Air Pollution and Wheeze in the Fresno Asthmatic Children's Environment Study

Jennifer Mann and the FACES Team

Valley Air Conference
June 9, Fresno, CA

Sponsors

- California Air Resources Board (2000-2005)
- National Institutes of Health, NHLBI (2006-2011)
- US Environmental Protection Agency (2002-2004)
- Mickey Leland National Urban Air Toxics Research Center (2006-2010)

Why the FACES study?

- Very little data on which asthmatics are susceptible to air pollutants
- Explore in detail air pollutants that have not been studied with respect to exacerbations of asthma
- No data on the relationship between the responses to short-term exposures and the long-term progression of asthma in children
- Fresno has some of the highest ambient air pollution in the US and disproportionately high asthma prevalence

Fresno Asthmatic Children's Environment Study (FACES)

- Study Population (n=315)
  - Children 6-11 yrs. old in Fresno/Clovis, CA who had a physician-diagnosis of asthma and active asthma
  - Prospective, longitudinal study with data collection from 2000-2008
- Principal Study Aim
  - Evaluate the short-term and long-term health effects of exposure to ambient air pollutants and bioaerosol components on lung function among children with asthma

Descriptive Statistics for FACES Cohort

Characteristic	**%**
Mean Age at baseline [s.d.]	8.1 [1.7]
Male (%)	57.0
Income less than $15,000 (%)	20.4
Hispanic (%)	39.7
Non-hispanic white (%)	41.9
African American (%)	15.6
Skin-test positive to at least one antigen (%)	62.7

Today

- Examine two studies from FACES that looked at air pollution and wheeze
  - 1.) Are short-term increases in air pollution (NO_2, $PM_{10-2.5}$, PM_{10}, O_3, NO_3) associated with wheeze?
    - Are there subgroups that are more vulnerable?
    - Central site exposures used as estimate of child’s exposure
  - 2.) Are short-term increases in PAHs associated with wheeze?
    - Does it make a difference to use modeled individual exposures
    - Are certain PAHs associated with greater effects?

Short-Term Effects of Air Pollution on Wheeze in Asthmatic Children in Fresno, California: Sensitive Subgroups

Jennifer Mann, John Balmes, Tim Bruckner, Kathleen Mortimer, Helene Margolis, Boriana Pratt, Katharine Hammond, Fred Lurmann, Ira Tager

Wheeze and Air Pollution: Subgroups?

- Are there subgroups of asthmatic children who are more likely to wheeze from air pollution?
  - Included interest in subgroups of atopic asthmatics

- Eligible children for this study, complete at least one “panel” by March, 2005
  - Panel included 14 days of spirometry 2x/day
  - Spirometer also asked about wheeze since last test
  - Analysis of **morning wheeze**
    - N=13,152 observations, 280 children

- Studied relationship of exposures in past 2 wks to:
  - NO_2, $PM_{10-2.5}$, $PM_{2.5}$, EC, NO_3, O_3
  - Measured at First Street monitoring station in Fresno

Allergy Skin Tests

Test	% Positive
Alternaria	32.9
Rye	31.4
Olive	31.4
Grass	30.2
House Dust Mite	23.1
Mugwort	21.2
Cat	20.2
Cladosporium*	20.2
Cockroach	11.6
Oak	11.2
Privet**	9.5
Cedar	6.2
Dog	5.4
Juniper	2.1

N=240; * *N=171; **N=130

Results in All Children

- Interested in effect of realistic change in air pollutant
  - Used 90th percentile of daily change in concentrations
- For Full Group, 2 pollutants associated with wheeze
  - **NO_2** : OR=1.10 (95%CI=1.02-1.20)
    - 2-12 day lags and averages had greatest effect
  - **$PM_{10-2.5}$**: OR=1.11 (95% CI=1.01-1.22)
    - 3- to 7- day lags were associated with wheeze
- Adjustment for covariates, repeated measures, temporal and seasonal trends removed

Subgroups?

- Considered the following
  - skin-test positive to each antigen
  - asthma severity level
  - income level
  - pets (dogs, cats, birds, rodents)
  - race/ethnicity

Identified Subgroups

- Two subgroups of atopic asthmatics based on allergy skin test results
  - Children allergic to cat dander
  - Children allergic to common fungi
    - *Alternaria* OR *Cladosporium*
- Boys with Mild Intermittent Asthma at baseline
  - “Post-hoc”

Atopic Subgroups

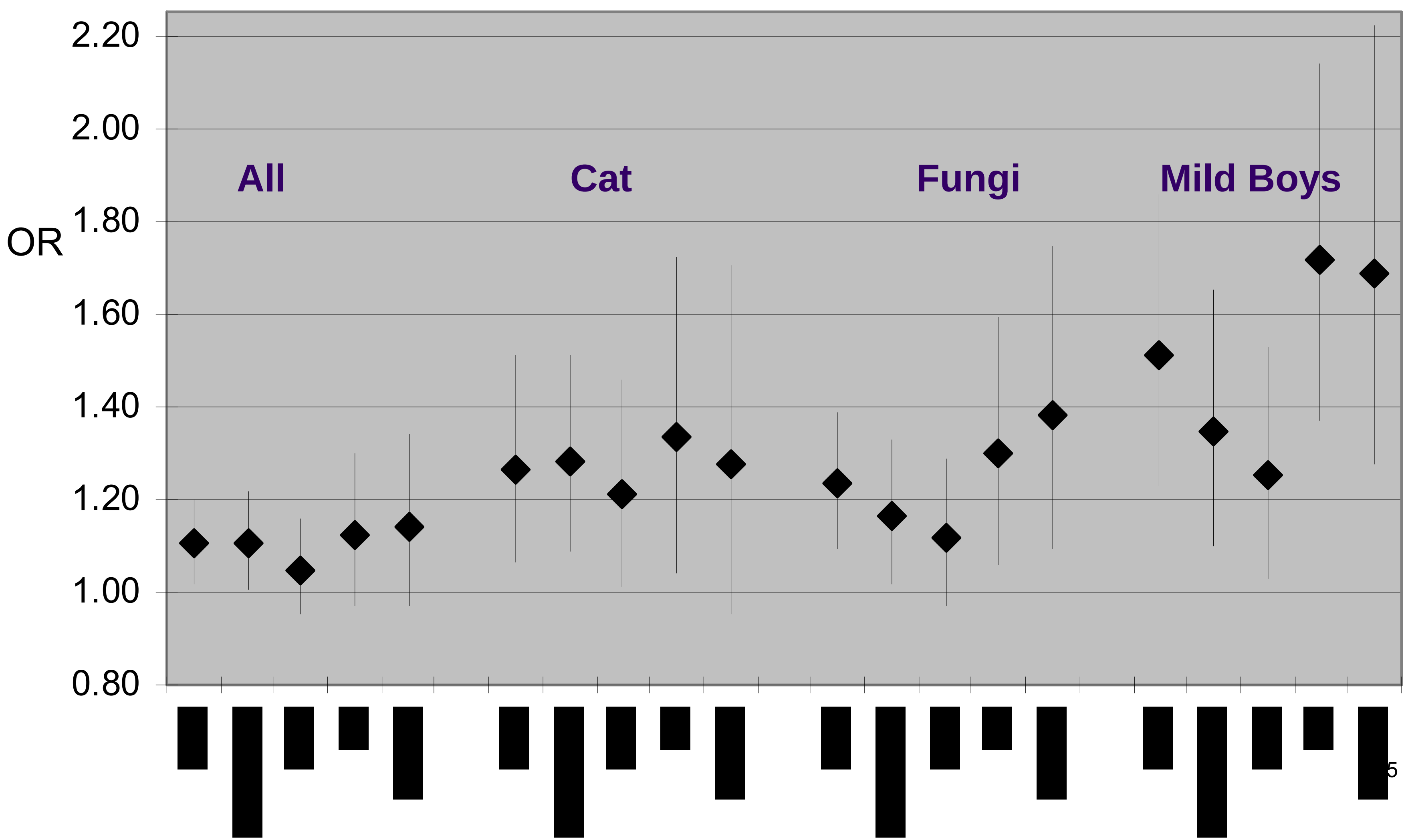
- *Alternaria*- and *Cladosporium*-allergic were grouped:
  - Not all children received *Cladosporium* skin test
  - 84% children who were allergic to *Cladosporium* were also allergic to *Alternaria*
  - 35.5% were allergic to either spore

Subgroup Results

- “Statistically significant associations” for at least 2 of 3 subgroups with
  - NO_2, NO_3, EC, $PM_{10-2.5}$, $PM_{2.5}$
- Effects greater in magnitude for all 3 subgroups
- No associations with O_3 in full group or any of the subgroups

Comparison of Results by Subgroup

Odds of Wheeze with Increased Air Pollutant Concentrations



Discussion/Conclusion

- **$PM_{10-2.5}$**
  - Only a few studies have shown that this pollutant is related to asthma
  - This is the first study to find association of coarse fraction with wheeze
- **NO_2** may be proxy for traffic or may directly effect child
  - Traffic associated with changes in lung function in this cohort
  - As marker of traffic associated with prevalent and incident asthma in Children's Health Study
  - Has been shown to enhance bronchoconstriction responses to inhaled aeroallergen in specifically sensitized adults with asthma

Discussion/Conclusion

- Fungi
  - Other groups have shown that *Alternaria* and/or *Cladosporium* spore concentration is associated with asthma exacerbation
  - *Alternaria* and *Cladosporium* are found in $PM_{10\text{-}2.5}$

Discussion/Conclusion

- **Boys with Mild Intermittent Asthma**
  - A few studies have seen greater effects among mild asthmatics
  - Some see greater effects in boys, but results are mixed.

Polycyclic Aromatic Hydrocarbon Exposure and Increased Wheeze in a Cohort of Children with Asthma in Fresno, CA

Sara Gale,[1] Elizabeth M. Noth, [2] Jennifer Mann,[2] Katharine Hammond, [2] Ira Tager[1]

1 Division of Epidemiology
2 Division of Environmental Health Sciences,
The University of California, Berkeley

Analysis Aim

- To assess the relation of short-term ambient air pollution (as measured by PAHs) on asthma morbidity (reported wheeze) among children with asthma in Fresno, CA
- To compare effects when using exposure estimated at central site with individual exposure estimates for each child on each day.

Data Structure

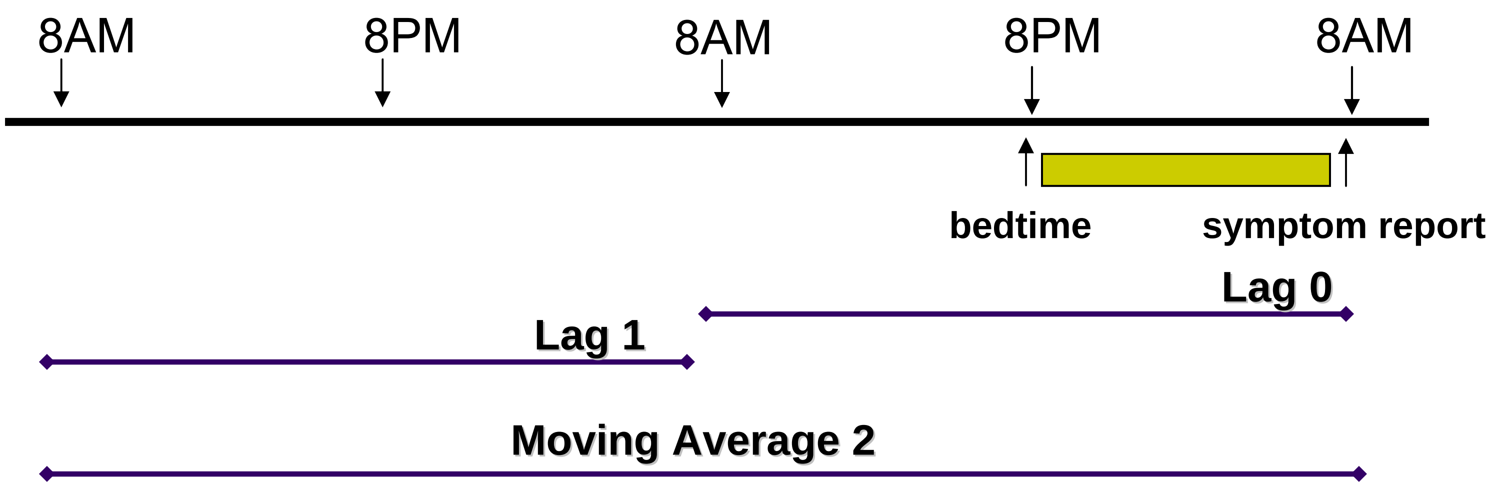
- Outcome: wheeze since bedtime
  - asked on EZ1 spirometer in AM
  - 2000-2007 (N=19,472)

- Exposures Average PAH exposure (ng/m^3)
  - the sum of PAH with rings 4, 5, or 6 (PAH_{456})
    - Central site
    - Individual exposure estimates
  - Phenantherene
    - Individual exposure estimates

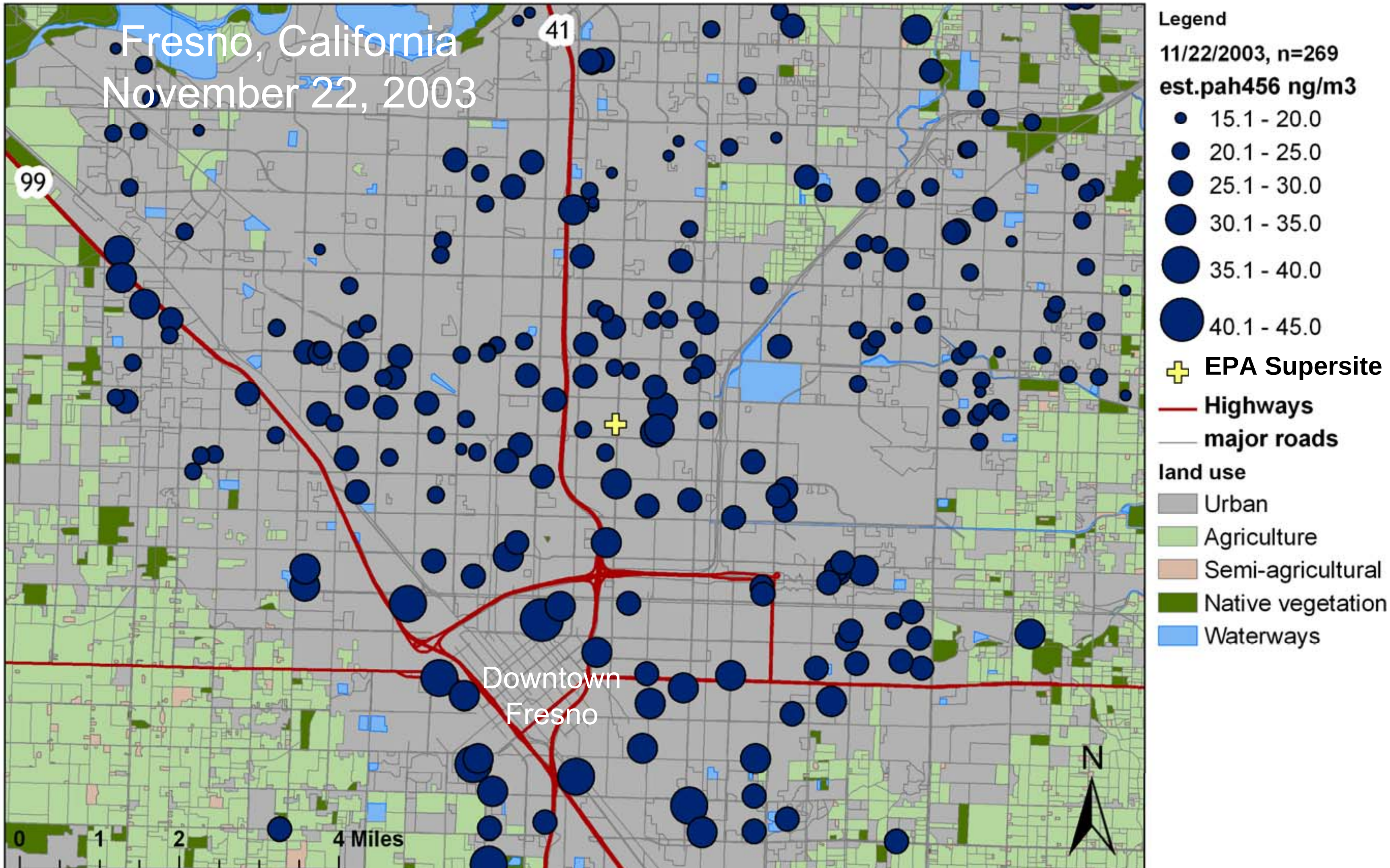
- Covariates/Adjustments
    - Demographics (e.g. age, sex, income, race/ethnicity)
    - Weather (temperature, humidity)
    - Seasonal patterns of wheeze removed with ARIMA model

Exposure Assessment

- EPA Super Site—daily measurements of particle-bound PAHs by continuous echo chem PAS 2000 monitor
- Land Use Regression (LUR) used to generate individual estimates by home address on each panel day 2000 – 2007
  - Additional PAHs measures captured from home, school and moving monitors



PAH exposure distribution



Results

PAH Estimate (10 ng/m3)	*PAH Central Site Odds Ratio (95% CI)*	*PAH 4,5,6 LUR Odds Ratio (95% CI)*	*Phenantherene LUR Odds Ratio (95% CI)*
Lag 0	1.08 (1.00, 1.16)	1.12 (0.93, 1.35)	1.23 (0.98, 1.56)
Lag 2	**1.10 (1.03, 1.18)**	**1.17 (0.97, 1.38)**	**1.35 (1.06, 1.72)**
Lag 5	1.11 (1.03, 1.18)	1.12 (0.93, 1.32)	1.22 (0.94, 1.61)
2-day MA	1.10 (1.01, 1.18)	1.19 (0.96, 1.34)	1.33 (0.98, 1.34)
5-day MA	**1.13 (1.03, 1.25)**	**1.22 (0.95, 1.53)**	**1.54 (1.06, 2.27)**
9-day MA	1.15 (1.04, 1.28)	1.20 (0.91, 1.55)	1.44 (0.96, 2.14)

Conclusions

- There is a consistent positive trend across PAH estimates: for every 10 ng/m^3 increase in PAH there is an increased odds for wheeze
- Phenantherene has the highest concentration of PAHs in our ambient air pollution measures second to naphthalene
- Phenantherene yields stronger associations with wheeze and has some significant lags and moving average estimates
- The odds of wheeze with increased PAH_{456} was greater when we used individual-level exposure estimates than when we used central site estimates.
- This is the first study to look at these associations, so needs to be replicated in future studies in other populations/locations.

The FACES Team

UC Berkeley

Ira Tager

Kathie Hammond

John Balmes

Sara Gale

Jennifer Mann

Betsey Noth

Boriana Pratt

Lucas Carlton

Jessie Murphy

Meagan Loftin

Fred Lurmann (STI)

Helene Margolis (UC Davis)

Tim Bruckner (UC Irvine)

Fresno

Leah Melendez

Cindy Appel

Raul Gallegos

Alex Galdabon

Thank You

Extra Slides

FACES Motivation

- Panel Design: 2-week intervals, 3 times/year
  - Capture lung function and symptom data
  - Wheeze: key asthma symptom
- Longitudinal Component
  - Changes in severity and lung function over time

Deletion/Substitution/Addition Algorithm (DSA)

- R add-on program
  - http://www.stat.berkeley.edu/~laan/Software/
- Flexible model fitting algorithm (machine learning), which uses **cross validation** to search for the “best” model from a sequence of models with polynomial predictors and their multiplicative interactions
- “best” is defined as the model that minimizes the mean-squared error of prediction
- Optimal model characteristics include:
  - Second order terms, two-way interactions, and a maximum of 12 terms for the final model

Land Use Regression

- PAS2000 measurement data collected continuously at the US EPA Supersite
  - PAH measurements taken at 83 FACES participant homes from 2/2002-2/2003
- Independent variables
  - Meteorology--wind, temperature, humidity, precipitation
  - Traffic (density, proximity to roadway), landuse, agricultural burning, demographic census variables, home heating, cars per capita per census block group
- Unlike toxic air pollutants with variability over regional or national areas, PAHs vary widely within a single city or urban area.

D/S/A Model Selection

DSA Model
$\text{Logit}[E[Y\|A=a, W]] = \beta_0 + \beta_1 a + \beta_2 w_1 + \ldots + \beta_8 w_7$ Y=wheeze (y/n) A=PAH 4,5,6 LUR; Phenantherene LUR or PAH 4,5,6 central site W=seasonal wheeze and D/S/A selected covariates—income, gender, asthma severity, smoker in home, dwelling type (squared), steroid use

Study Limitations

- Scientific inference may be limited to children with asthma in the California Central Valley

- Exposure assessment
  - from a single EPA monitor
  - from a land use regression model
    - These estimates may not be what children are actually exposed to (the concentrations might not equal the actual dose)

- Associations are presented here
  - An analysis with “marginal structural models” will give us the interpretation of what happens in a population where everyone’s exposures are reduced.