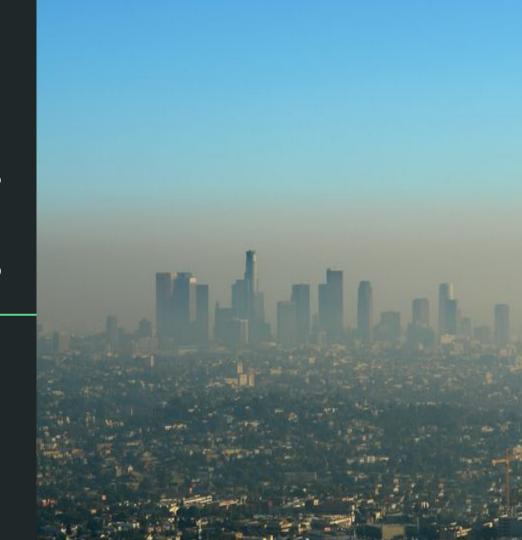
Ozone & Asthma Hospitalizations Amongst Adolescents in Los Angeles, US

Group 2: Haoran Cheng, Thao Lam, Xiajie Lyu, Marisa Wong, Lifan Yang

EH 530 April 22th, 2022



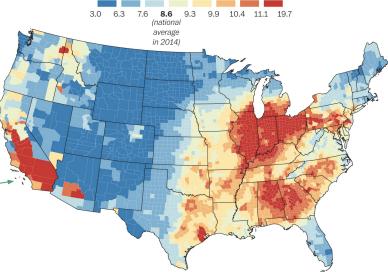
Is there an association between exposure to ozone and hospital visits due to asthma in adolescents (aged 13-18 years old) in Los Angeles, USA?

Background and Motivation

- Why adolescents? (<u>Silverman & Ito, 2010</u>)
 - Age-related association
 - Age: significant effect modifier for asthma hospitalizations
- Why Los Angeles, CA? (Moore et al., 2008)
 - Time trends study
 - High density + intense weather
- Why ozone vs. asthma? (Moore et al., 2008, Schwarz et. 2021)
 - Time trends study
 - O₃ main pollutant associated
 - Contributing living factors study
- Why this study?
 - Focus on Los Angeles' extreme heat and high air pollution
 - Focus newly on ozone-linked asthma hospitalization in adolescents, not just children

The map of American air pollution

Daily average small particulate matter (PM2.5) concentration in 2014



Source: Robert Wood Johnson Foundation County Health Rankings

THE WASHINGTON POST



Asthma and Biomarkers

- Condition in which airways inflamed, narrow, swollen; extra mucus, difficulty breathing
- Symptoms vary from person to person

Ozone and asthma

- Ozone demonstrated to worsen airway inflammation
- Increases airway response to inhaled allergen
- Increases nonspecific airway responsiveness

Allergen IgE-mediated Inflammation Association of IgE with Clinical Disease Histamine Leukotriene IL-4 IL-13 Platelet-activating factor Association of IgE with Clinical Disease Food Allergy Urticaria Allergic Rhinitis Allergic Asthma Atopic Dermatitis

IgE and asthma

- High serum IgE was observed in patients with asthma
- IgE immunoglobulin, mediates type 1 hypersensitivity reactions, plays a key role in pathogenesis of allergic asthma
- Increase allergen sensitivity, leading to thickening of the bronchial wall and exacerbating the symptoms

Study Design

Retrospective case-control analysis of a cohort in Los Angeles, USA

- Adolescents aged 13 to 18 in Los Angeles, USA from 2022-2032
- Recruitment:
 - 500 asthma participants (cases)
 - Cases will participate as cases and controls in case-crossover
 - 500 non-asthma participants (controls)
 - Have blood samples drawn from all patients every half year
 - Asthma patients have additional blood samples drawn every time they have an attack

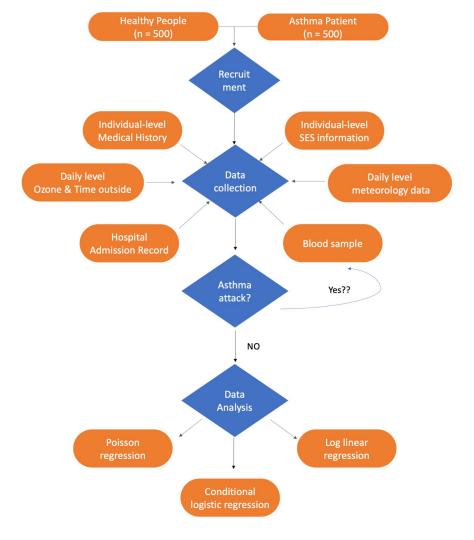


Study Design

- Ozone concentration and hospital admissions
 - Total number of hospital visits per day
 - Occurrence of asthma attack for each individual
- Ozone concentration and biomarker levels
 - IgE levels between different groups
 - Healthy
 - Asthma w/o attack
 - Asthma w/ attack



Flowchart



Data Sources

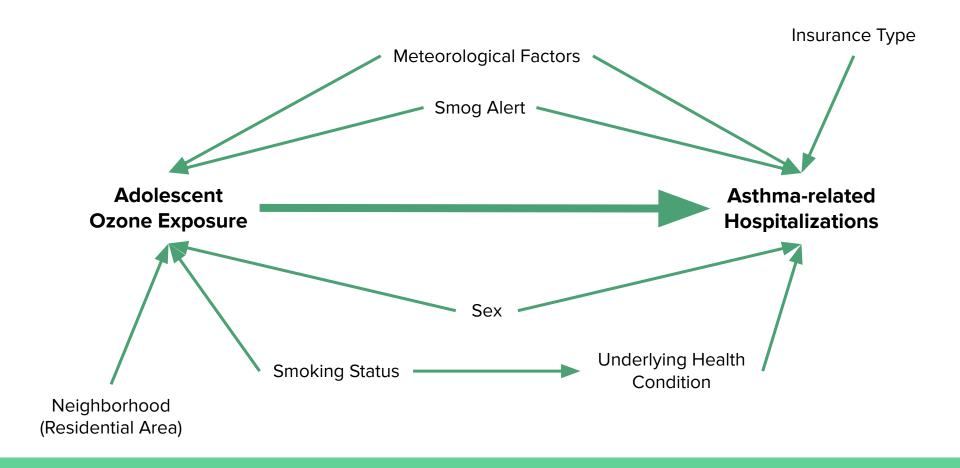
- Air pollution and weather data
 - Daily pollution ozone concentration data and pollutant standards index (PSI), smog alert from SCAQMD (South Coast Air Quality Management District) monitors in Los Angeles city limits.
 - Weather data -obtained from the National Climatic Data Center
- Medical history and personal information data
 - Hospital admission history
 - Enrollment questionnaire for all participants' information
- Data on time spent outside
- Factors that shift the amount of time spent outside:
 Air quality forecasts and smog alerts
 - Questionnaire on average daily outdoor time



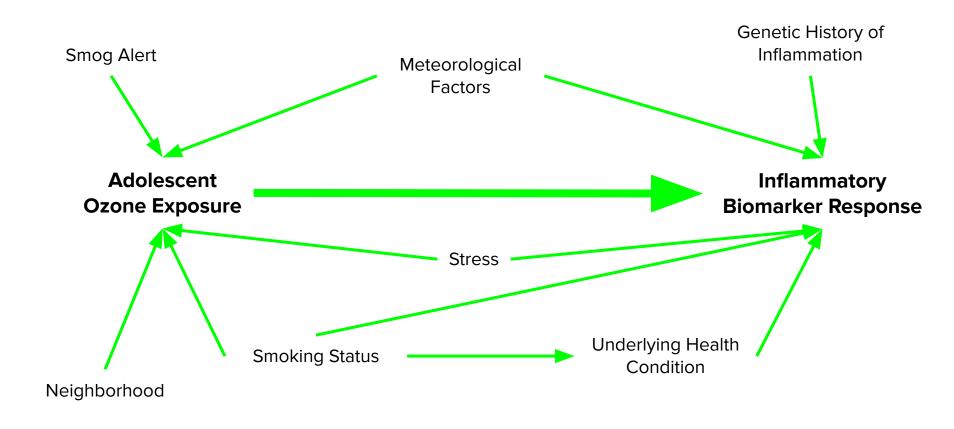
Key Variables

- Exposure
 - Daily maximum 8-hour average concentration of ozone exposure in adolescents (13-18 yo)
- Outcome
 - Hospital Admission due to Asthma
 - Inflammatory biomarker-IgE levels
- Potential Covariates and Confounders
 - Issuance of smog alert (via PSI index)
 - Socioeconomic factors
 - Meteorological factors
 - Underlying Health Conditions
 - Behavioral factors

DAG for Asthma-Related Hospitalizations



DAG for Inflammatory Biomarker Response



Analytical Approach – hospital admissions

- Ozone concentration and hospital admissions
 - Poisson regression model for population level data

$$\circ Y_i = e^{(\beta_0 + \beta_1 * Ozone + \beta_2 * PSI + \beta_3 * Met)}$$

Conditional logistic regression model for individual level data

$$\log\left(\frac{Y=1}{Y=0}\right) = \beta_0 + \beta_1 * Ozone + \beta_2 * Outdoor + \beta_3 * Ozone * Outdoor + \beta_4 * PSI + \beta_5$$

$$* Met + \beta_6 * SES + \beta_7 * MH$$

- Sensitivity analysis
 - Lag effect models
 - o 1 day, 2 days, 3 days, 7 days lag
 - Unnested models for covariates
 - Depending on variable

Analytical Approach – targeted biomarker

- Ozone concentration and inflammatory biomarkers
 - Univariate analysis: ANOVA for IgE levels
 - o G1: w/o asthma vs G2: w/ asthma & w/o attack vs G3: w/ asthma & w/ attack
 - Post-hoc analysis for multiple comparison adjustment
 - Multivariate analysis: Log-linear regression
 - $\circ \quad \log(I_{IgE}) = \beta_0 + \beta_1 * Group + \beta_2 * Ozone + \beta_3 * Outdoor + \beta_4 * Ozone * Outdoor + \beta_5$ $* PSI + \beta_6 * Met + \beta_7 * SES + \beta_8 * MH$
 - Sensitivity analysis
 - Ordinal logistic regression
 - \circ Flip $\log(I_{IgE})$ and group to see if $\log(I_{IgE})$ can be a good predictor of outcome

Study Assumptions

- Any missing data from our identified sources is truly missing, where organizations were unable to collect that information
 - Missingness does not have further implications
- No deadline post-study to finalize analytical results
- Unlimited budget
 - Hiring research assistants
 - Providing generous incentives to study participants



Sources of Error & Other Challenges

Sources of Error	Other Challenges
 Information Bias National Climatic Data Center Sources SCAQMD Air Pollution Monitors Medical History (not included pass respiratory diseases) Biomarker measurement Selection Bias Loss to follow-up Confounding Additional variables not identified in our assumptions Recall Bias 	 External Validity to the greater US Collaboration with Hospitals and Air monitoring center

Questions?

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