Air Pollution and Adult Asthma In The Sister Study

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Adult Asthma: Background

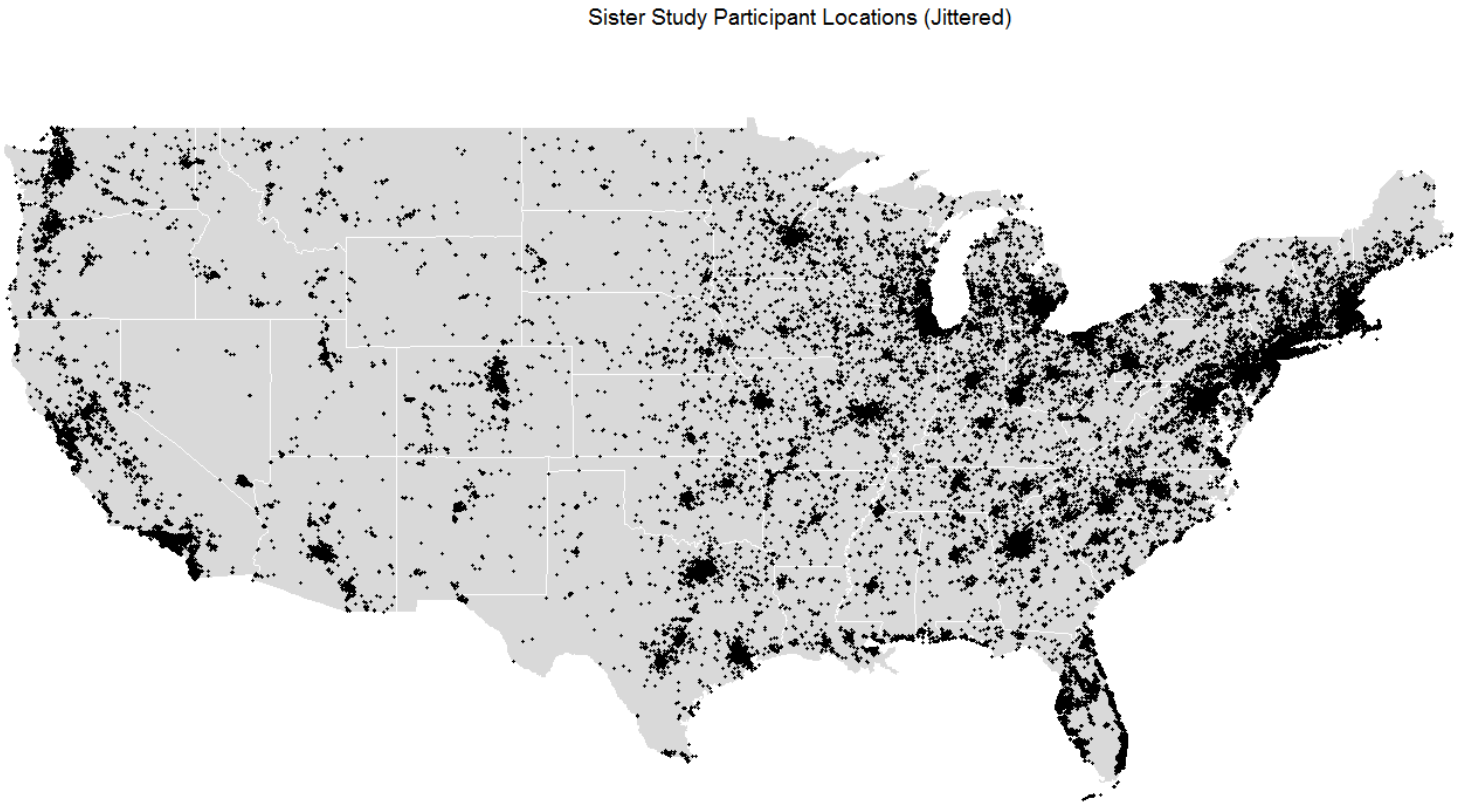
- U.S. Prevalence: 8.1% in women
- Asthma accounts for 1% of all disability adjusted life-years, globally
- Two phenotypes of Adult Asthma:
  - Childhood asthma persisting/recurring in adulthood
  - Adult incident asthma

Specific Aims

- Specific Aim 1: Does ambient air pollution lead to adult recurrence of childhood asthma?
- Specific Aim 2: Does ambient air pollution lead to adult incident asthma?
- Specific Aim 3: Does ambient air pollution lead to adult incident respiratory symptoms?

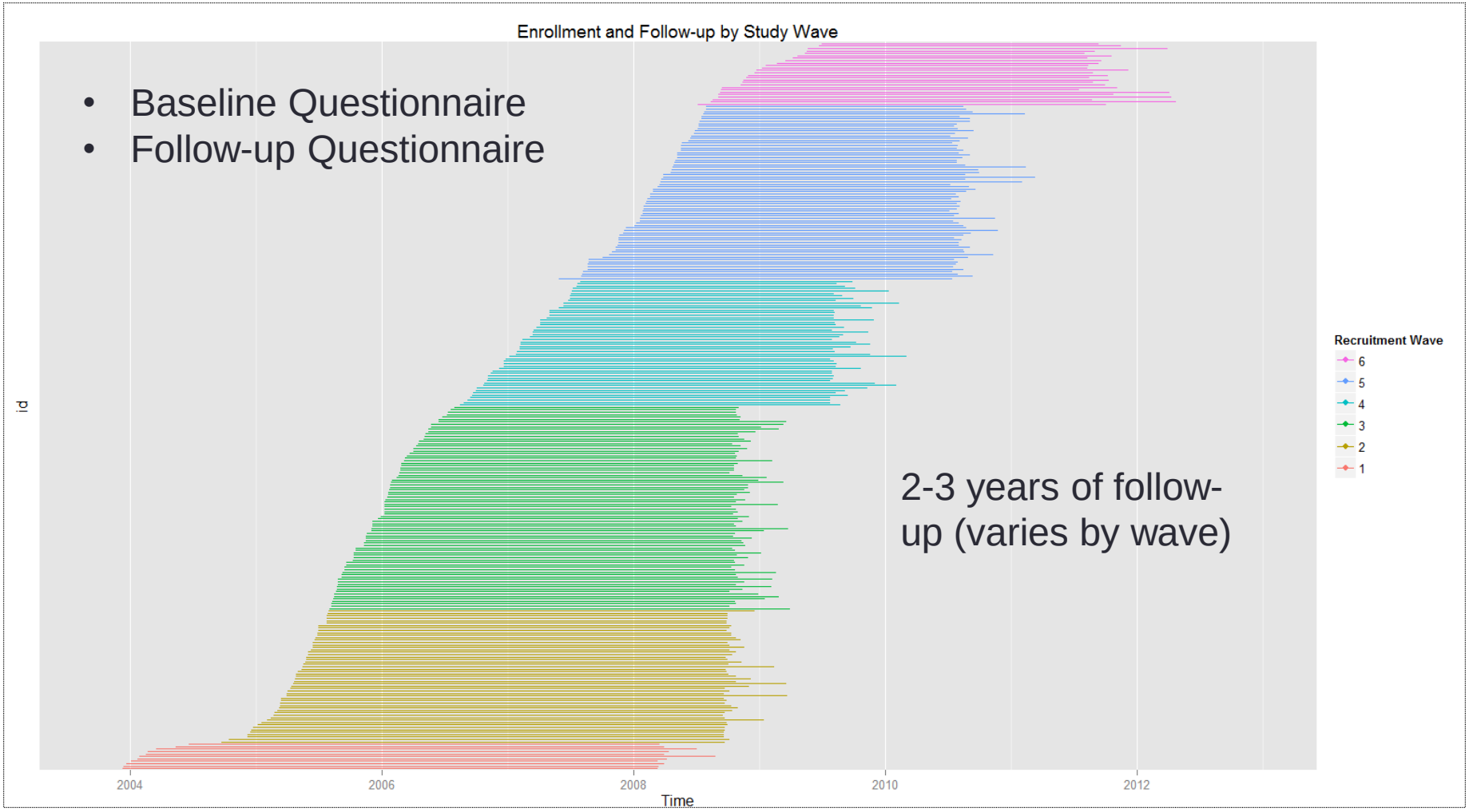
METHODS

Study Design
The NIEHS Sister Study



- National recruitment (AK and HI not shown)
- n=50,884

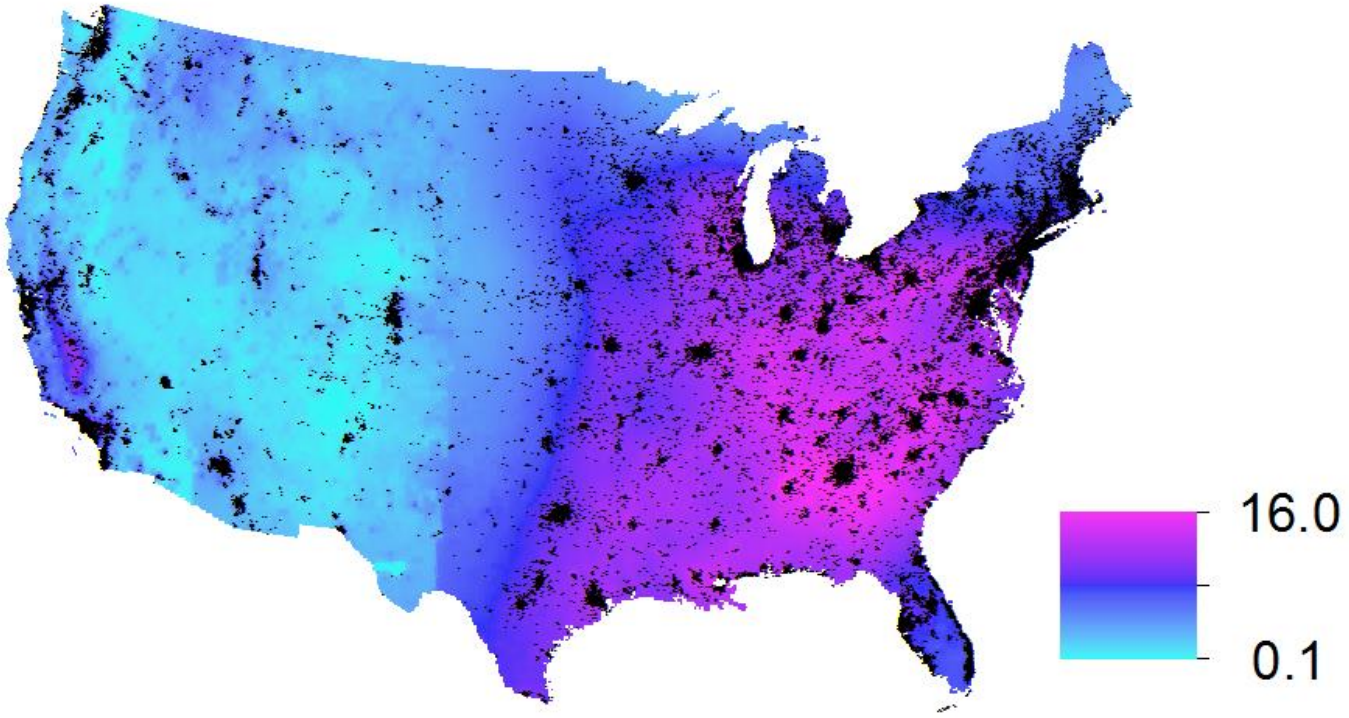
Study Design



Exposure Model

- Two exposures:
  - $PM_{2.5}$
  - NO_2
- Year 2006 annual average
- Modeled nationally using:
  - National air quality monitors
  - land-use covariates
  - A spatial smoothing
- Predicted at participant baseline address

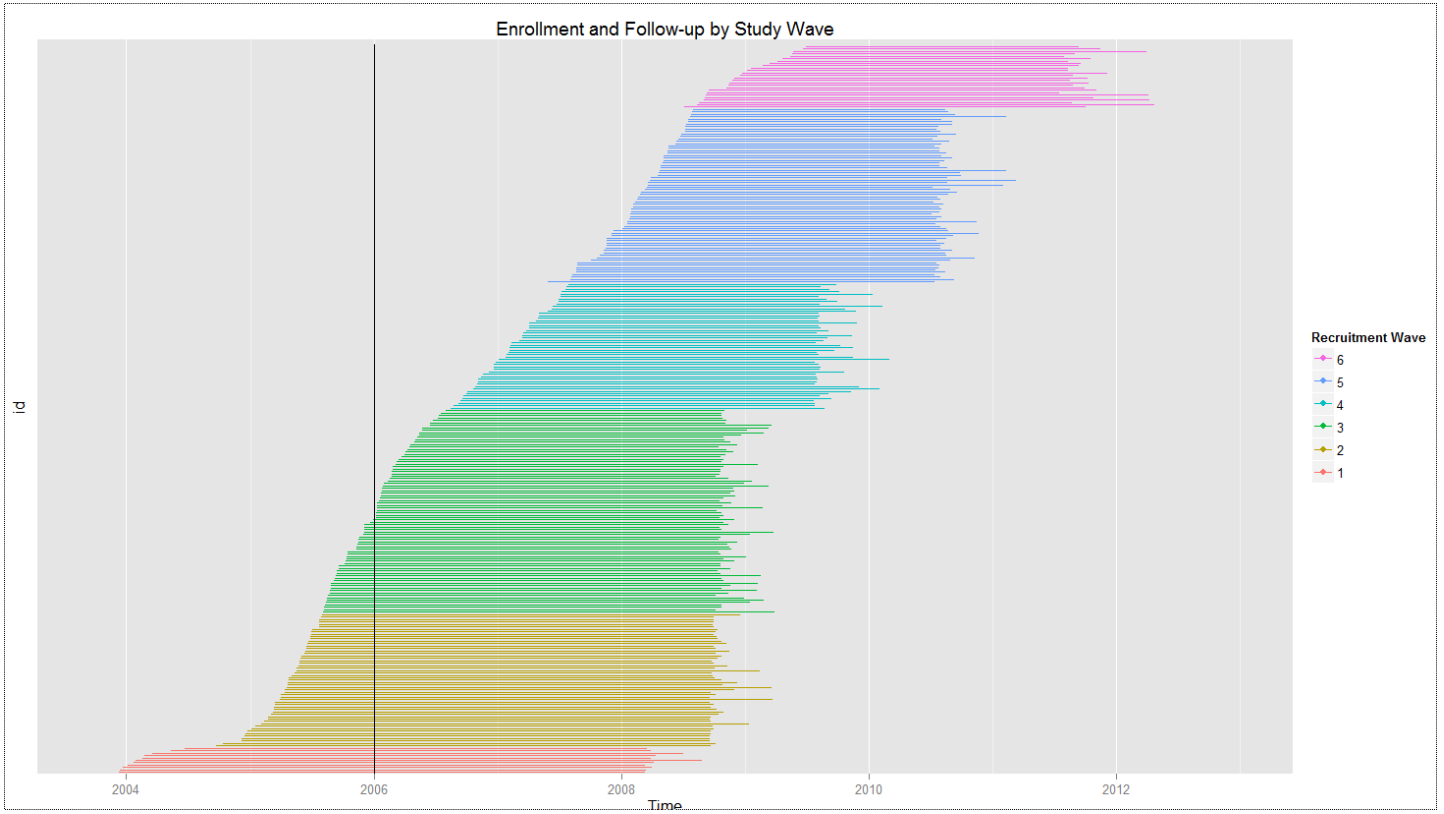
Exposure



$PM_{2.5}$ predictions ($\mu g/m^3$) with Sister Study participant home address locations overlaid in black

Year 2006 Exposure and Enrollment

- Year 2006 corresponds to baseline enrollment



Outcomes
Adult Recurrence of Asthma (Specific Aim 1)

- Restrictions:
  - Asthma started before age 13
  - Asthma stopped by age 21
  - Neither wheeze nor frequent cough at baseline
  - No medication use at baseline
- Adult recurrence at follow-up:
  - Report of cough, wheeze, or asthma symptoms at follow-up

Outcomes
Adult Incident Asthma (Specific Aim 2)

- Restrictions
  - Non-asthmatic
  - No wheeze or no cough at baseline
- Incident asthma at follow-up if:
  - Diagnosed with asthma since baseline AND
  - Used asthma medications since baseline AND
  - Had asthma symptoms or cough or wheeze in the last 12 months

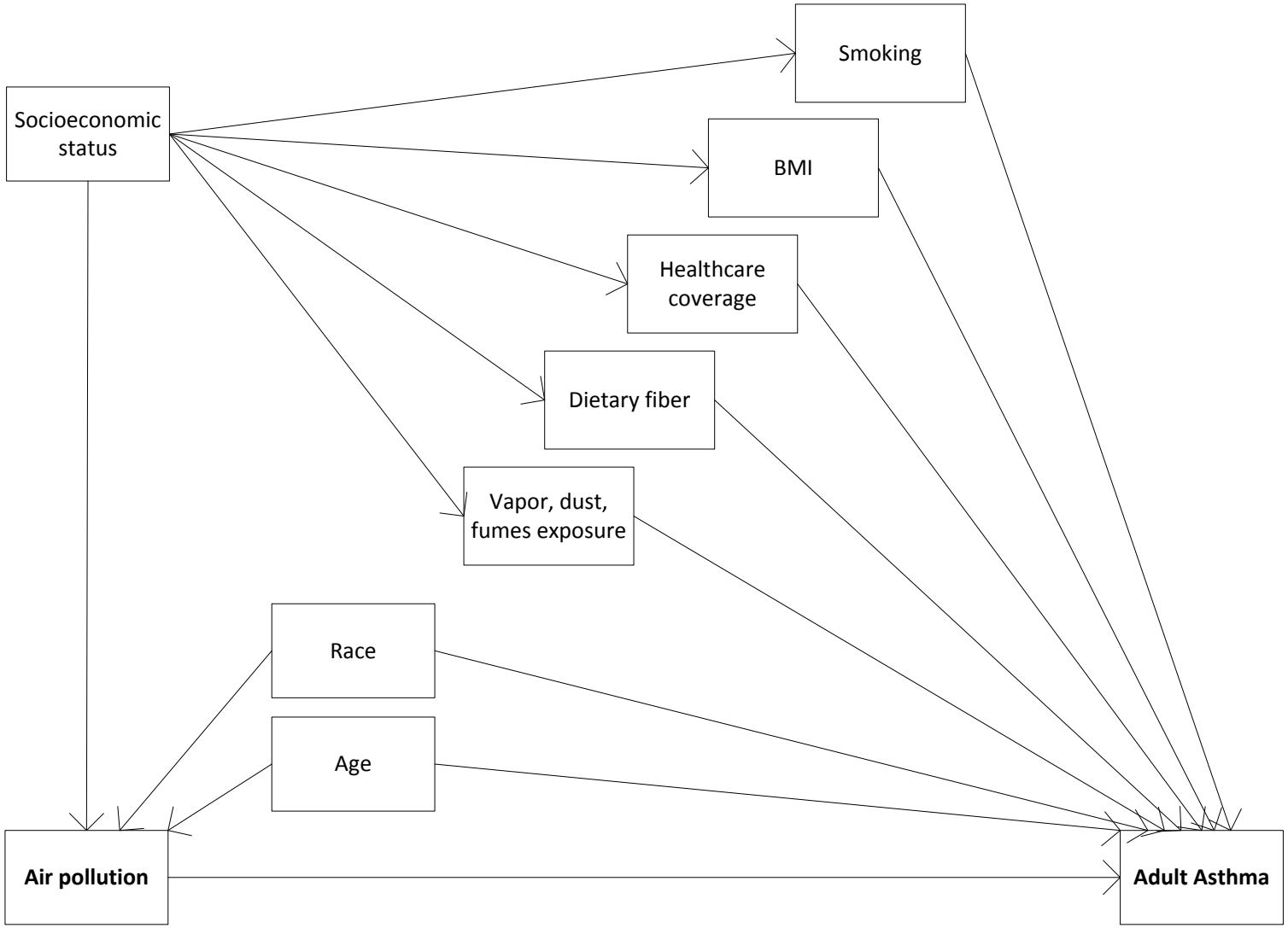
Outcomes
Onset Respiratory Symptoms (Specific Aim 3)

- Restrictions
  - Non-asthmatic
  - No wheeze at baseline
  - No cough at baseline
- Three outcomes:
  - Frequent cough in the last year (before follow-up)
  - Wheeze in the last year
  - Wheeze *and* cough in the last year

Confounding

- Adjustment Models
  - Age-adjusted
  - **Fully Adjusted**
    - Age
    - Race
    - Education
    - Occupational Vapor/Fumes exposure
    - Baseline smoking status
    - Age started smoking
    - Smoking status at follow-up
    - Childhood second-hand smoke exposure
    - Healthcare coverage
    - Dietary fiber consumption
  - Data-driven

Causal Model



Effect Modification

- Pre-specified potential effect modifiers
  - Smoking Status
  - BMI
  - Family history of asthma

Statistical Analysis

- Logistic Regression
- Cox Proportional Hazards Model
  - sensitivity analysis—Incident asthma outcome only

RESULTS

Population Characteristics by Quartiles of $PM_{2.5}$ exposure (ug/m^3)

		[0.7,6.8]	(6.8,9.3]	(9.3,12.6]	(12.6, 31.5]
n		12367	12367	12367	12367
Age (years)		55.7 ± 8.8	54.9 ± 9.0	54.9 ± 9.0	55.1 ± 9.1
BMI		27.5 ± 5.8	27.5 ± 5.9	27.6 ± 6.2	27.6 ± 6.3
Daily fiber consumption (g)		16.9 ± 8.3	16.8 ± 8.3	17.1 ± 8.6	17.3 ± 8.7
Baseline Smoking status %					
	Current smoker	8.6	7.7	7.9	8.7
	Never smoked	53.6	54.8	53.9	51.7
	Past smoker	35.7	35.2	35.8	37.3
	Social smoker	2.1	2.3	2.3	2.4
Education %					
	Less than high school	1.1	0.9	0.9	1.2
	High school or GED	16.8	15.2	13.1	11.4
	Some college	21.2	19.7	19.1	19
	Bachelors	24.9	26.8	27.7	28.1
	Associate, tech, or nursing	16.6	14.6	13.6	11.7
	Masters/Doctoral	19.3	22.9	25.6	28.7
Race %					
	Black	4.6	7.8	10.6	13.4
	Hispanic	2.1	2.6	2.8	5.2
	Non-Hispanic White	90.3	87.3	84.2	78.7
	Other	3	2.3	2.3	2.7

Continuous variables are expressed as mean ± standard deviation.

Population Characteristics by Quartiles of NO_2 exposure (ppb)

		[1.9,8.8]	(8.8,10.8]	(10.8,12.4]	(12.4,18]
n		12367	12367	12367	12367
Age (years)		55.7 ± 8.9	55.3 ± 9.1	54.9 ± 8.9	54.6 ± 9.0
BMI		27.0 ± 5.7	27.5 ± 6.1	27.5 ± 6.0	28.1 ± 6.5
Daily fiber consumption (g)		17.4 ± 8.5	17.0 ± 8.3	17.0 ± 8.6	16.8 ± 8.6
Baseline Smoking status %					
	Current smoker	7.3	8.4	8	9.2
	Never smoked	52.8	53.1	53.6	54.6
	Past smoker	37.8	36.3	36	33.8
	Social smoker	2.2	2.2	2.4	2.4
Education %					
	Less than high school	0.8	1.1	1	1.2
	High school or GED	13.7	14.8	14.9	13.1
	Some college	20.4	20.3	18.5	19.7
	Bachelors	27.7	25.8	27	27.1
	Associate, tech, or nursing	14.8	15.1	13.7	12.9
	Masters/Doctoral	22.6	22.9	25	26.1
Race %					
	Black	2.1	5.1	9.4	19.9
	Hispanic	3.5	3.4	2.5	3.3
	Non-Hispanic White	91.8	88.6	85.7	74.4
	Other	2.6	2.9	2.4	2.4

Continuous variables are expressed as mean ± standard deviation.

Results

- The interquartile ranges of $PM_{2.5}$ and NO_2 were 3.53 ug/m^3 and 5.84 ppb, respectively.
- The observed incidence rate of adult asthma was 2.5 cases per 1000 person-years.

Outcome	Cases	n
Asthma Recurrence	84	368
Incident Asthma	282	39,350
Cough and Wheeze	222	34,489
Cough	1,711	36,515
Wheeze	1,143	36,926

Effect Estimates—$PM_{2.5}$

		Fully Adjusted	
Exposure (IQR)	Outcome	OR (95% CI)	P Value
$PM_{2.5}$ (3.53 µg/m^3)	Asthma Recurrence	1.20 (0.79, 1.82)	0.388
	Incident Asthma	1.20 (0.99, 1.45)	0.069
	Cough and Wheeze	0.93 (0.74, 1.15)	0.491
	Cough	0.95 (0.88, 1.02)	0.175
	Wheeze	1.13 (1.02, 1.25)	**0.015**

Effect Estimates—NO_2

		Fully Adjusted	
Exposure (IQR)	Outcome	OR (95% CI)	P Value
NO_2 (5.84 ppb)	Asthma Recurrence	1.00 (0.71, 1.40)	0.989
	Incident Asthma	1.12 (0.96, 1.30)	0.150
	Cough and Wheeze	1.01 (0.84, 1.22)	0.907
	Cough	1.00 (0.93, 1.07)	0.930
	Wheeze	1.08 (1.00, 1.17)	0.053

Effect Modification

- **NO_2 was significantly associated with onset wheeze in nonsmokers** with an OR of 1.13 (95% CI: 1.04-1.24, p=0.007) for an IQR difference in NO_2.
- No other effects in pre-specified subgroup analyses were significant

Sensitivity Analyses

- Age-adjusted models were consistent with fully adjusted models
- Data-driven models identified no important confounders other than age
- The Cox proportional hazards model provided similar results to the logistic model for the incident asthma analysis

DISCUSSION

Discussion

- We found a statistically significant association between estimated $PM_{2.5}$ exposure and incident wheeze.
- The association between $PM_{2.5}$ exposure and incident asthma approached significance.
- NO_2 was significantly associated with incident wheeze in non-smokers only.

Discussion

- Primary **limitations** of this analysis include the possibility of undiagnosed asthma at baseline and the potential for exposure misclassification.
- **Strengths** of this study are its prospective design, national cohort, and advanced exposure models.
- In conclusion, $PM_{2.5}$ exposure may be a risk factor in the development of incident asthma or wheeze, the cardinal symptom of asthma, in adult women, but further research is needed to confirm these observed associations.

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Questions?

Effect Estimates

		Minimally Adjusted		Fully Adjusted	
Exposure (IQR)	Outcome	OR (95% CI)	P Value	OR (95% CI)	P Value
$PM_{2.5}$ (3.53 µg/m^3)	Asthma Recurrence	1.24 (0.87, 1.76)	0.236	1.20 (0.79, 1.82)	0.388
	Incident Asthma	1.19 (0.99, 1.42)	0.059	1.20 (0.99, 1.45)	0.069
	Cough and Wheeze	0.98 (0.81, 1.19)	0.855	0.93 (0.74, 1.15)	0.491
	Cough	0.98 (0.91, 1.06)	0.621	0.95 (0.88, 1.02)	0.175
	Wheeze	1.17 (1.07, 1.28)	0.001	1.13 (1.02, 1.25)	0.015
NO_2 (5.84 ppb)	Asthma Recurrence	1.00 (0.75, 1.32)	0.989	1.00 (0.71, 1.40)	0.989
	Incident Asthma	1.12 (0.97, 1.28)	0.123	1.12 (0.96, 1.30)	0.150
	Cough and Wheeze	1.00 (0.85, 1.18)	0.977	1.01 (0.84, 1.22)	0.907
	Cough	0.99 (0.93, 1.05)	0.680	1.00 (0.93, 1.07)	0.930
	Wheeze	1.05 (0.98, 1.13)	0.151	1.08 (1.00, 1.17)	0.053