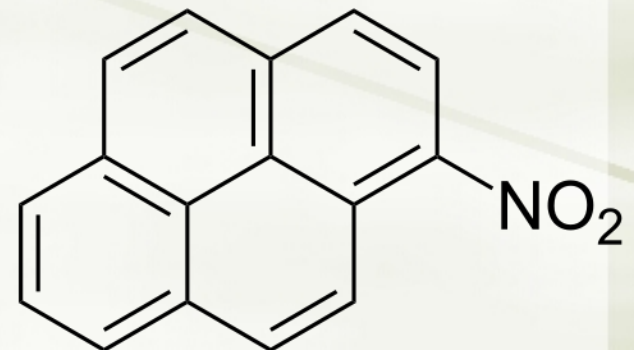# *New results for 1-nitropyrene metabolites in children and underground miners*

## *Christopher Simpson*

# 1-Nitropyrene (1-NP)

- 1-NP is formed by nitration of poly aromatic hydrocarbons (PAHs) within diesel engines
  - 1-NP is the most abundant particle-associated nitro-PAH in DE.

- It is a much more specific measure of DE than other commonly used surrogates (e.g. Black Carbon)

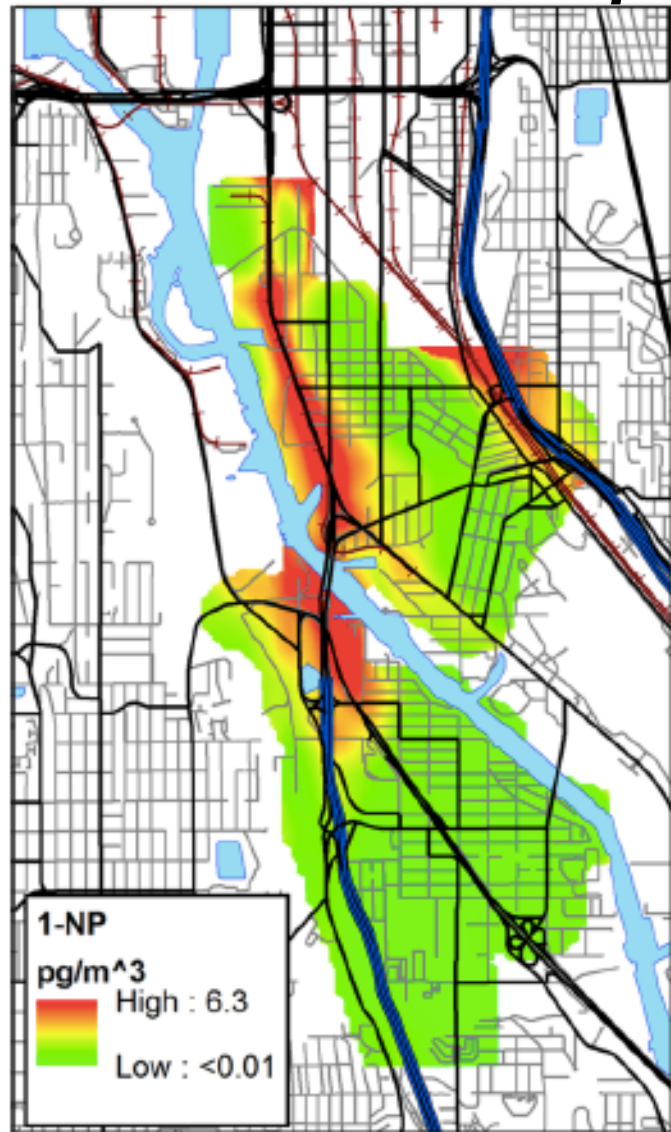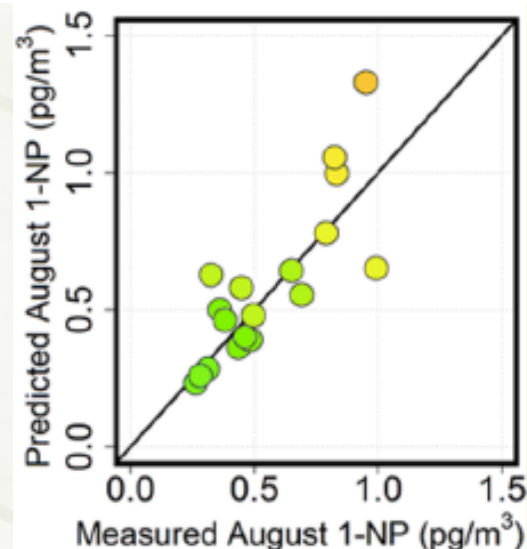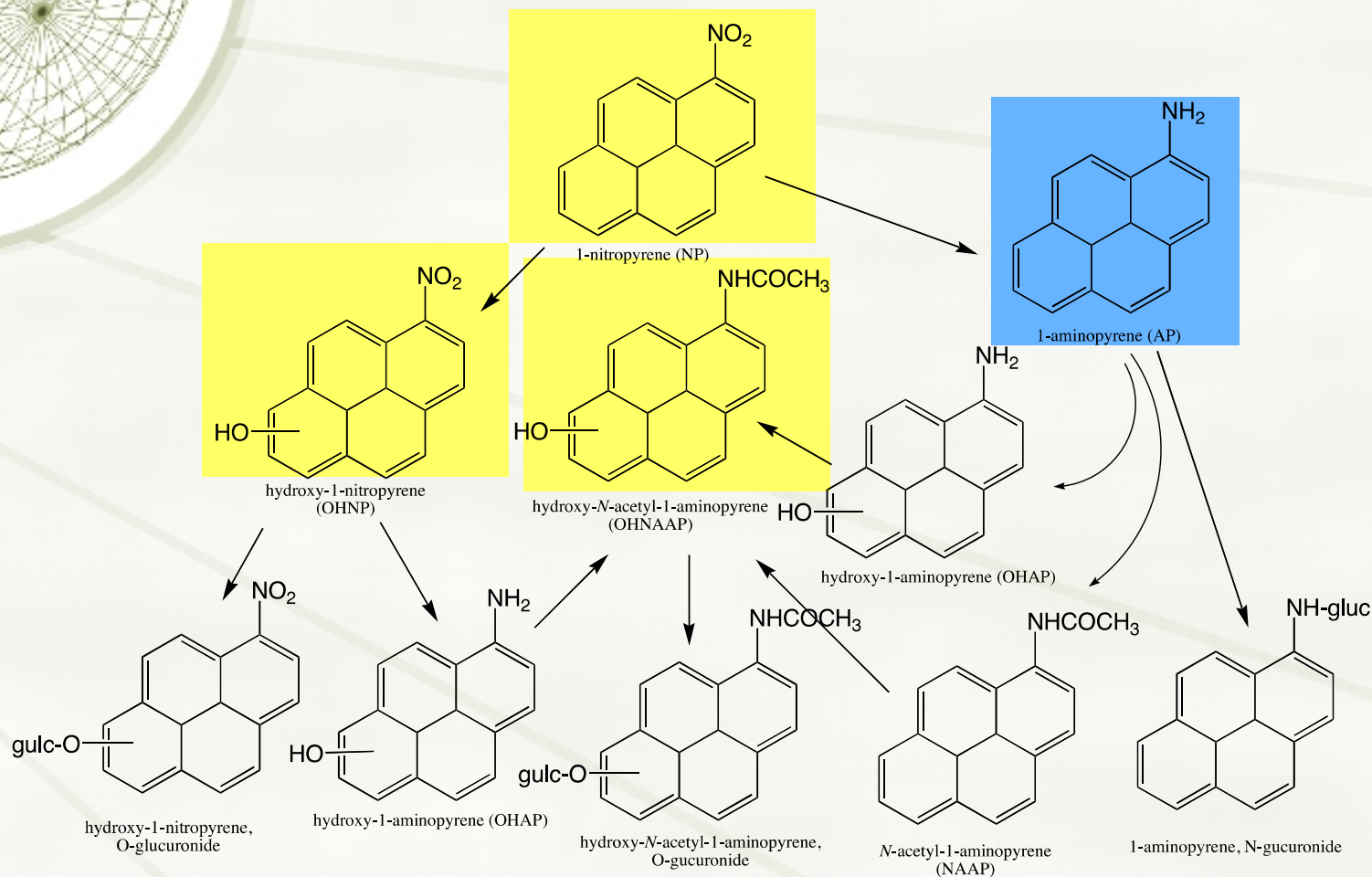- Metabolites of 1-NP can be measured in urine as an exposure biomarker



Scheepers et al. 1995; Toriba et al. 2007; http://en.wikipedia.org/wiki/1-Nitropyrene

# Spatial modeling of 1-NP



1-Nitropyrene

1-NP

pg/m^3

High : 6.3

Low : <0.01

## Table 3. Summary of August NPAH Regression Models

| model | covariate | $\beta$ | std error | $t$ value | $p > |t|$ |
|---|---|---|---|---|---|
| $\log_{10}$ August 1-NP | $\log_{10}$ m to railroad | −0.18 | 0.081 | −2.2 | 0.04 |
| | high-intensity development in 150 m | 0.0025 | 0.0010 | 2.4 | 0.03 |
| | CAL3QHCR truck estimate in 4500 m | 0.29 | 0.20 | 1.5 | 0.16 |
| | mean $\log_{10}$ mobile BC in 300 m | 1.3 | 0.41 | 3.2 | 0.01 |

*Schulte, J.K., Fox, J.R., Oron, A.P., Larson, T.V., Simpson, C.D., Paulsen, M., Beaudet, N., Kaufman, J.D. & Magzamen, S. Neighborhood-Scale Spatial Models of Diesel Exhaust Concentration Profile Using 1-Nitropyrene and Other Nitroarenes. Environ. Sci. Technol., 2015, 49 (22), pp 13422–13430*

# Biological monitoring of exposure to 1-NP

# Relationship Between Urinary Concentration of 8-Hydroxy Nitropyrene and 1-Nitropyrene Exposures



Error bars represent 95% CI; Note $\log_{10}$ scale on x-and y-axes

# *DE exposures in an underground mine*

- ✦ Large underground mine metal (~1,300 workers)
- ✦ Extensive use of diesel engines
- ✦ Observational cohort study
  - ✦ 20 subjects
  - ✦ Surface, face, and shop job locations
- ✦ 4 sampling campaigns
  - ✦ 2-3 months apart (March, 2014 – October, 2014)
  - ✦ 4 days each
    - ✦ Subjects worked 4 days on 4 days off

# *Sample Collection*

- Personal Air Samples
  - 1-NP & EC
  - Subjects 1 – 10  collected on days 1 & 3
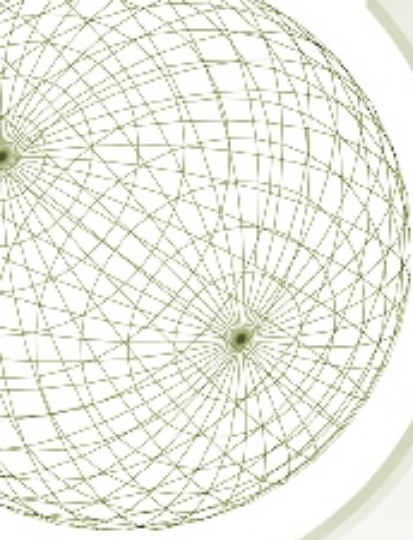  - Subjects 11 – 20 collected on days 2 & 4
- Urine Samples
  - Pre-shift collected daily
  - Post-shift collected daily
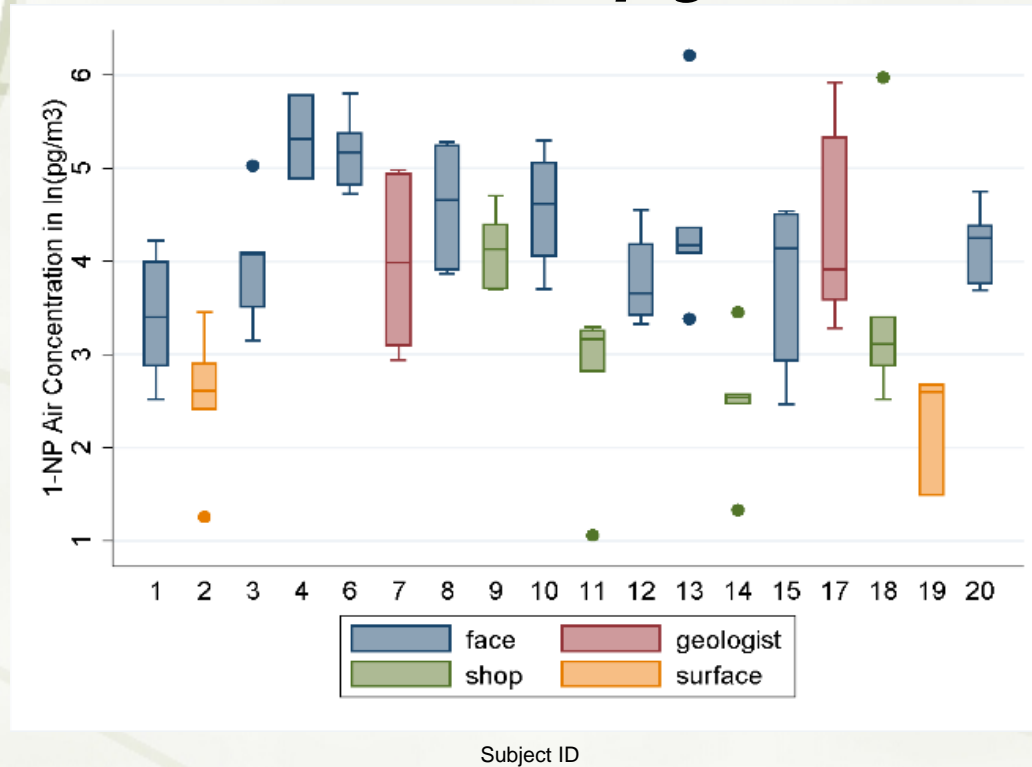- Job Task/Activity Surveys
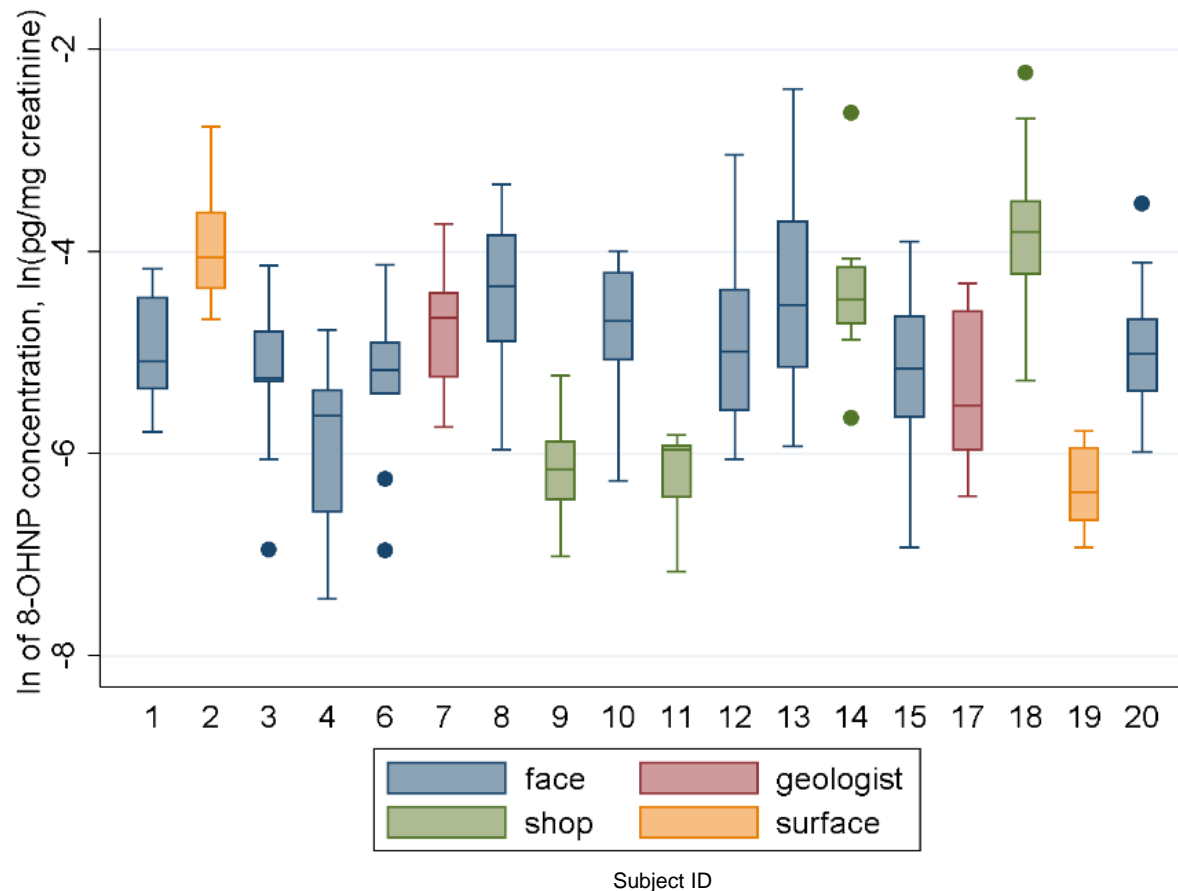  - Time spent underground & time exposed to diesel exhaust
  - Collected daily

# 1-Nitropyrene in Air
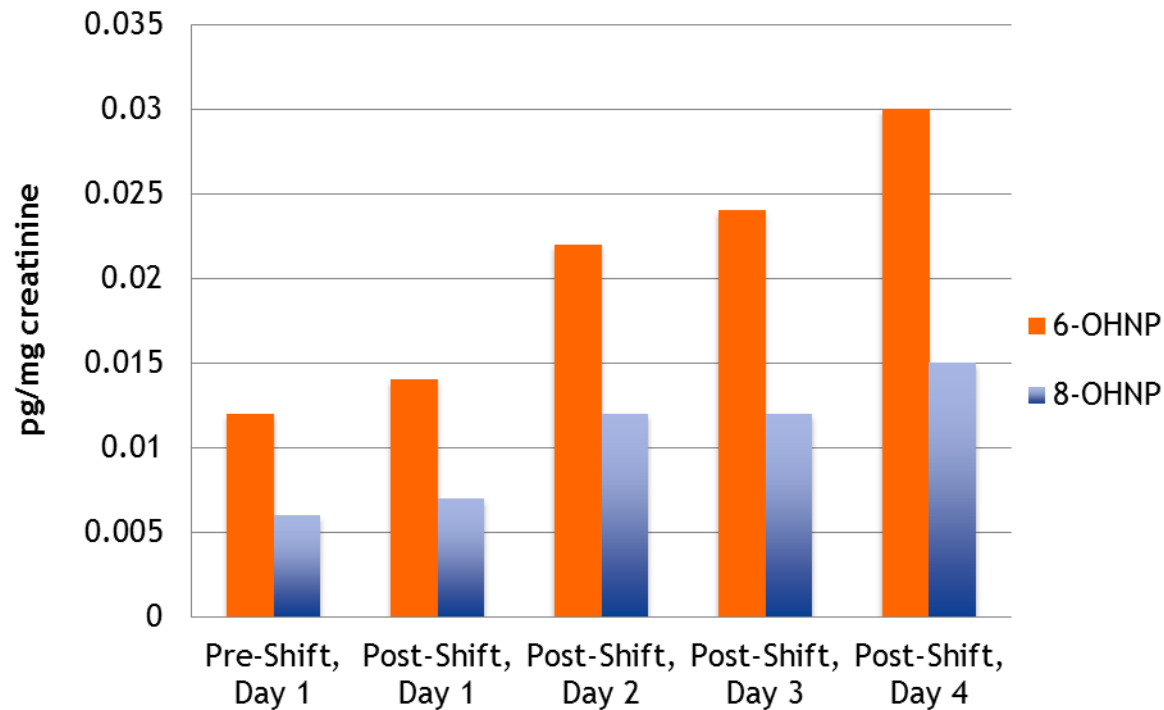


Subject ID

**1-NP and EC Personal Air Concentrations by Location Group**

| Job Group | n | Median 1-NP (95% CI), pg/m$^3$ | Median EC (95% CI), µg/m$^3$ |
|---|---|---|---|
| face | 67 | 64.8 (50.3-79.7) | 12.7 (9.58-13.6) |
| shop | 21 | 26.9 (19.6-41.1) | 5.55 (3.01-7.39) |
| surface | 15 | 6.03 (2.24-29.9) | 1.90 (1.32-8.04) |

# Metabolite Levels: 8-OHNP

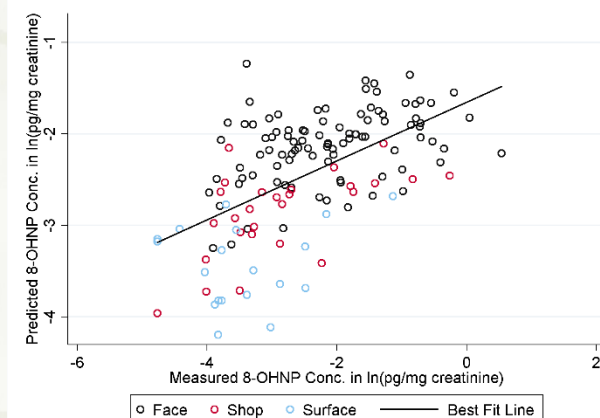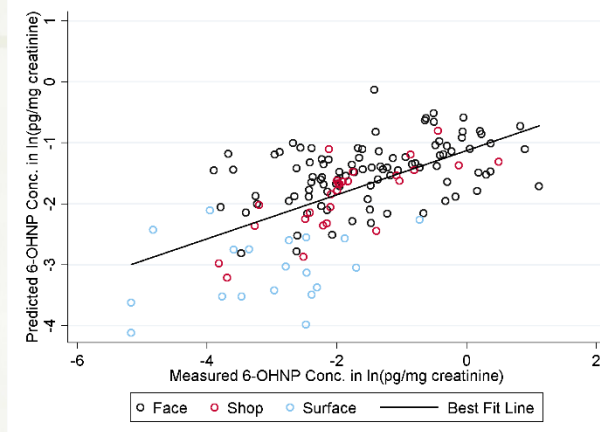# *Cross-week variation in metabolite levels*



Data shown is for 'face' group, similar trend observed for 'shop' group

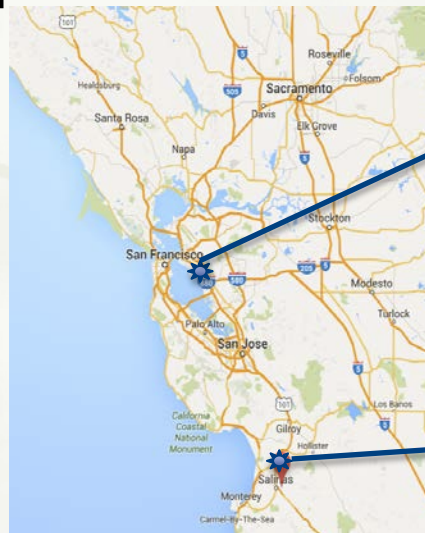# Prediction Models for Post-Shift 6-OHNP Levels in Urine

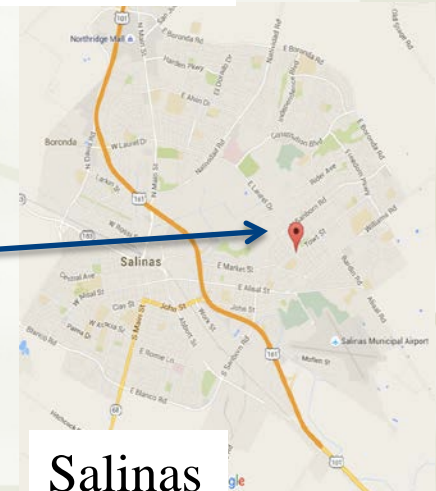| | β (SE) | p | 95% Conf. Interval | In-sample $R^2$ (RMSE) | Out-of-sample $R^2$ (RMSE) |
|---|---|---|---|---|---|
| Model A | | | | 0.36 (1.02) | 0.28 (1.05) |
| Shop* | -0.15 (0.23) | 0.529 | (-0.61, 0.31) | | |
| Surface* | -0.89 (0.30) | 0.004 | (-1.48, -0.29) | | |
| Time DE (hr) | 0.10 (0.03) | <0.001 | (0.05, 0.16) | | |
| Respirator Use (%) | 0.85 (0.34) | 0.013 | (0.18, 1.52) | | |
| Time between Voids (hr) | 0.20 (0.06) | 0.001 | (0.08, 0.32) | | |
| Day of Week | 0.30 (0.08) | <0.001 | (0.14, 0.46) | | |
| Intercept | -3.75 (0.39) | <0.001 | (-4.53, -2.97) | | |
| Model B | | | | 0.38 (1.01) | 0.32 (1.03) |
| Time UG (hr) | 0.12 (0.03) | 0.001 | (0.05, 0.18) | | |
| Time DE (hr) | 0.09 (0.03) | 0.002 | (0.03, 0.15) | | |
| Respirator Use (%) | 0.85 (0.33) | 0.011 | (0.20, 1.50) | | |
| Time between Voids (hr) | 0.23 (0.06) | <0.001 | (0.11, 0.34) | | |
| Day of Week | 0.34 (0.08) | <0.001 | (0.18, 0.49) | | |
| Intercept | -4.98 (0.40) | <0.001 | (-5.76, -4.20) | | |

*reference location is Face

# *Children's exposure to DEP in California*

✦ Pilot study using archived urine samples collected from children

✦ 10 "high" exposed and 10 "low" exposed
  - ✦ "High" DE exposure: children living in Oakland
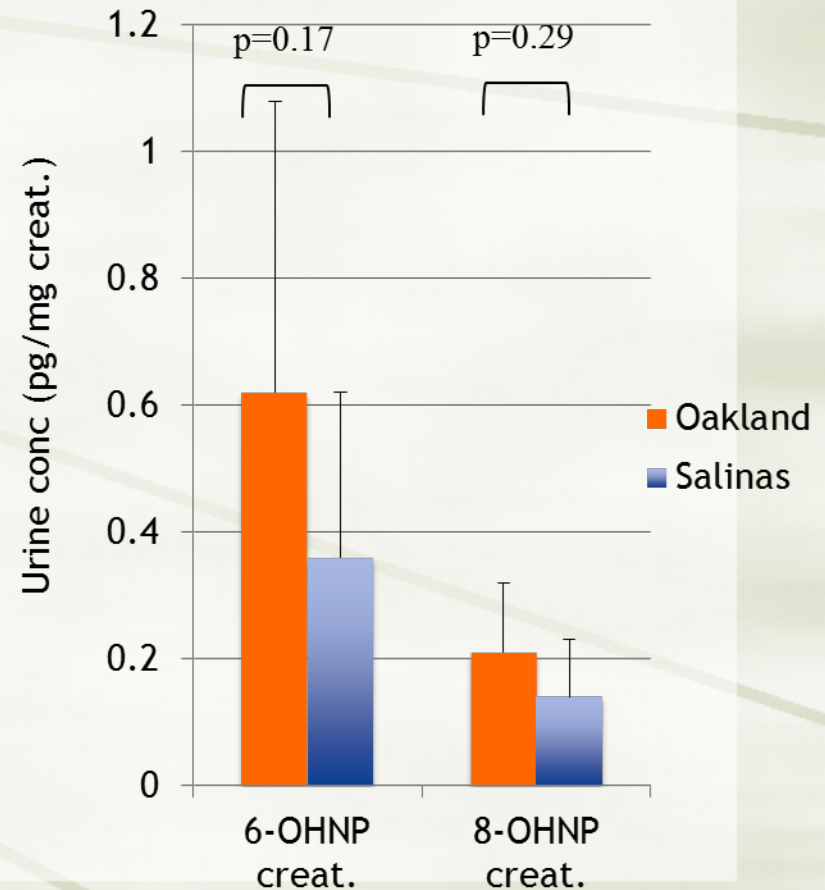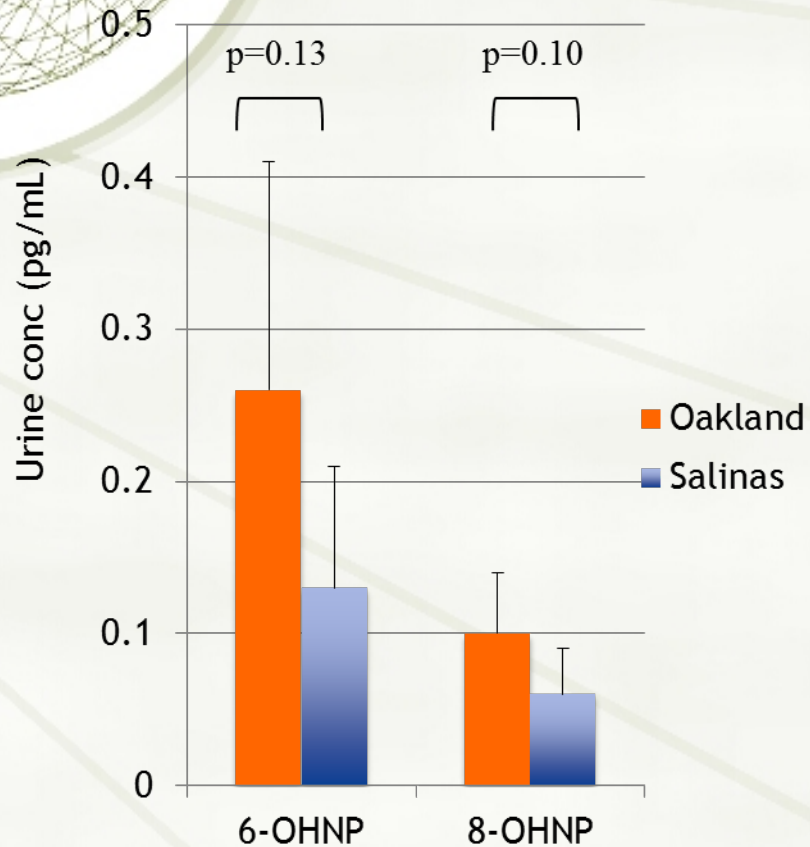  - ✦ "Low" DE exposure: children living in Salinas Valley



Oakland



Salinas

# 1-NP Biomarker levels

# *Association with traffic exposure*

We examined the correlation between creatinine corrected 1-NP metabolite levels, and traffic density within various circular buffers (500 m, 1000 m, 2000 m) of the subjects' homes.

Although not statistically significant, we observed positive correlations between increasing traffic density and increasing urinary biomarker levels.

| Traffic Density | 6-OHNP | 8-OHNP |
|---|---|---|
| 500 m | r=0.09 | -r=0.03 |
| 1000 m | r=0.24 | r=0.08 |
| 2000 m | r=0.37 | r=0.22 |

# *Conclusions*

- 1-NP metabolites can be reliably detected in human urine samples, including from individuals exposed to ambient concentrations of DE.

- The existing data strongly suggest that urinary 1-NP metabolites increase as exposure to DE increases.

- We don't yet know the extent to which exposures other than DE contribute to urinary 1-NP metabolite levels.

- We don't yet know how strong the relationship is between inhaled 1-NP and urinary metabolite levels, nor how reliably urinary biomarker levels might predict inhalation exposure.

- We don't fully understand the pharmacokinetics of 1-NP metabolite formation following inhalation exposures to DE.