rev Toxicol. 2021 ;51 (6):467–508. doi:10.1080/10408444.2021.1965086 [PubMed: 34569909]

Highlights

- Long-term exposure to low levels of ozone is associated with respiratory morbidity
- Respiratory effects of long-term ozone exposure are worse in poorer neighborhoods
- Ozone may act in synergy with other exposures common in poor neighborhoods

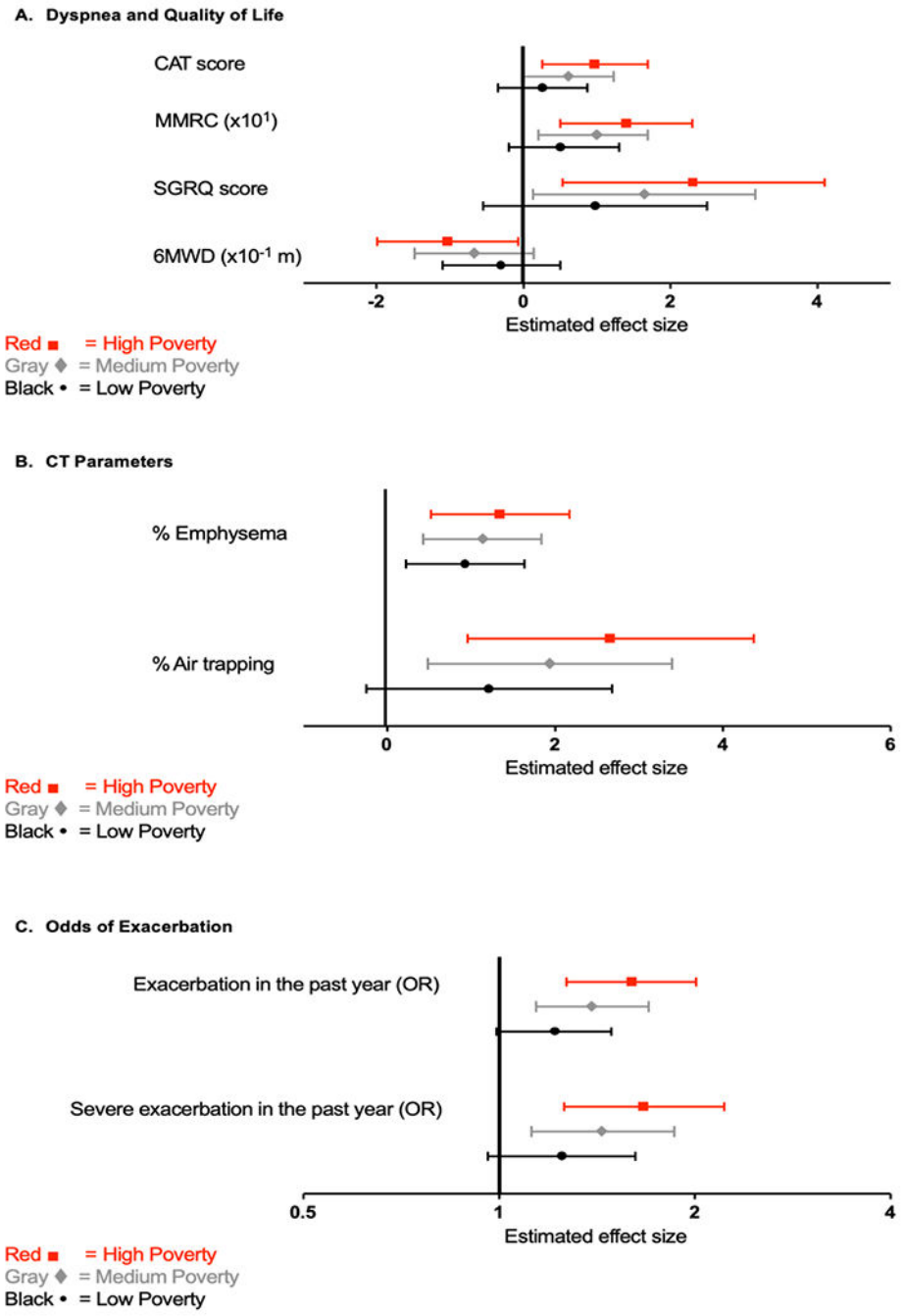


Fig. 1.

Effect of 5 ppb Increase in Ozone Between Low, Medium, and High Poverty Neighborhoods on Dyspnea and Quality of Life (A), CT Parameters (B), and Odds of Exacerbation (C). The point estimates and 95% confidence intervals were obtained based on performing multivariable regression analysis with two-way interaction between ozone and poverty rate, adjusted by age, sex, race, educational attainment, annual household income, body mass index, current smoking status, smoking pack-years, occupational exposure, and study sites.

Table 1.

Baseline Participant Characteristics, Mean ± SD or N (%)

	All N=1874	Low Poverty (<5%) N=779	Medium Poverty (5%-20%) N=830	High Poverty (>20%) N=265
Age, y	64.5 ± 8.8	66.8 ± 7.7	63.6 ± 8.8	60.4 ± 9.5
Sex, n (% female)	859 (46%)	330 (42%)	399 (48%)	130 (49%)
Race, n (% white)	1478 (79%)	706 (91%)	657 (80%)	115 (43%)
Education, n (% above HS grad)	1188 (64%)	578 (75%)	484 (59%)	126 (48%)
Income, annual household				
<$35,000	631 (34%)	183 (24%)	309 (37%)	139 (53%)
≥$35,000	889 (47%)	442 (57%)	382 (46%)	65 (25%)
Decline to answer	354 (19%)	154 (20%)	139 (17%)	61 (23%)
Body Mass Index	28.0 ± 5.3	27.7 ± 5.0	28.1 ± 5.3	28.2 ± 5.8
Current Smoker, n (% yes)	687 (37%)	234 (30%)	309 (38%)	144 (55%)
Pack-Years, y	49.8 ± 28.9	50.2 ± 24.1	51.2 ± 34.5	44.6 ± 21.3
Postbronchodilator FEV_1% Predicted	74.7 ± 25.8	75.5 ± 25.4	74.3 ± 25.5	73.5 ± 28.0
Comorbidity Index, #	2.2 ± 1.5	2.2 ± 1.5	2.2 ± 1.5	2.4 ± 1.7
Occupational Exposure, n (% yes)	904 (49%)	346 (45%)	414 (50%)	144 (55%)
10-yr mean $PM_{2.5}$ concentration, $\mu g/m^3$	11.2 ± 2.3	10.4 ± 2.3	11.3 ± 2.1	12.8 ± 1.9
10-yr mean Ozone concentration, ppb	24.7 ± 5.2	25.8 ± 4.8	25.2 ± 4.9	20.4 ± 5.2
Neighborhood Poverty Rate, %	9.9 ± 10.3	2.3 ± 1.5	10.7 ± 4.2	30.2 ± 10.1

Table 2.

Interaction Between Neighborhood Poverty Rate and 10 Yr Average Ambient Ozone Concentration on COPD Outcomes

	Ozone Effect Estimate (95% CI)[a]			Interaction Effect Est. (95% CI)[b]	
	Low Poverty[c]	Medium Poverty[d]	High Poverty[e]	Difference in Ozone Effect Estimate by 1-SD Increase in Poverty Rate	$P_{interaction}$
Respiratory Morbidity					
CAT	0.26 (−0.35, 0.87)	**0.61 (0.004, 1.23)**	**0.97 (0.25, 1.69)**	**0.49 (0.12, 0.85)**	**0.010**
MMRC	0.05 (−0.02, 0.13)	**0.10 (0.02, 0.17)**	**0.14 (0.05, 0.23)**	**0.06 (0.02, 0.11)**	**0.007**
SGRQ	0.98 (−0.55, 2.50)	**1.65 (0.13, 3.16)**	**2.31 (0.53, 4.10)**	0.92 (−0.004, 1.84)	0.051
FEV1 % Predicted	**−2.05 (−3.99, −0.10)**	**−2.53 (−4.47, −0.59)**	**−3.01 (−5.29, −0.74)**	−0.66 (−1.81, 0.49)	0.258
6MWT	−3.06 (−11.07, 4.96)	−6.69 (−14.78, 1.41)	**−10.3 (−19.9, −0.75)**	**−4.97 (−9.77, −0.18)**	**0.042**
CT-measured outcomes					
Airway Thickness ($x10^{-2}$)	−0.03 (−0.57, 0.51)	−0.01 (−0.55, 0.54)	0.01 (−0.62, 0.65)	0.03 (−0.29, 0.35)	0.860
% Emphysema	**0.93 (0.23, 1.63)**	**1.14 (0.43, 1.84)**	**1.34 (0.52, 2.17)**	0.28 (−0.13, 0.69)	0.176
% Air Trapping	1.21 (−0.25, 2.68)	**1.94 (0.48, 3.40)**	**2.66 (0.96, 4.37)**	**0.99 (0.13, 1.86)**	**0.025**
Exacerbations in the past 12 mo					
Any exacerbation, OR	1.22 (0.99, 1.49)	**1.39 (1.14, 1.70)**	**1.60 (1.27, 2.01)**	**1.21 (1.07, 1.36)**	**0.002**
Severe exacerbation, OR	1.25 (0.96, 1.62)	**1.44 (1.12, 1.86)**	**1.67 (1.26, 2.22)**	**1.22 (1.06, 1.42)**	**0.007**

[a] Ozone effect estimate represents the mean change for respiratory morbidity and CT-measured outcomes or odds ratio for exacerbations per 5 ppb increase in ozone concentration. The ozone effect estimate was obtained at each neighborhood poverty level (low, medium, high) by holding constant the neighborhood poverty rate at the defined level (5%, 12.5%, and 20%) using linear or logistic regression model with two-way interaction (ozone x poverty). All models were adjusted for age, sex, race, educational attainment, annual household income, BMI, current smoking status, smoking pack-years, occupational exposure, and study site.

[b] The interaction effect estimate represents the predicted change in the mean change for respiratory morbidity and CT-measured outcomes or odds ratio for exacerbations per 5 ppb increase in ozone concentration for every 1-SD increase in neighborhood poverty rate.

[c] For estimating ozone effect at “low poverty”, the neighborhood poverty rate was fixed at 5%.

[d] For estimating ozone effect at “medium poverty”, the neighborhood poverty rate was fixed at 12.5%, which is the median value of the 5~20% poverty range.

[e] For estimating ozone effect at “high poverty”, the neighborhood poverty rate was fixed at 20%.