Air Pollution, Polycyclic Aromatic Hydrocarbons and Early Cardiovascular Effects

A Natural Experiment in Travelers from Los Angeles to Beijing

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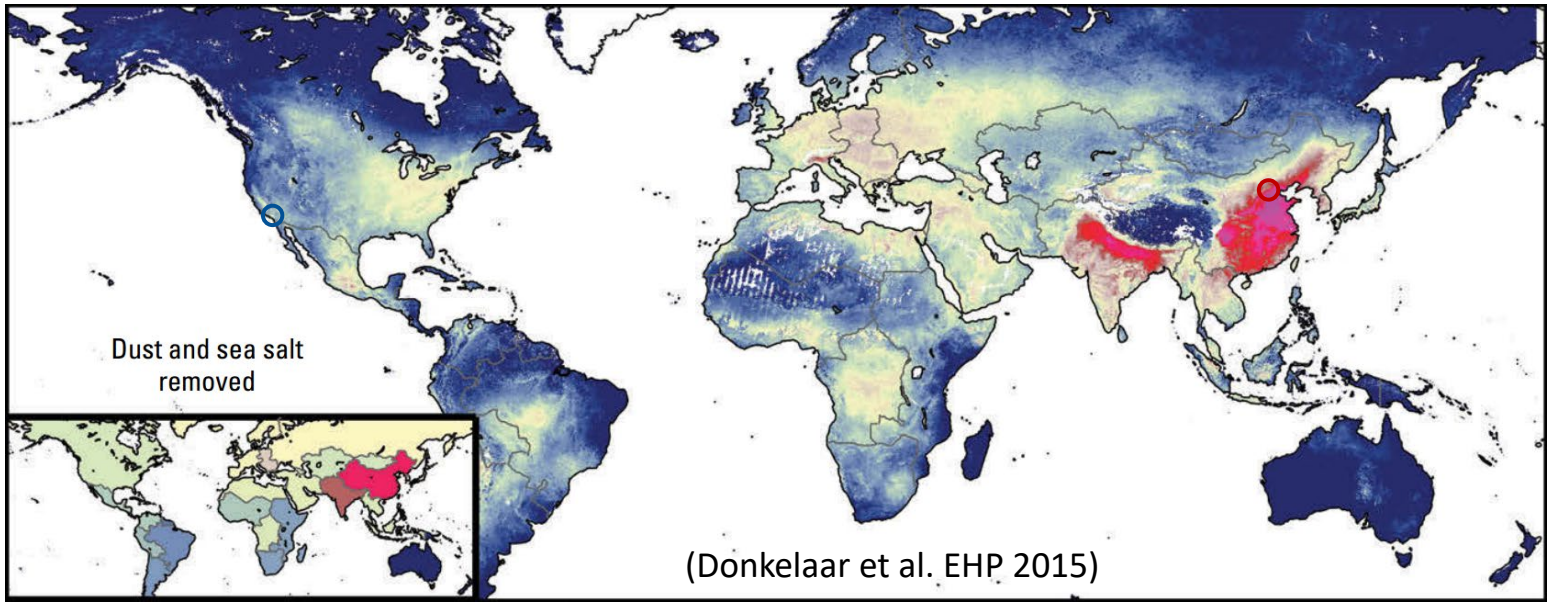
Air Pollution is a Global Problem



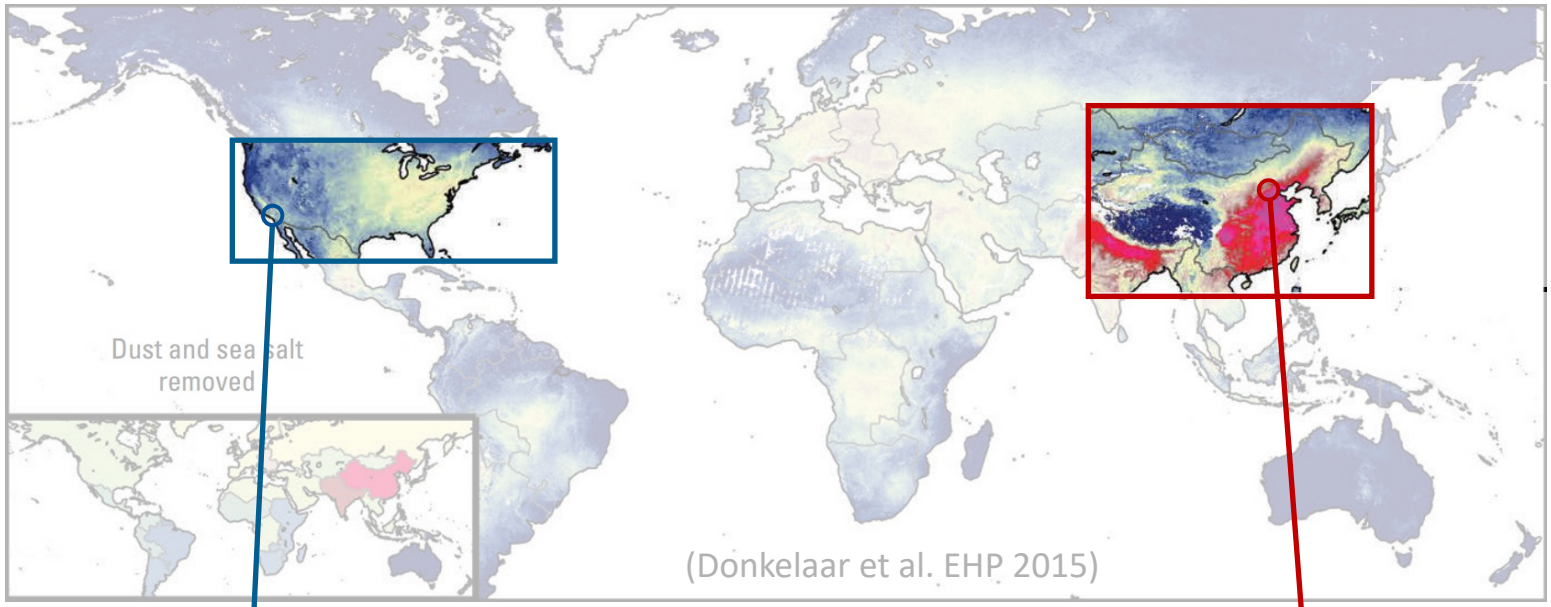
(Donkelaar et al. EHP 2015)

- 87% of the global population breathed unhealthy air in 2013;
- Ambient PM pollution caused up to 8.9 million death in 2015;
- Large spatial variability in $PM_{2.5}$ exposure:

  10.7 μg/m^3 in USA vs. 54.3 μg/m^3 in China

（Brauer et al. EST 2016; Burnett et al, PNAS 2018）

Air Pollution and Cross-boundary Travels



UCLA (Los Angeles)
$PM_{2.5}$ levels：5~30μg/m^3

Biospecimen Collection（LA-before）

Biospecimen Collection（Beijing）

Biospecimen Collection（LA-after）

Peking University (Beijing)
$PM_{2.5}$ levels：10~250μg/m^3

Summer Student Exchange

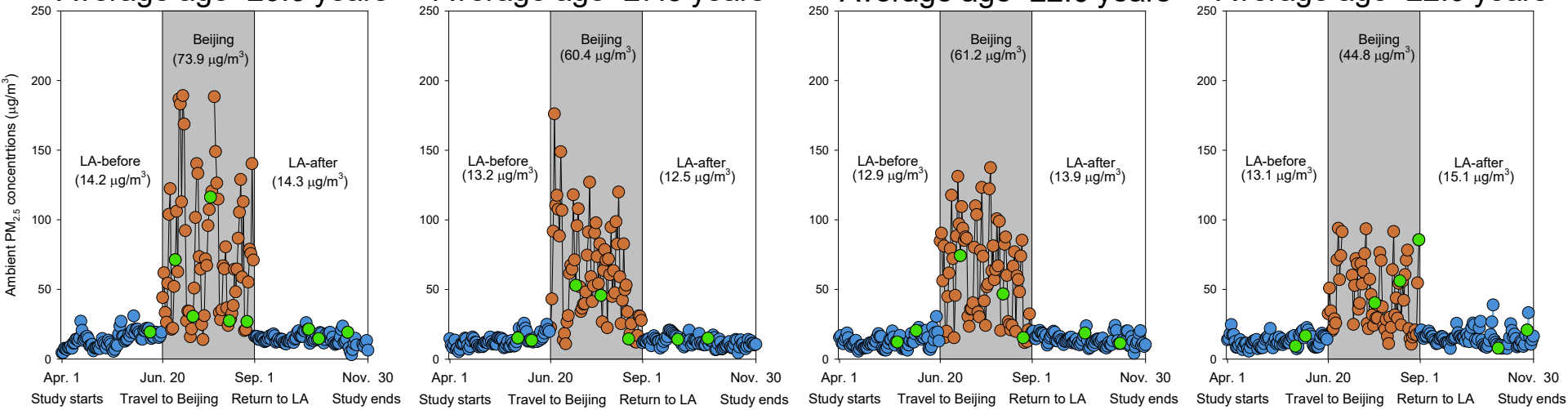
Air Pollution and Exchanged Students

Panel 2014
14 students
5 men and 9 women
Average age=23.3 years

Panel 2015
13 students
3 men and 10 women
Average age=27.8 years

Panel 2016
8 students
3 men and 5 women
Average age=22.6 years

Panel 2017
10 students
8 men and 2 women
Average age=22.0 years



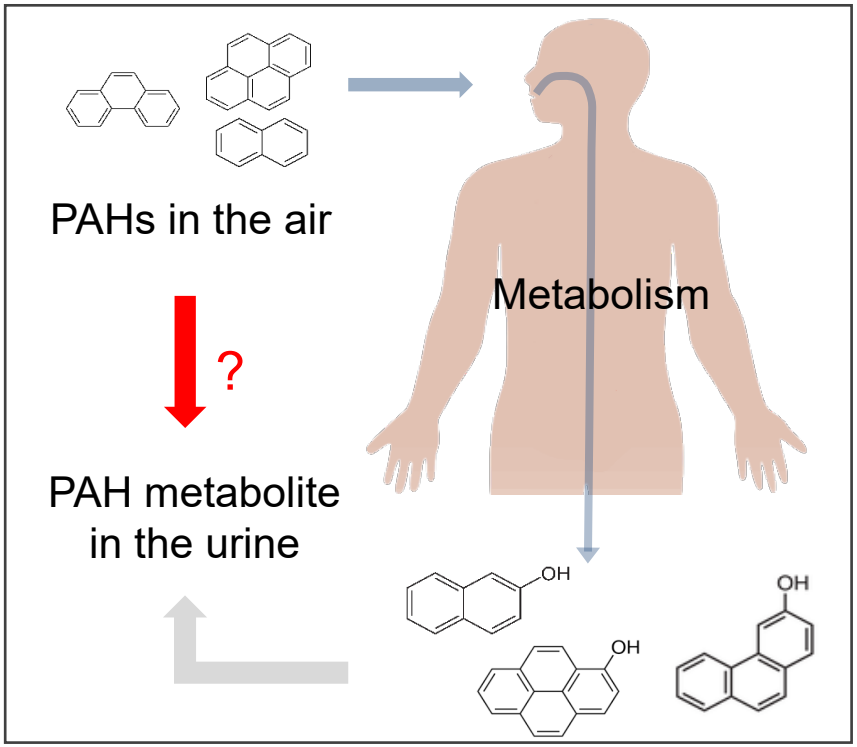
Ambient $PM_{2.5}$ levels in Los Angeles Ambient $PM_{2.5}$ levels in Beijing Urine Collection

（Data source: national air quality monitors within 30 km of the UCLA (n=4) and Peking University (n=18）

Air Pollution and PAHs

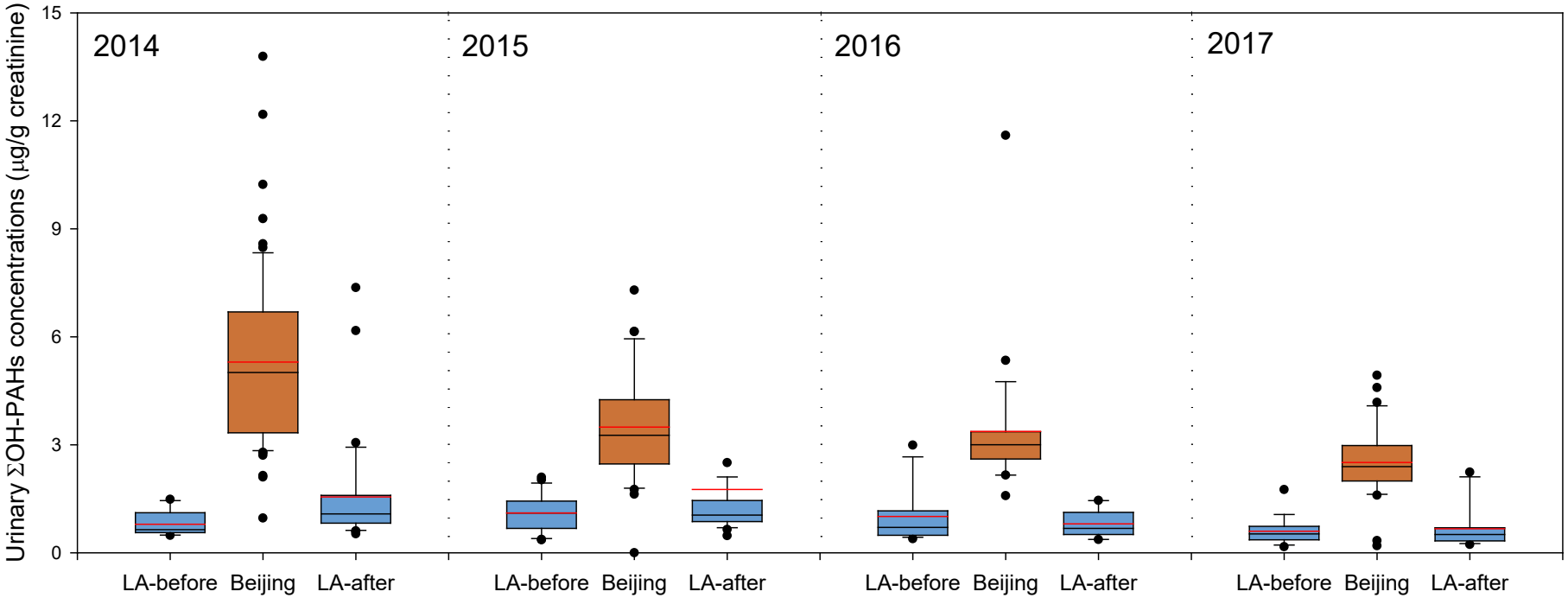
Polycyclic Aromatic Hydrocarbons (PAHs)

- ✓ **Source**: combustion (e.g. vehicle emission)
- ✓ **Exposure routes**: inhalation and ingestion
- ✓ **Health effects:**
  Group 1 carcinogen by the International Agency for Research on Cancer (IARC)



Question: Does traveling to a city with severe air pollution cause increased levels of polycyclic aromatic hydrocarbons (PAHs) metabolites in the urine?

Urinary PAH Metabolites



Levels of urinary PAH metabolites were

- Higher in Beijing
- Decreased from 2014 to 2017 in Beijing
- Associated with ambient NO_2 and $PM_{2.5}$ levels

Air Pollution and Cardiovascular Diseases

Air pollution causes

Systemic Oxidation & Inflammation → Atherosclerosis → Cardiovascular Diseases

Can occur in healthy people after hours' or days' exposures.

Occurs after years' exposures.

Occur in susceptible people after years' exposures.

(Møller et al, EHP 2010; Kuenzli et al, EHP 2005; Miller et al, NEJM 2007)

Systemic Oxidation and Inflammation

Pro-oxidative/inflammatory

Anti-oxidative/inflammatory

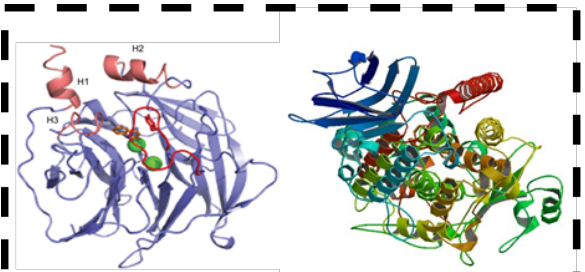
Lipoxygenase (LOX)

- Directly catalyzes the lipid peroxidation unsaturated fatty acid;
- Leads to the synthesis of pro-inflammatory leukotrienes.

Paraoxonase 1 (PON1)

- Exhibits both anti-oxidative and anti-inflammatory activities;
- Serves as the major functional enzyme bond to HDL particle.

Effects of Air Pollution on LOX and PON1?



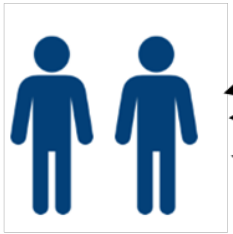
Initiation of Atherosclerosis

Animals

PON1 ↓

LOX ↑

2-10 weeks' air pollution exposures



$PM_{2.5}$

PM_{10}

O_3

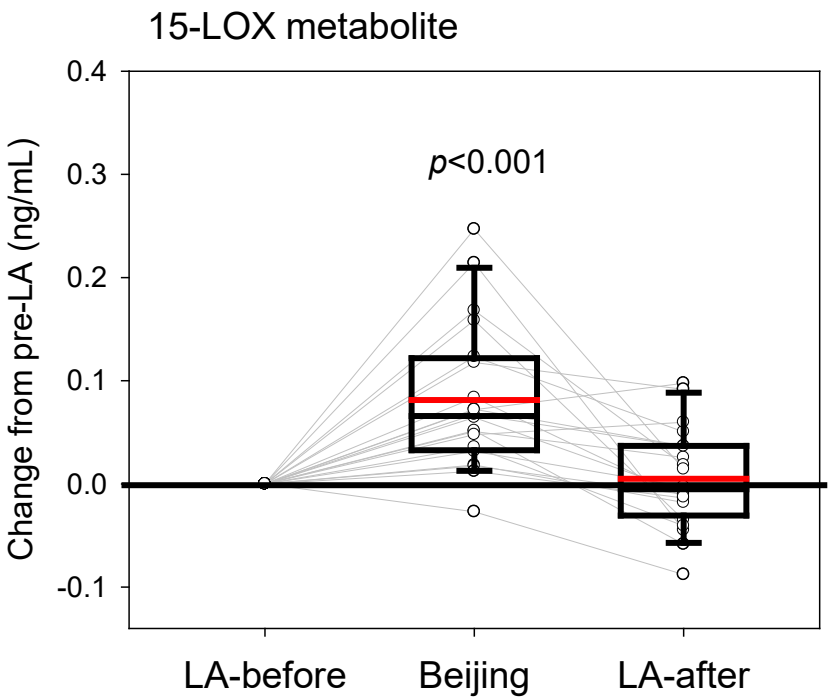
Controlled exposure experiments
No changes in PON1 or LOX

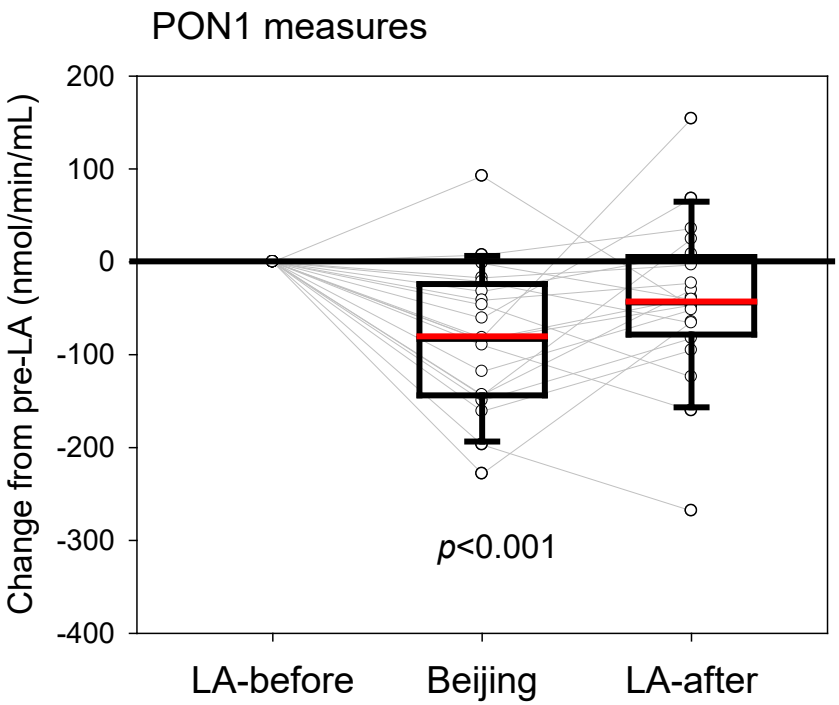
2 hours' exposure

Longer exposure required?

（Spanbroek et al, PNAS 2003; Shih et al, Nature 1998; Fen et al, ATVB, 2011; Ramanathan et al, PFT 2016）

LOX and PON1 Measures in Beijing





- Blood was collected from 26 healthy students in 2014 and 2015 for biomarker measurements;
- In Beijing, blood was collected 6 - 8 weeks after the arrival.
- In LA-after, blood was collected 4 - 7 weeks after the return.

（Lin et al, Circulation 2019）

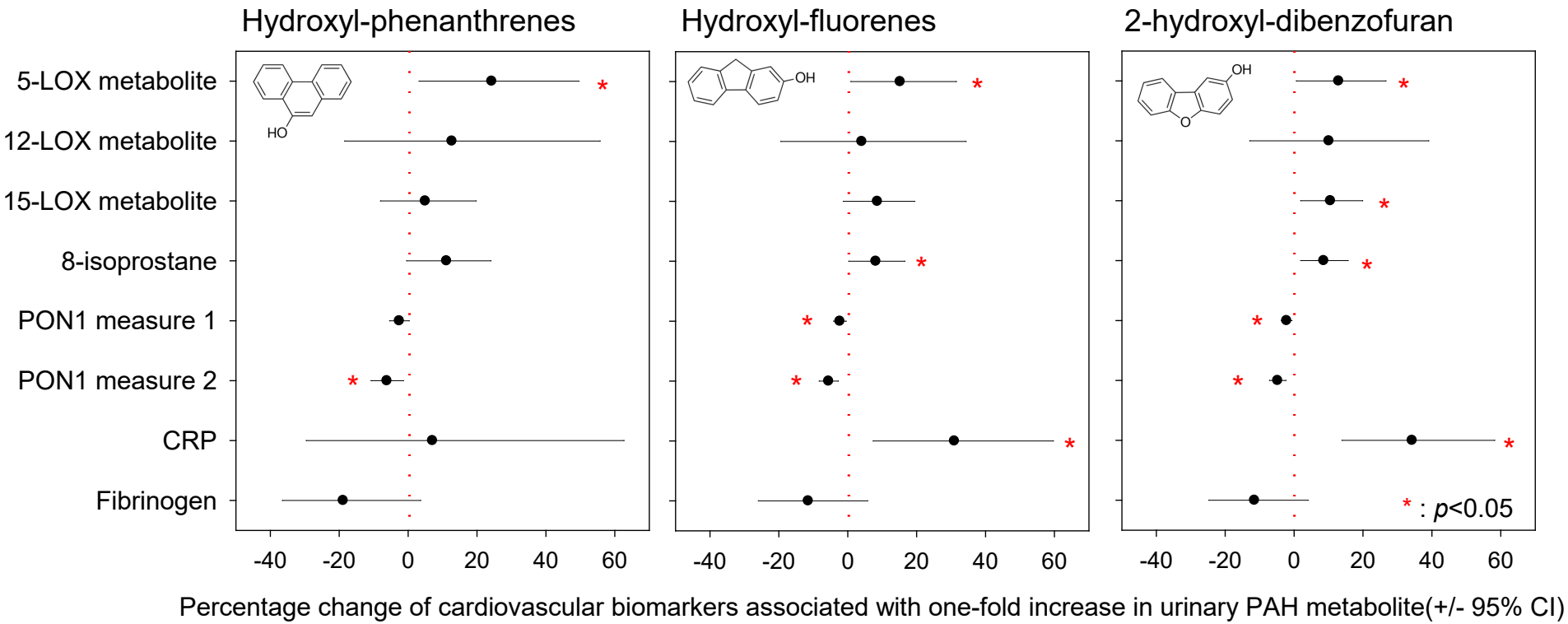
Systemic Oxidation and Inflammation in Beijing

Table. Changes of traditional cardiovascular biomarker before, during, and after the travel from Los Angeles to Beijing

Biomarker	Biomarker concentrations, geometric mean (IQR)		
	LA-before	Beijing	LA-before
Systemic oxidation, pg/mL			
8-isoprostane	2.88 (1.37 -5.10)	3.46 (1.67 - 7.38)	2.85 (1.85 - 3.46)
Systemic inflammation, μg/mL			
C-reactive protein	0.69 (0.24 - 1.15)	1.37 (0.70 - 4.07)	0.67 (0.30 - 1.24)
Fibrinogen	0.43 (0.27 - 0.48)	0.64 (0.55 - 0.81)	0.40 (0.26 - 0.47)
von Willebrand factor	5.79 (4.44 - 11.9)	9.12 (6.77 - 13.6)	7.08 (4.73 - 10.6)
Cholesterol, mg/dL			
Total	84.9 (69.6 - 103)	80.5 (65.6 - 94.0)	90.5 (71.8 - 108)
HDL	32.1 (29.0 - 39.2)	31.7 (26.2 - 40.3)	33.0 (28.4 - 39.1)

（Lin et al, Circulation 2019）

Associations with Urinary PAH Biomarkers



Changes in cardiovascular biomarkers were associated with PAHs exposure.

（Lin et al, Circulation 2019）

Summary

- Traveling from less-polluted Los Angeles to more-polluted Beijing increases exposure to PAHs.
- Traveling from Los Angeles to Beijing induced systemic oxidation and inflammation, suggesting increased risk of cardiovascular diseases.
- Changes in PAH exposures and health biomarkers reversed after returning to Los Angeles.

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