Modulation of PM2.5-Mediated Cardiometabolic Indicators in Wildfire-exposed Individuals Through Residential Air Filtration

Session 55: Future of Fire Safety (Symposium)
Society of Toxicology Meeting 2023, Nashville, TX

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Duke | NICHOLAS SCHOOL OF THE ENVIRONMENT

JAMA Pediatrics | Original Investigation

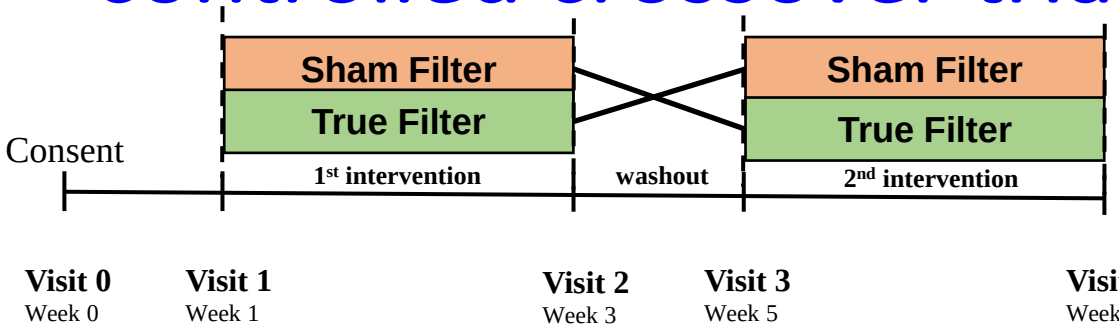
Association Between Bedroom Particulate Matter Filtration and Changes in Airway Pathophysiology in Children With Asthma

Xiaoxing Cui, PhD, BMED, MSPH; Zhen Li, MD; Yanbo Teng, PhD; Karoline K. Barkjohn, PhD; Christina L. Norris, MSc; Lin Fang, BS; Gina N. Daniel, MEM; Linchen He, MEM; Lili Lin, MD; Qian Wang, MD; Drew B. Day, PhD; Xiaojian Zhou, MD; Jianguo Hong, MD; Jicheng Gong, PhD; Feng Li, MD, PhD; Jinhan Mo, PhD; Yinping Zhang, PhD; James J. Schauer, PhD, MBA; Marilyn S. Black, PhD; Michael H. Bergin, PhD; Junfeng (Jim) Zhang, PhD

IMPORTANCE Fine particles (particulate matter 2.5 μm in size [$PM_{2.5}$]), a ubiquitous air pollutant, can deposit in the small airways that play a vital role in asthma. It appears to be unknown whether the use of a $PM_{2.5}$ filtration device can improve small airway physiology and respiratory inflammation in children with asthma.

Supplemental content

Double-blind, placebo-controlled crossover trial



43 asthmatic children living in Shanghai

each received both true filtration and sham filtration

Filtration duration = 2 weeks
Washout period = 2 weeks

Portable Air Filtration in Bedrooms

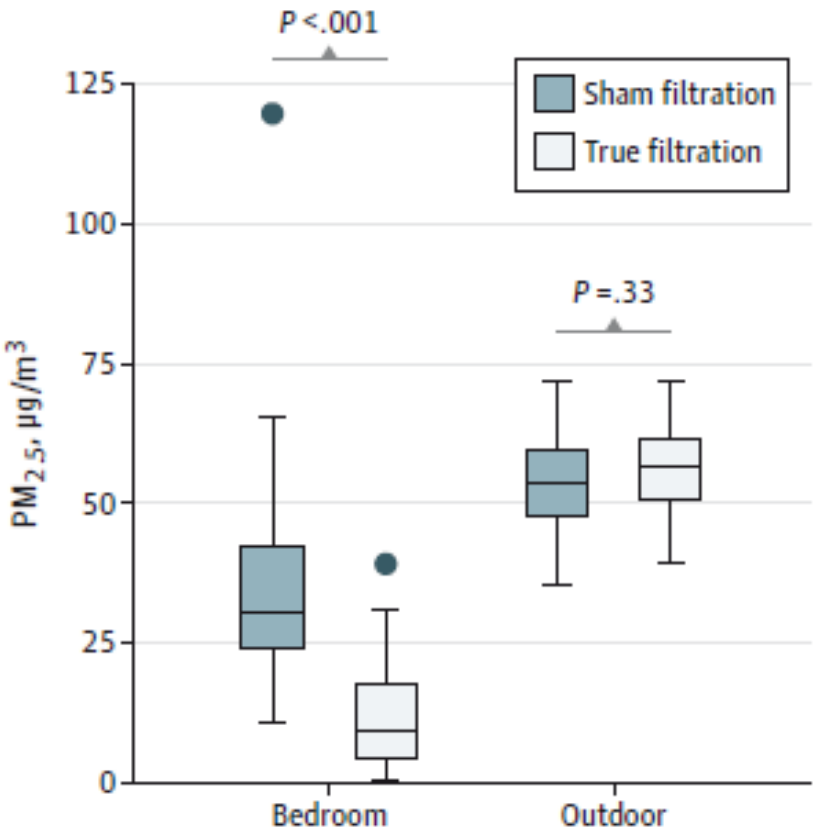
Air →  →  →  →

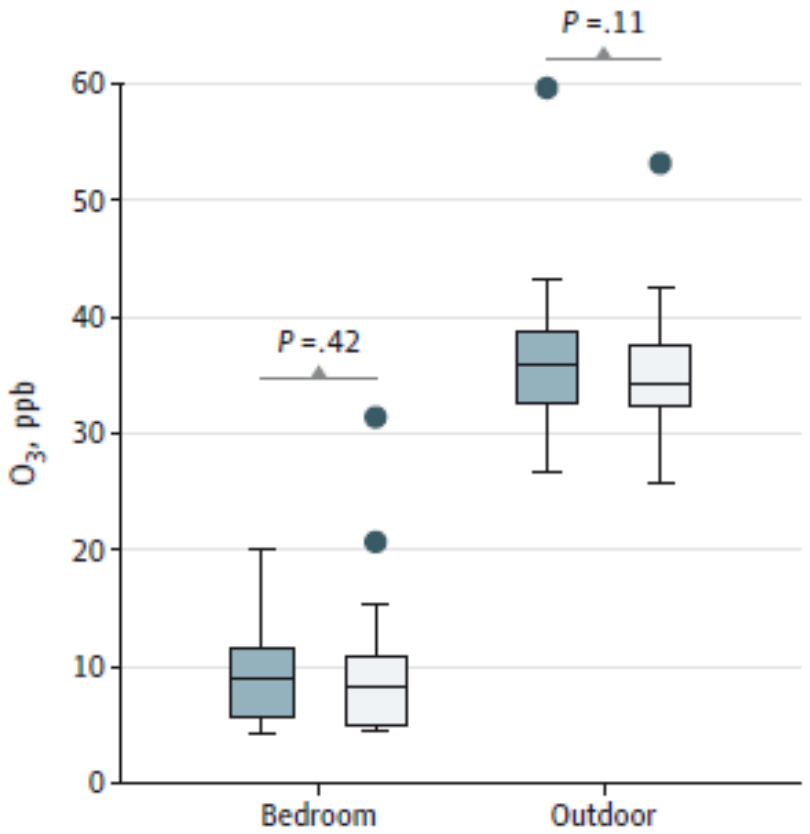
Pre-Filter **HEPA Filter** **Activated Carbon Filter**

HEPA and activated carbon filters were removed from sham filtration devices

PM2.5 Exposure Reduction

Figure 1. Pollutant Concentrations in Bedrooms and Outdoors by Filtration Status

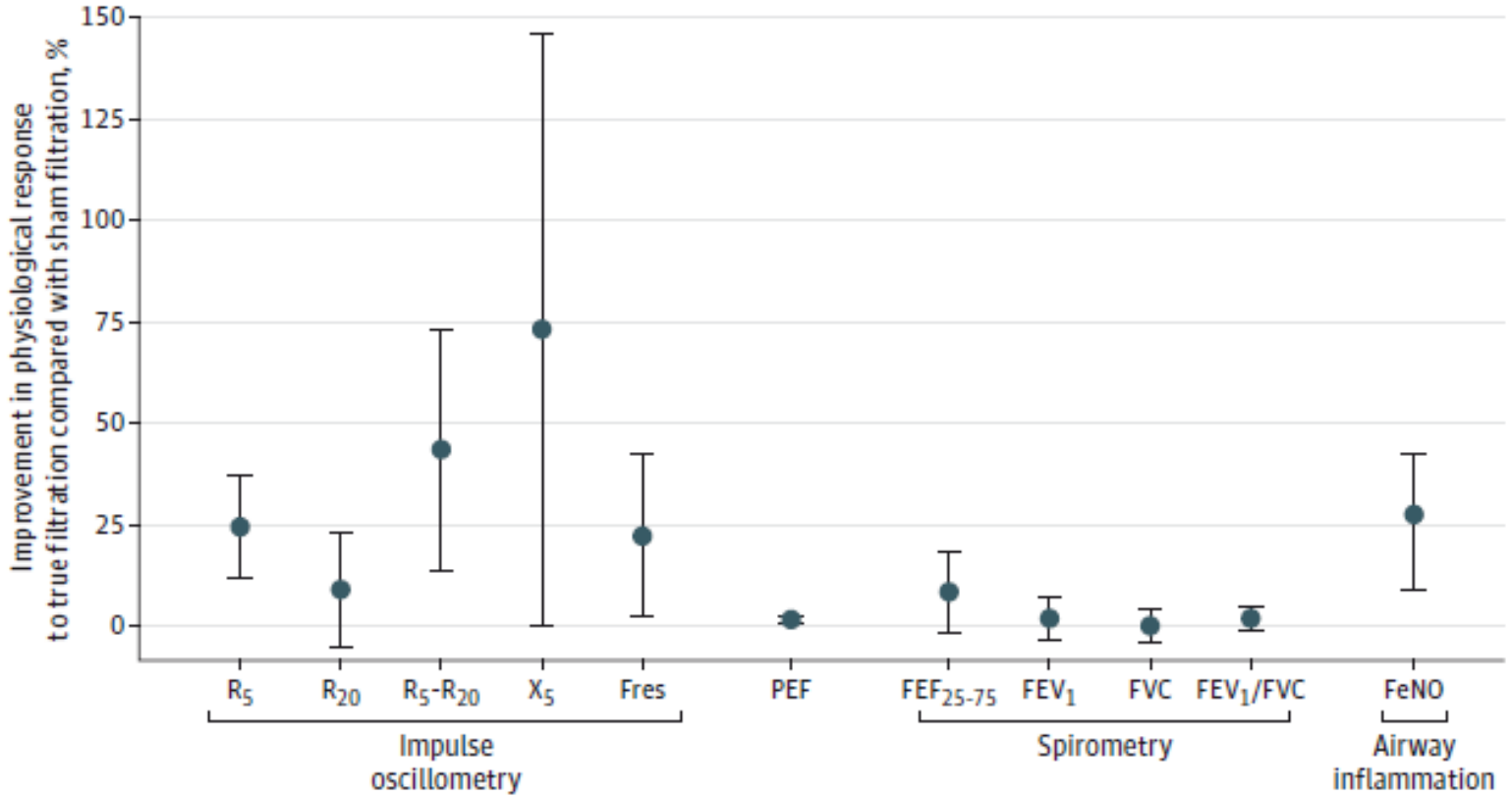




Concentrations graphed were 2-week mean values. Statistical significance in median concentrations was determined using a Wilcoxon signed rank test. $PM_{2.5}$ indicates particulate matter 2.5 µm in size.

Intervention Effectiveness

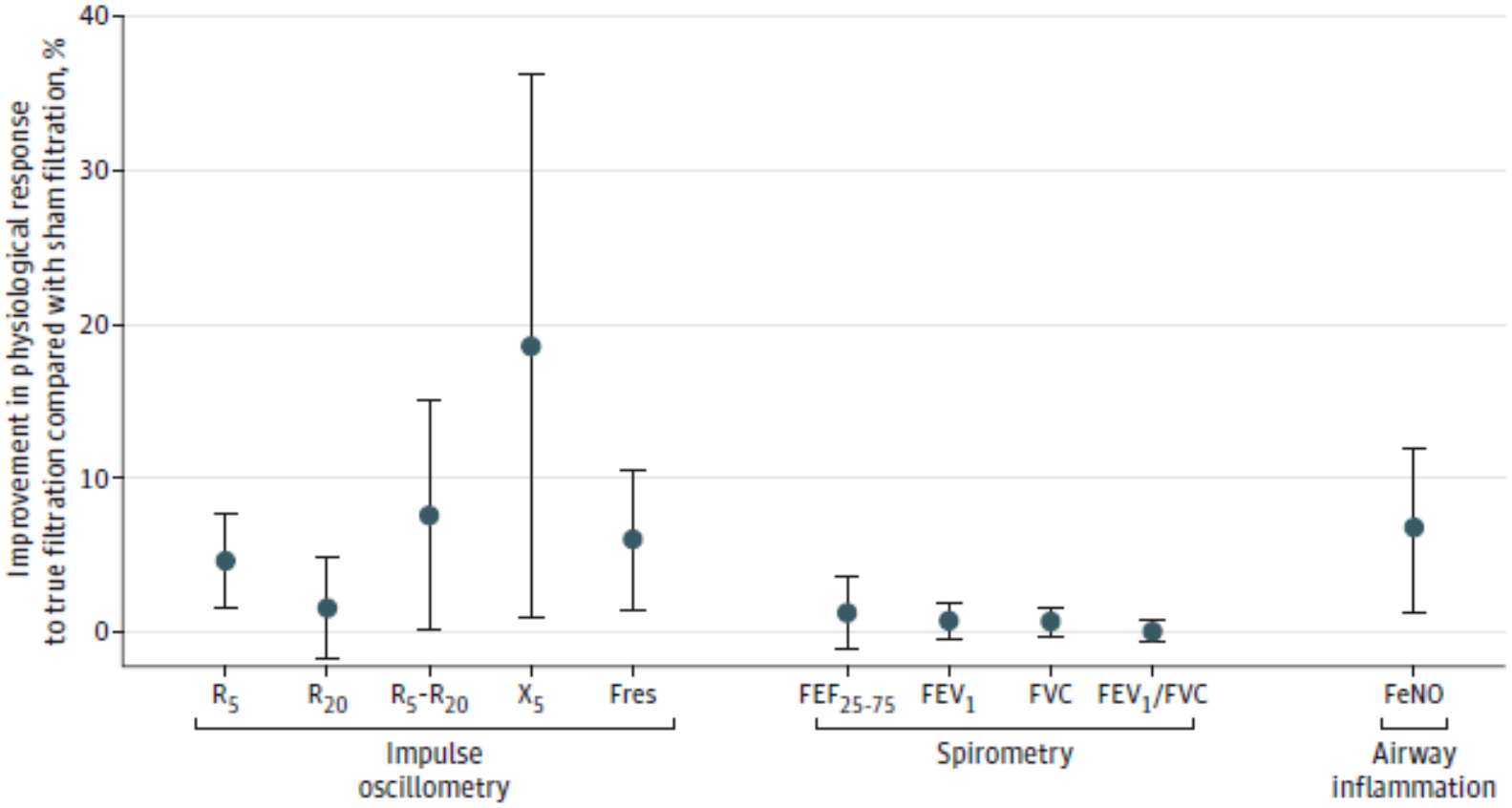
Figure 2. Outcomes of True Filtration Compared With Sham Filtration



For all outcomes except peak expiratory flow (PEF), the points and bars show mean and 95% CIs for outcome improvements when comparing filtration changes in outcome levels between true filtration and sham filtration. For PEF, the point and the bar show the mean and 95% CIs when comparing PEF values measured during the true filtration period with PEF values measured during the sham filtration period. For all outcomes, positive values indicate improvements and negative values indicate deterioration. For fractional exhaled nitric oxide (FeNO) data, the analysis was performed on log-transformed FeNO data and the result was converted back to untransformed data for presentation in this figure. FEF_{25-75} indicates forced expiratory flow during 25% to 75% of forced vital capacity; FEV_1, forced expiratory volume during the first second; Fres, resonant frequency; FVC, forced vital capacity; $PM_{2.5}$, particulate matter 2.5 µm in size; R_5, airway resistance measured at 5 Hz; R_{20}, airway resistance measured at 20 Hz; R_5-R_{20}, the difference between R_5 and R_{20}, reflecting small airway resistance; X_5, airway reactance measured at 5 Hz.

Dose-Response by Exposure Reduction

Figure 3. Outcomes of Bedroom Fine Particle ($PM_{2.5}$) Exposure Reduction



Points and bars show mean and 95% CIs for outcome improvements associated with a 10-μg/m^3 reduction in bedroom $PM_{2.5}$ concentration from outdoor levels. For all indicators, positive values indicate improvements and negative values indicate deterioration. For fractional exhaled nitric oxide (FeNO) data, the analysis was performed on log-transformed FeNO data, and the result was converted back to untransformed data for presentation in this figure. FEF_{25-75} indicates forced expiratory flow during 25% to 75% of forced vital capacity; FEV_1, forced expiratory volume during the first second; Fres, resonant frequency; FVC, forced vital capacity; PEF, peak expiratory flow; R_5, airway resistance measured at 5 Hz; R_{20}, airway resistance measured at 20 Hz; R_5-R_{20}, the difference between R_5 and R_{20}, reflecting small airway resistance; X_5, airway reactance measured at 5 Hz.

Research

JAMA Pediatrics | Original Investigation

Association Between Bedroom Particulate Matter Filtration and Changes in Airway Pathophysiology in Children With Asthma

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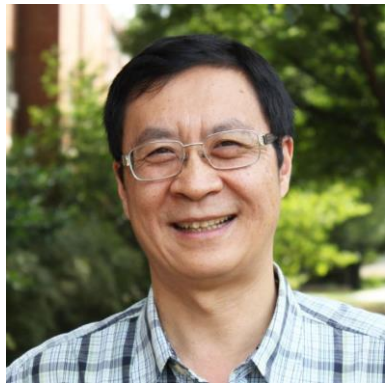
CONCLUSIONS AND RELEVANCE Per these results, indoor $PM_{2.5}$ filtration can be a practical method to improve air flow in an asthmatic lung through improved airway mechanics and function as well as reduced inflammation. This warrants a clinical trial to confirm.

The Study is funded in part by Underwriters Laboratories – UL1 Study

UL2 Study Team – Duke University



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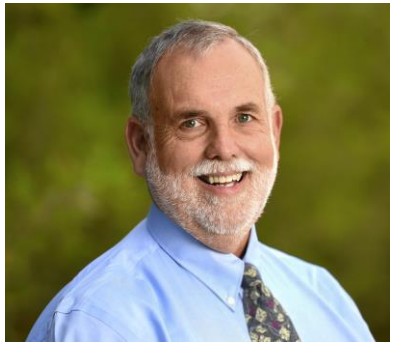
Emily Craig, PhD Student

Using Indoor Air Filtration to Reduce PM2.5 Cardiometabolic Effects in At-risk Individuals Funded by Underwriter's Laboratories (3/2022- 12/2025)

UL2 Study Team – University of Southern California



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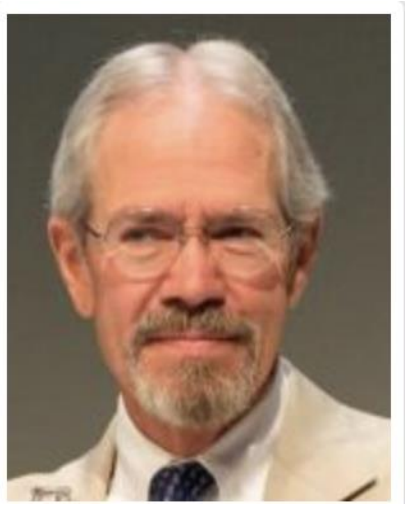
Using Indoor Air Filtration to Reduce PM2.5 Cardiometabolic Effects in At-risk Individuals Funded by Underwriter's Laboratories (3/2022- 12/2025)

UL2 Study Team – UL & Rutgers University



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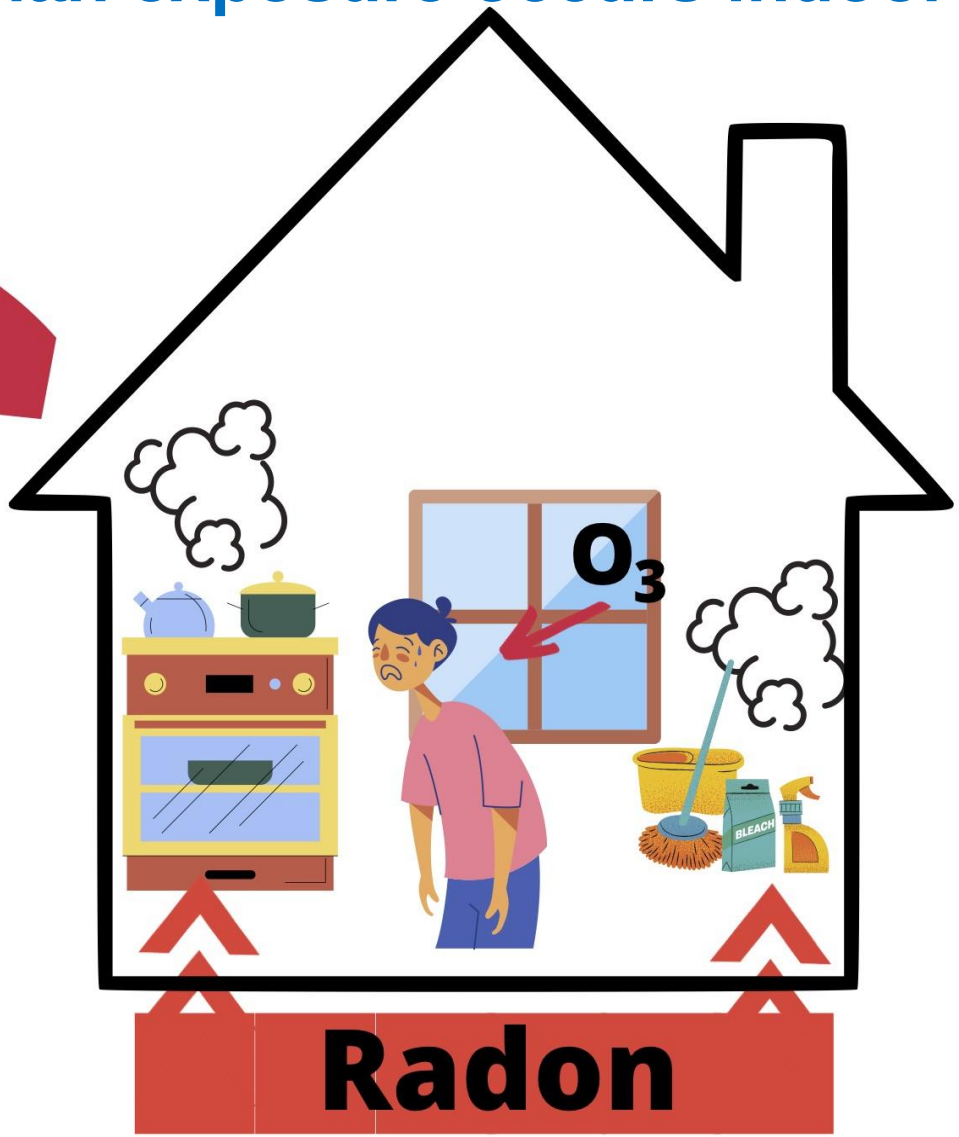
Using Indoor Air Filtration to Reduce PM2.5 Cardiometabolic Effects in At-risk Individuals Funded by Underwriter's Laboratories (3/2022- 12/2025)

$PM_{2.5}$ Effects from Short- and Long-term Exposures
(EPA Integrated Science Assessment, 2019)

	Health Category	Causality Determination
Short-term Exposure	Cardiovascular Effects	Causal
	Mortality	Causal
	Respiratory Effects	Causal
	Central Nervous System	Inadequate
Long-term Exposure	Cardiovascular Effects	Causal
	Mortality	Causal
	Respiratory Effects	Likely to be Causal
	Reproductive and Developmental	Suggestive
	Cancer	Suggestive

Even for outdoor-generated pollution (e.g., wildfires), most of human exposure occurs indoors!



Made by Emily Craig, with Canva

In the absence of indoor sources and absence of air purification:

Indoor/Outdoor ratios	Windows closed	Windows open
$PM_{2.5}$	~0.7	~1
O_3	~0.2	~0.7
NO_2	~0.8	~ 1

HEPA Air Purifiers

- **Previous studies:**
  1. using HEPA air purifiers can **reduce indoor PM2.5 levels by 40% to >90%**
  2. using HEPA air purifiers for a short period (3 days to 2-month) can **improve acute cardiovascular and respiratory health outcomes**.

- **Current gaps:** no published studies have evaluated the potential benefits of a longer-term indoor HEPA filtration intervention in improving cardio-metabolic profiles in at-risk adults.

- **UL2 study trial:**
  1. Longer-duration residential HEPA intervention trial, providing an opportunity to observe more chronic changes in health outcomes
  2. During the trial, wildfire exposure will be captured

UL2 Study Aims

- **Aim 1: Assess the effect of a 6-month residential HEPA** intervention on changes of type 2 diabetes-related metabolic outcomes (*fasting glucose, HbA1C, HOMA-IR, lipids and blood pressure*) in 52 adults. (**Intervention Effectiveness**)
- **Aim 2: Examine the association between reduction in indoor $PM_{2.5}$** exposure brought by the intervention **and changes in metabolic outcomes** adjusting for ambient $PM_{2.5}$ exposure. (**Dose-Response**)
- **Aim 3: Explore pathophysiologic biomarker changes** pertinent to the cardio-metabolic profile of type 2 diabetes in response to the intervention and changes in $PM_{2.5}$ exposure. (**Molecular Mechanisms**)
- **Aim 4: Explore the impact of wildfires on HEPA intervention effectiveness and the impact of HEPA intervention on wildfire-PM exposure.** (**Wildfire Impact)**

Portable Air Purifiers –
Google it to see numerous on the market

olekule Mini Air Purifier with eco Purification Technology, hite
1 ★★★★☆ 11
one Free · Energy: A+++
60.00
ay
5.00 delivery

Pure Enrichment True HEPA Portable Air Purifier - White
4.8 ★★★★★ 203
HEPA Filter
$44.99
Best Buy
Free delivery by Sep 6 & Free 15-day ...
4.6/5 ★ (694 store reviews)

AROEVE Air Purifiers for Home, H13 HEPA Air Purifiers Air Cleaner for Smoke ...
HEPA Filter · White
$59.99
Amazon.com - Seller
Free delivery

Levoit Air Purifier for Home, H13 True HEPA Filter for Allergies an Pets
4.7 ★★★★½ 12
HEPA Filter · Ozone Free
$89.99
Levoit
Free delivery by Mon, Sep 5

Dyson Pure Cool TP01 purifying fan White/Silver)
$299.99 $399.99
Dyson US
★★★★☆ (524)
Free shipping

MA-40 Air Purifier for Homes and Offices White /...
$496.99
Medify Air
★★★★½ (481)
Free shipping

TRACS TM250 HEPA-Certified Portable UV-C Air...
$779.00
tracspurifiers.com
Free shipping

Oransi mod HEPA Air Purifier Gray, White
$599.00
Oransi
★★★★½ (317)
Free shipping

Dyson Purifier Cool Formaldehyde TP09 (White/Gold)
$519.99 $669.99
Dyson US
★★★★☆ (62)
Free shipping

UP3000 UltraPure Air Cleaner - Allergy Buye…
$599.00

BISSELL MyAir Personal Air Purifier For…
$77.69 $93

EdenPURE OxiLeaf II Thunderstorm | Air Purifier …
$129.00

Austin Air Healthmate Air Purifier, 1500 sq ft, HM40…
$714.99

UV Air Sanitizer Portable Air Filter UV Air…
$158.20

Wynd - Smart Portable Air Purifier + Air Quality Sen…
$199.00

Westinghouse Portable Medical Grade Patented Air Purifier, Light Beige
4.9 ★★★★★ 16
HEPA Filter · Ionic
$129.99

Pure Enrichment PureZone Halo True HEPA Air Purifier
4.8 ★★★★★ 238
HEPA Filter · White
$99.99

Air Health Skye 5-Stage Quiet, Smart, Large Room Portable Air Purifier | w/ H13 ...
HEPA Filter
$463.99

Bissell MYair Personal Air Purifier Purple | 2780P
4.7 ★★★★½ 519
$92.69

Air Purifier Selection

Honeywell HPA100
$120, CADR=100 ft^3/min,
14.0 x 8.9 x 13.5 inches

Low Noise
Bedroom use

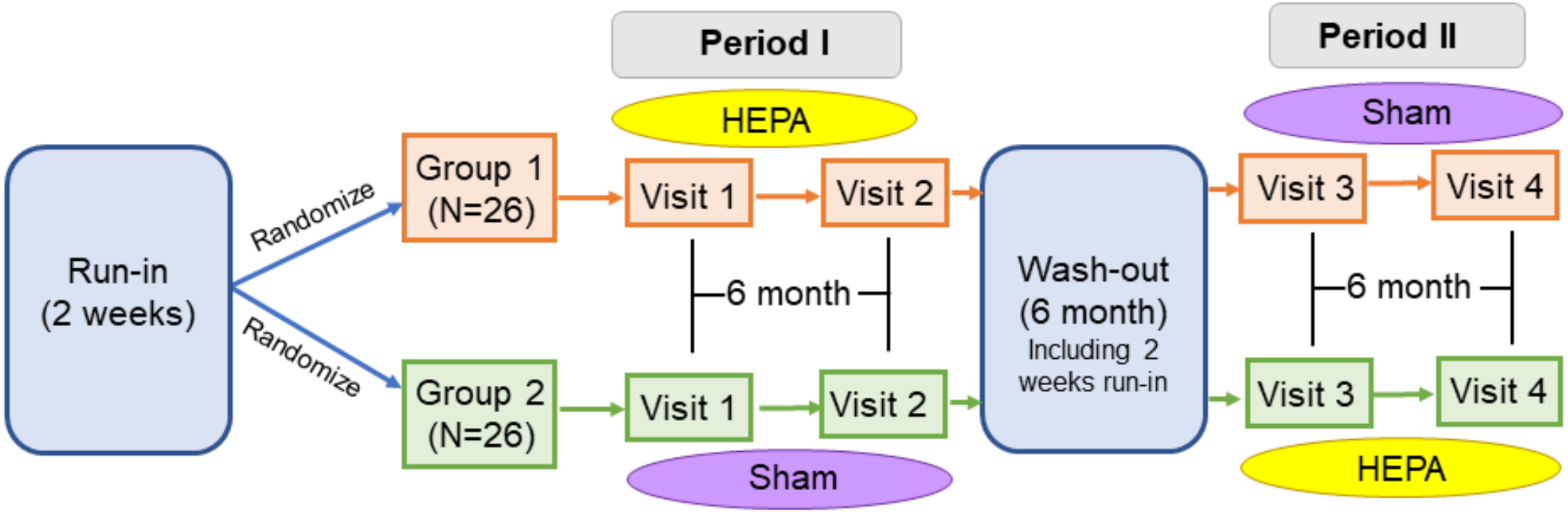
TOPPIN C2
$75, CADR=100 ft^3/min,
7.6 x 7.6 x 14.8 inches

Moderate Noise
Livingroom use

In preliminary test in LA homes , either purifier can decrease indoor $PM_{2.5}$ concentrations by 40%-85%

UL2 Study Design

- Cross-over study
- Prioritize census tract-level with historical PM2.5 exposure ≥ 12 µg/m3

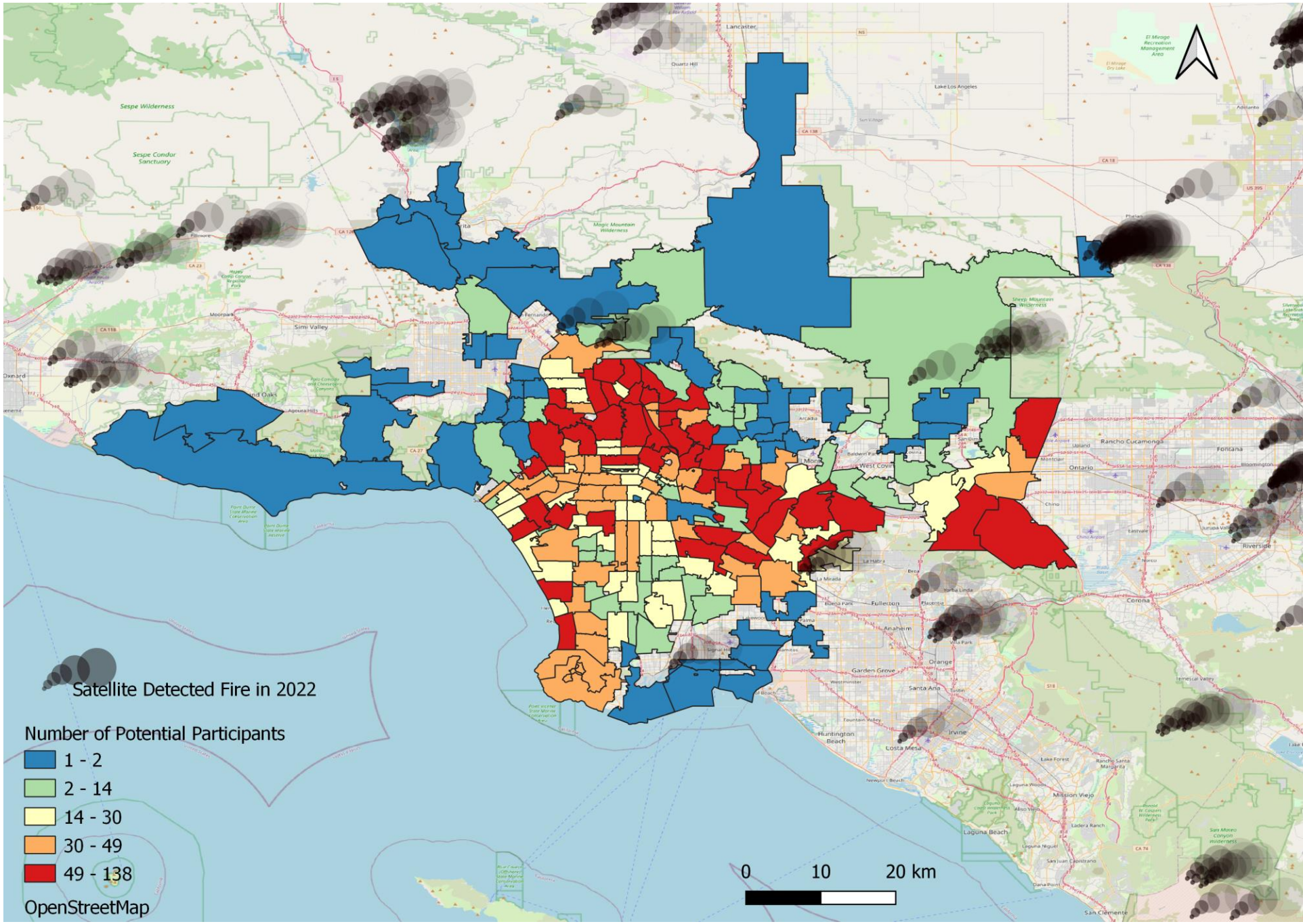


UL2 study design flowchart

Subject pool: EMR of USC hospitals, n=6285

Residential locations and proximity to wildfires in 2022

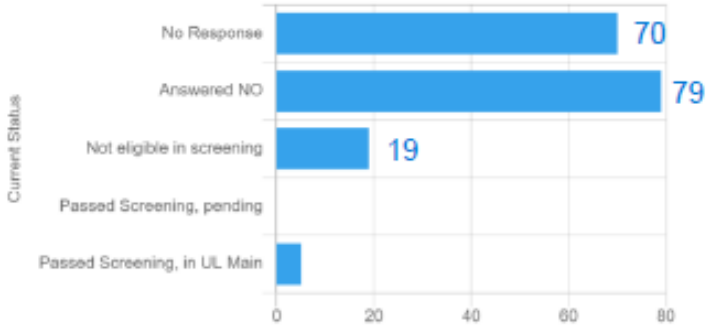
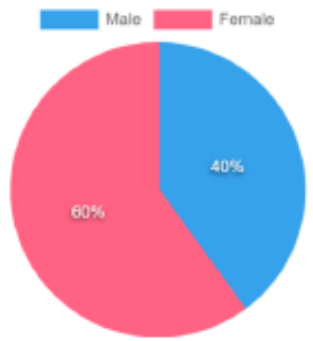
https://firms.modaps.eosdis.nasa.gov/



As of March 14, 2023

ClinicalTrials.gov Identifier: NCT05718245

CONSORT chart

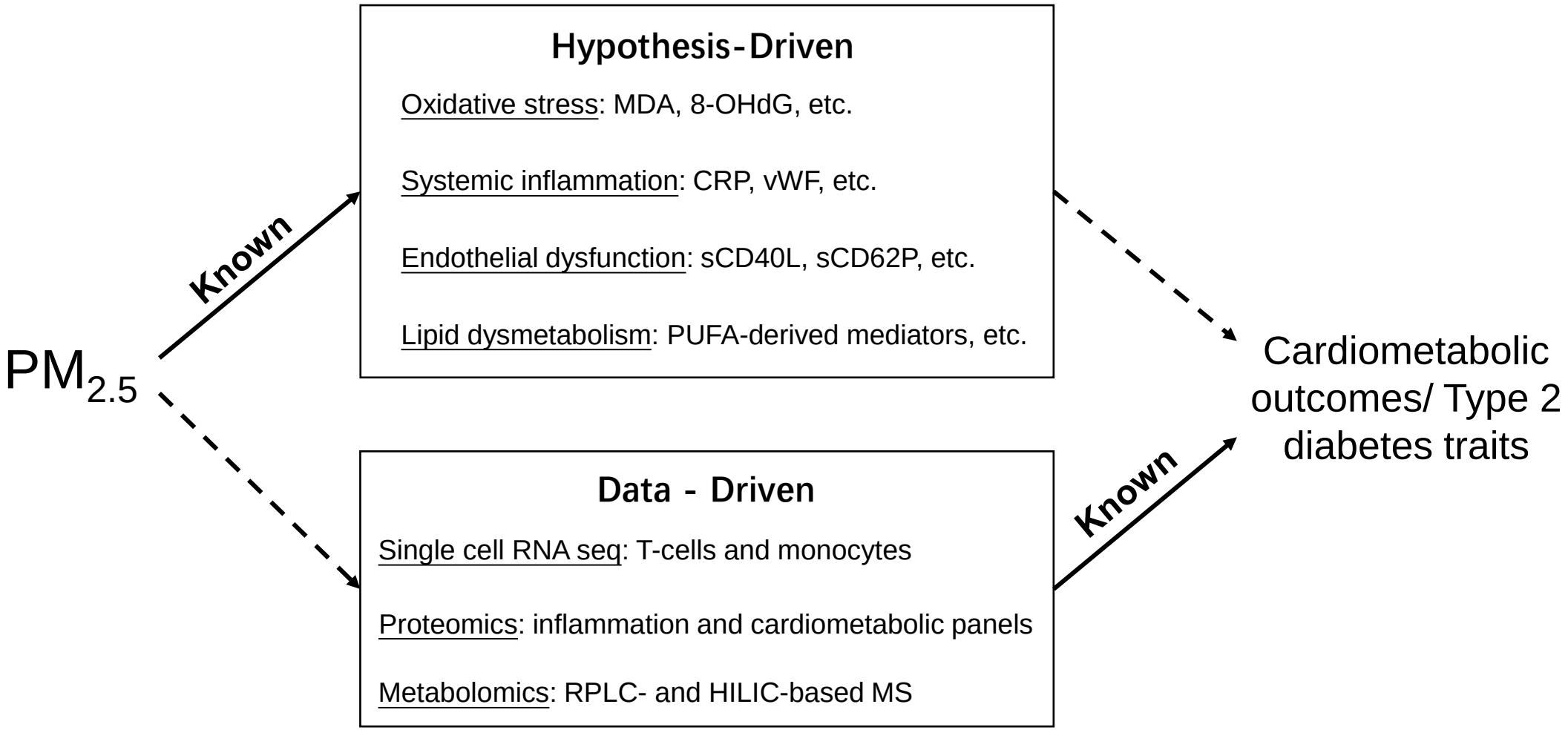
Number of participants invited:	**200**
Number of participants responded email:	4
Number of participants responded SMS:	5
Total number of participants responded (either by email or SMS):	**9**
Number of participants phone screened:	**200**
Phone screened status:	
Passed screening, eligible for pre-home screening and willing to participate (Number of participants moved to UL Main)	**5**
Passed screening participants by gender (female/male)	

Health Outcomes

- **Home visits every 6 months**
  1. Cardiometabolic outcomes/Type 2 diabetes traits
     - BMI, continuous glucose (CGM) and BP monitoring - home
     - Glucose, lipids, insulin resistance, HbA1C - lab
  2. Molecular mechanisms along pathophysiologic pathways
     - Oxidative stress, inflammation, lipid mediation – targeted markers
     - Single-cell RNA Seq, proteomics, metabolomics - untargeted

- **Covariates to be considered:**
  1. Health related lifestyles – questionnaire data
  2. Exposure related lifestyles – questionnaire data
  3. Dietary recall data

Molecular Mechanisms and Novel Biomarker Exploration



Exposure Assessment

- **Air quality monitoring:**
  - Paired indoor and outdoor low-cost pollutant monitors
  - Data real-time transmitted to the project computer;
  - Daily basis monitoring to check for potential abnormal data output and make timely correction actions.
- **Biomonitoring of source-specific air pollutants:**
  - Amino-PAHs and PAH-tetrol in blood
  - Hydroxy-, amino-, and carboxy-PAHs in the urine

Low-Cost Sensor Protocols

- **Air Quality Sensors (*TSI*)**
  - **Outdoor:** BlueSky (PM2.5 & PM10)
  - **Indoor:** 6-gases AirAssure (PM2.5 , PM10, CO, CO2, SO2, O3, NO2, tVOCs)

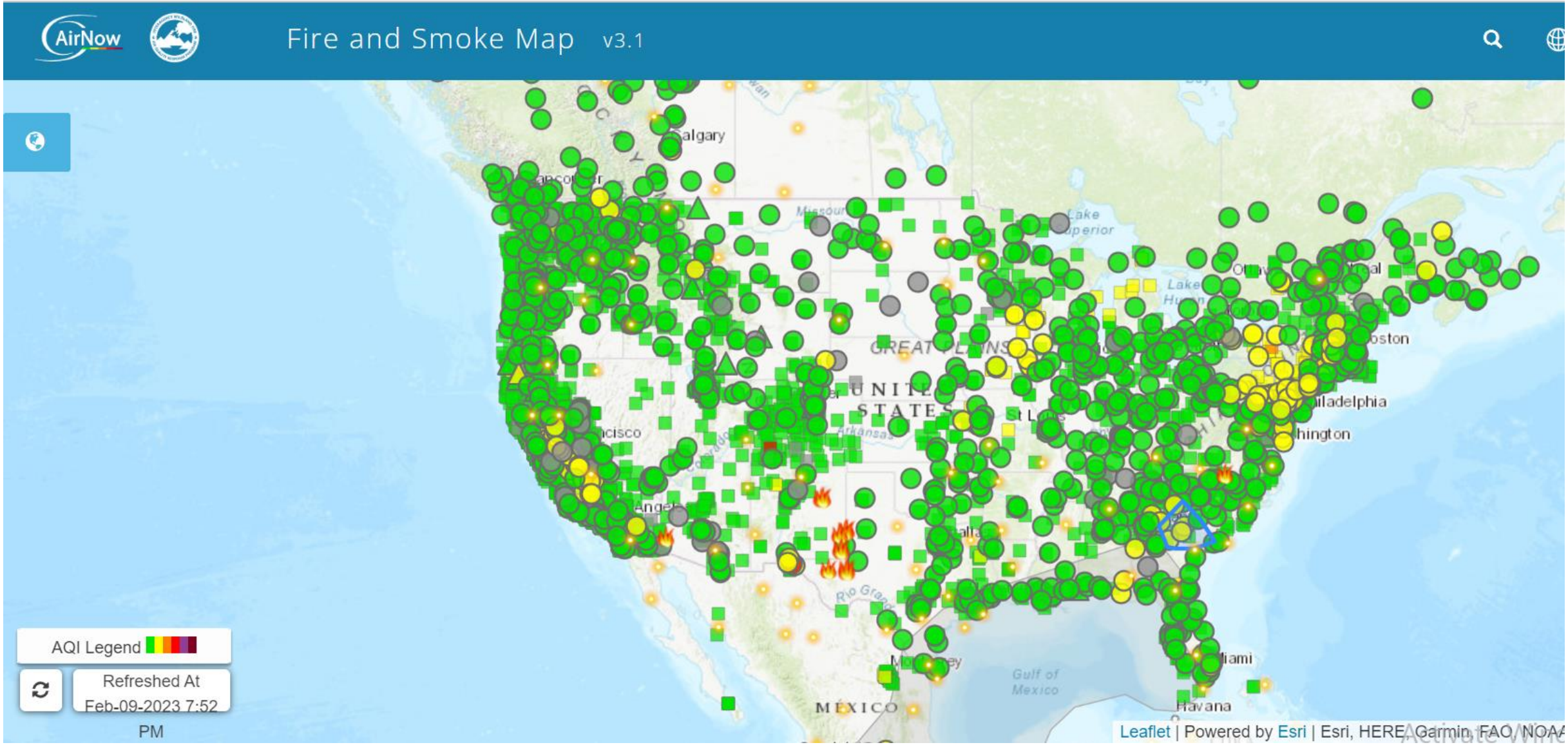
- **3-Step Calibration Process**
  1. Calibration for external sensors
  2. Calibration for internal sensors
  3. Calibration with AQMD reference monitors

Photo Credit: UL2 Research Team

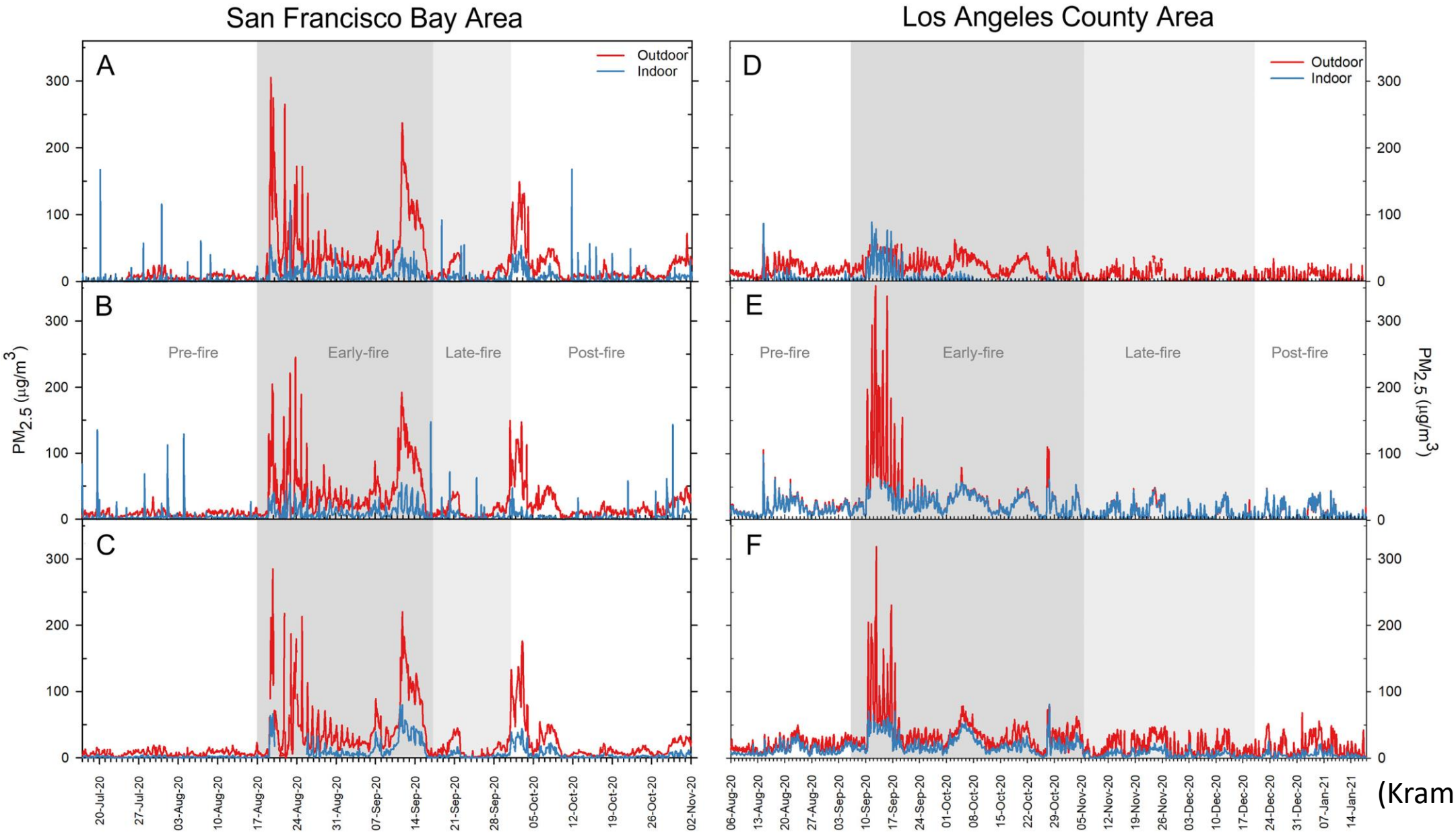
Photo Credit: TSI

Wildfire events detection:

https://fire.airnow.gov/#.

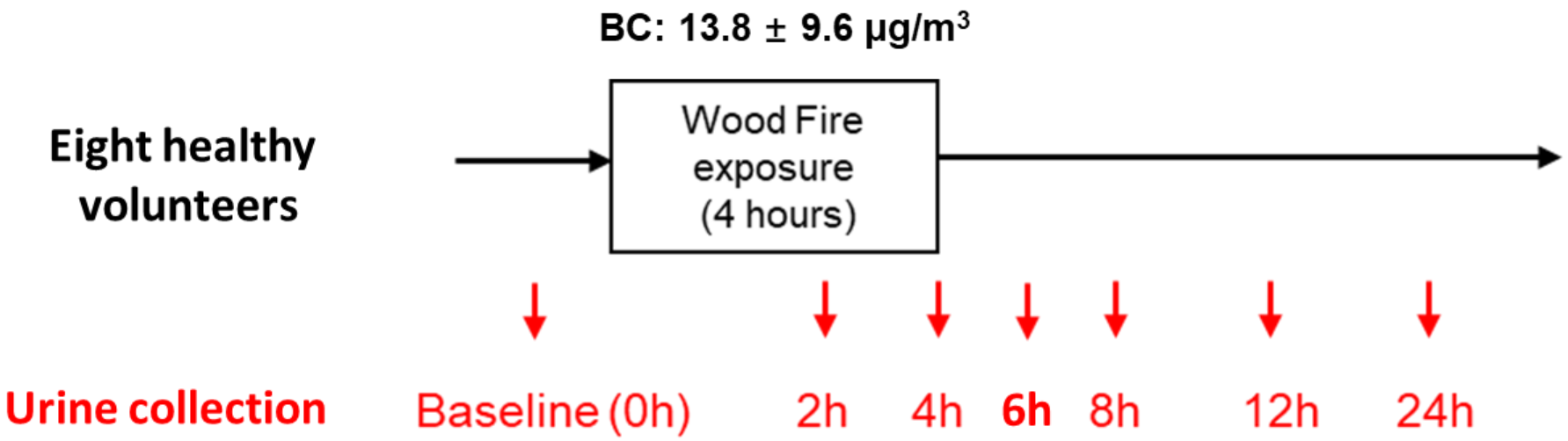


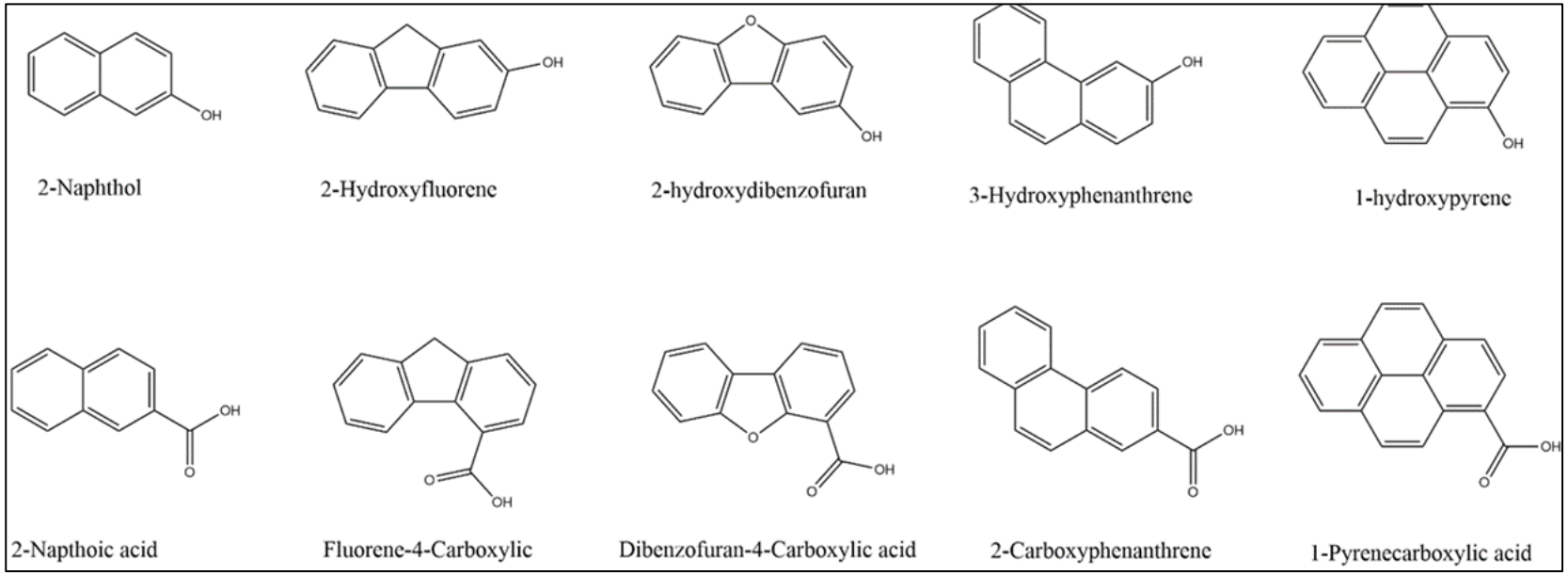
Wildfire Exposure Assessment: Low-cost PM2.5 sensors



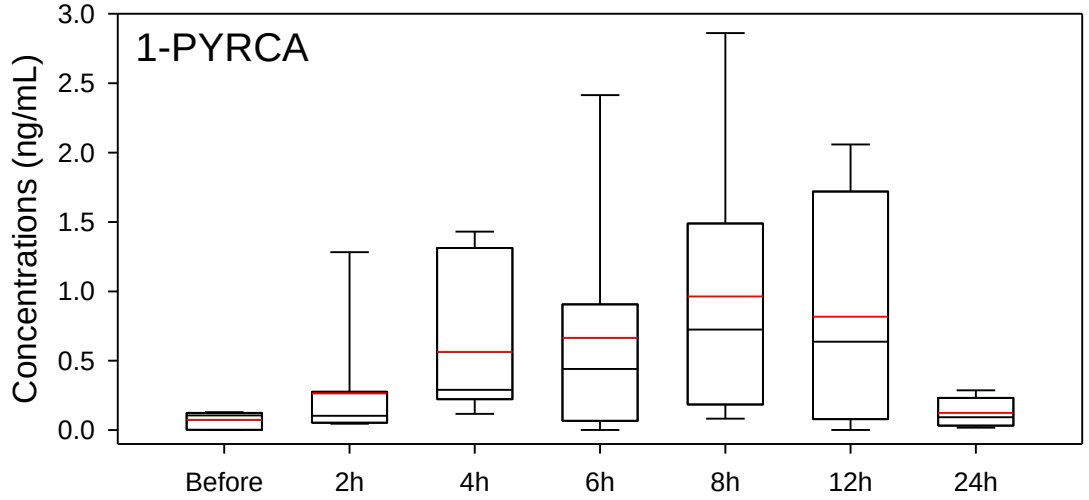
(Kramer et al, 2023)

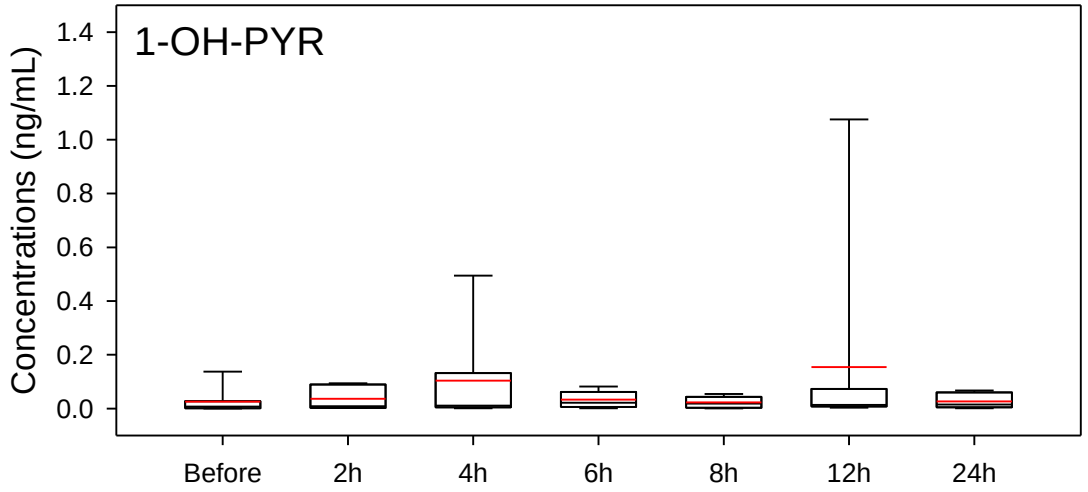
Identifying Exposure Biomarkers of Wildfire

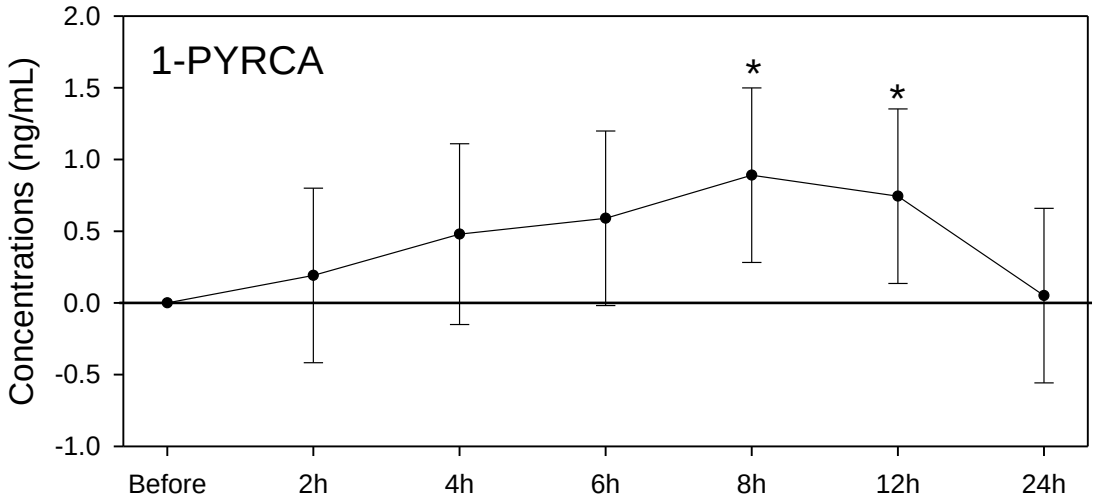


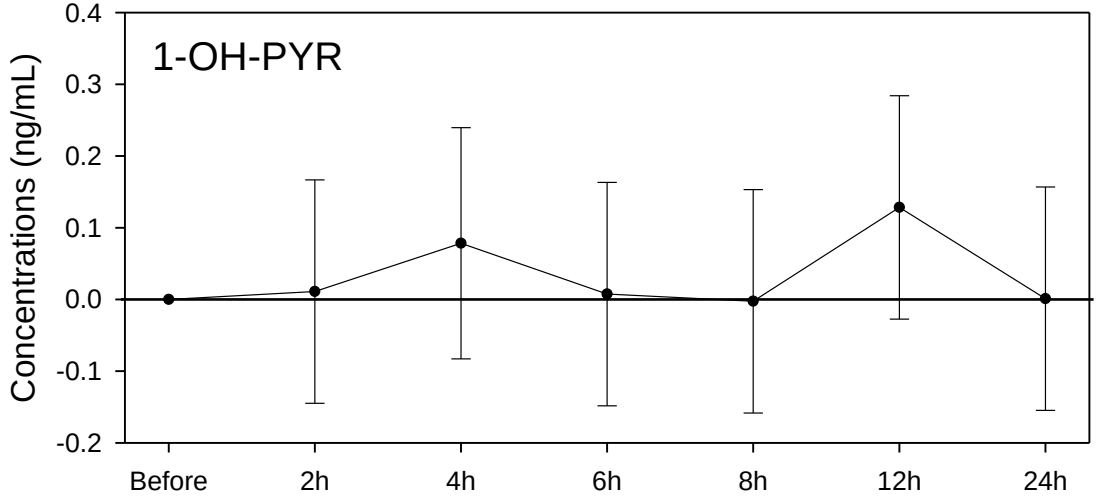


Urinary 1-Pyrene carboxylic acid (PYRCA) is responsive to campfire





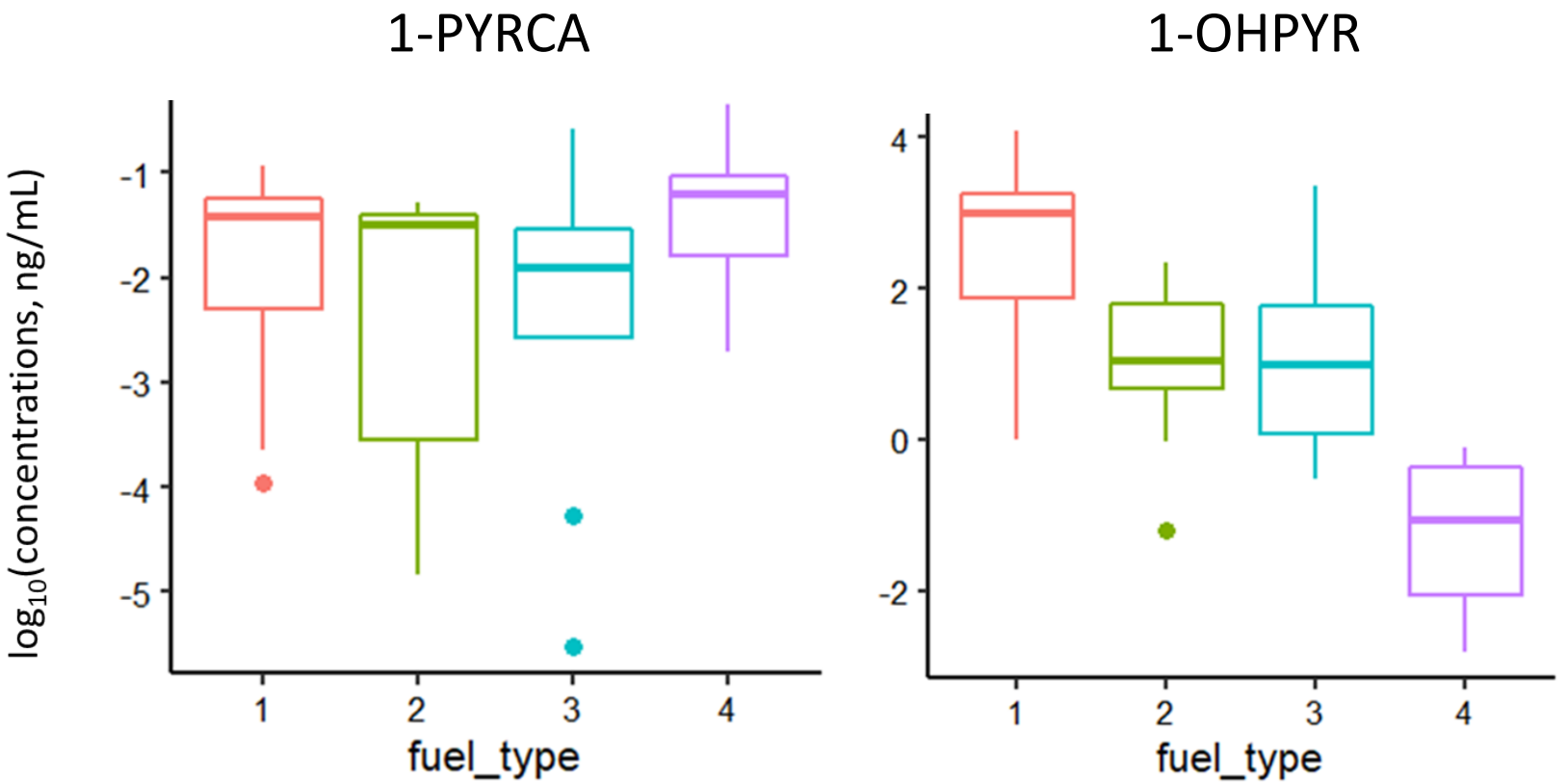




Urinary 1-PYRCA were not detected among people exposed to traffic sources

- Urinary 1-OH-PYR was associated with traffic sources (and outdoor NO_2 at residence) among 306 Rochester pregnant women.
- 1-PYRCA was detected in none of the samples, suggesting non-significant contribution of traffic exposure to this wood-smoke exposure biomarker.

Urinary 1-PYRCA is not responsive to coal combustion



Fuel:

1=Laibin smoky coal without chimney;

2=Laibin smoky coal with chimney;

3=Smokeless coal;

4=Electricity

Data Analysis Plan

- Aim specific analyses (Aims 1-3)
- Wildfire impact analysis (Aim 4):
  1. If a wildfire event occur during the intervention, we will attempt to add daily health assessment and biospecimen collections during the event. This will allow us to assess the impact of HEPA intervention on acute health responses to wildfire exposure.

  2. We will examine the associations of health outcomes with indicators of wildfire exposure (e.g., proximity to wildfire, PM2.5 exposure attributable to wildfire, exposure biomarker). We will further examine whether HEPA intervention modifies the associations.

  3. We will assess the impact of wildfire exposure on the overall effectiveness of HEPA intervention.

Thank You!