Traffic-related UFP and cardiovascular health: Findings from a community-based study in Boston, MA

Doug Brugge, June 2017
CAFEH is a series of studies: Reported here are primary findings from the first study which is largely completed.

Grant proposal written:
STEP, CPA, CRA, CBPH, TU, HSPH

HUD grant awarded:
STEP, TU, COS

Kresge grant awarded:
MAPC, BPHC, TU, CPA, STEP, COS

NIEHS grant awarded:
TU, BUSSW, STEP, CPA, CRA, MAPC

EPA STAR grant awarded:
BUSPH

NIEHS grant awarded:
STEP, CPA, CRA, CBPH, TU, HSPH

NHLBI grant awarded:
NEU, UML, TU, STEP, CBPH

EPA STAR grant awarded:
TU

Somerville Community Requests Technical assistance

All are community-based participatory research
Somerville – air conditioning reduces PNC indoors

Figure 3. Time-series data for two homes monitored simultaneously on 14 June 2010 for indoor (thick line) and outdoor (thin line) particle number concentration. Note the different scales of the y-axes.

Chinatown –PNC concentrations do not decline much, most of the time up to 35 meters

PNC at Countway (central site), but not near highway or modeled, is associated with our biomarkers for short term exposure.

![Diagram showing relationships of biomarkers with central site (SPH) ambient particle number concentration.](image-url)

*Fig. 2.* Relationships of biomarkers with central site (SPH) ambient particle number concentration. Expected change in the biomarker is expressed as percent change (coefficient and 95% CI) per 5000 particles/cm³ change in exposure for IL-6, hs-CRP, and TNF-RII and absolute change (coefficient and 95% CI) per 5000 particles/cm³ change in exposure for fibrinogen.
Community Assessment of Freeway Exposure and Health (CAFEH)

- Mobile Monitoring on 162 days
- 704 surveys
- 451 clinic visits

PNC Models → Ambient residential PNC → Time-activity adjustment → CRP

CRP Association??
TAPL Details
Somerville: on-road, residential – model predicts PNC reasonably well.

Hourly predictive models with about 20 meter resolution. Not very transferable from geographic area to area.
There was differential error in geographic position assignment that we corrected.
Exposure Time-Activity Adjustment (TAA-PNC)

Model 1. Residential Ambient + Model 2. Work

Model 3. Other + Model 4. Highway
Time activity adjustment differentially reduced exposures for near highway participants.

Comparison of PNC Annual Average Exposure Models (N=140)

Lane et al. *Journal of Exposure Science and Environmental Epidemiology* (2015), 506 – 516
Adjusting for time activity improved linearity of association with CRP (and IL-6) – Somerville data only

Figure 3. GAM model comparison of the effect of PNC exposure models on LN hsCRP.
A higher PNC of 10,000 particles/cm\(^3\) was associated with higher DBP of 2.40 mmHg \((p = 0.03)\), independent of other factors in the model.

There were no significant associations for PM2.5 or BC.

Associations of DBP with PNC were more pronounced among obese individuals than non-obese individuals. “

*Chung et al., Int. J. Environ. Res. Public Health 2015, 12*

Marginal associations of TAA-PNC with S/IHD and hypertension, but not diabetes, except possibly in Asians

*Li et al., IJERPH, 2016*
TAA-PNC is associated positively, after adjusting for several confounders (negative confounding) but not significantly with CRP, IL-6 and TNFRII and negatively with fibrinogen. Stronger in white participants than Asian.

Table 4
Comparison of regression models for association between an interquartile-range change in time-activity adjusted annual average particle number concentration (IQR = 10.000 particles/cm²) and biomarkers of systemic inflammation (hsCRP, IL-6 and TNFRII) and coagulation (fibrinogen).

<table>
<thead>
<tr>
<th>Model</th>
<th>hsCRP % change (95% CI)</th>
<th>IL-6 % change (95% CI)</th>
<th>TNFRII % change (95% CI)</th>
<th>Fibrinogen % change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>-8.0% (-23.3%, 11.7%)</td>
<td>-2.1% (-12.9%, 10.2%)</td>
<td>-0.05% (-6.1%, 5.4%)</td>
<td>-3.3% (-7.0%, 0.4%)</td>
</tr>
<tr>
<td>Adjusteda</td>
<td>9.8% (-8.3%, 31.4%)</td>
<td>5.8% (-5.6%, 18.5%)</td>
<td>3.6% (-1.9%, 9.4%)</td>
<td>-1.9% (-5.5%, 1.6%)</td>
</tr>
<tr>
<td>Adjustedb</td>
<td>14.0% (-4.6%, 36.2%)</td>
<td>8.9% (-2.6%, 21.8%)</td>
<td>5.1% (-0.4%, 10.9%)</td>
<td>-1.9% (-5.5%, 1.6%)</td>
</tr>
<tr>
<td>Adjustedc</td>
<td>14.8% (-4.1%, 37.4%)</td>
<td>8.1% (-3.6%, 21.2%)</td>
<td>4.6% (-1.0%, 10.5%)</td>
<td>-2.1% (-5.7%, 1.5%)</td>
</tr>
</tbody>
</table>

a Adjusted for age, sex, continuous BMI, smoking status and education.

Adjusted for age, sex, continuous BMI, smoking status, education and race/ethnicity.

Table 5
Comparison of regression models for association between an interquartile-range change in time-activity adjusted annual average particle number concentration (IQR = 10.000 particles/cm²) and biomarkers of systemic inflammation (hsCRP, IL-6 and TNFRII) and coagulation (fibrinogen) stratified into white non-Hispanic and East Asian participants.

<table>
<thead>
<tr>
<th>Model</th>
<th>hsCRP % change (95% CI)</th>
<th>IL-6 % change (95% CI)</th>
<th>TNFRII % change (95% CI)</th>
<th>Fibrinogen % change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White non-Hispanic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>36.3% (-0.9%, 73.5%)</td>
<td>28.7% (4.4%, 53.0%)</td>
<td>15.5% (7.3%, 7.8%)</td>
<td>2.3% (-5.6%, 10.2%)</td>
</tr>
<tr>
<td>Adjusteda</td>
<td>32.7% (3.7%, 67.2%)</td>
<td>22.6% (-0.2%, 45.5%)</td>
<td>16.8% (5.8%, 27.7%)</td>
<td>-0.02% (-0.7%, 0.7%)</td>
</tr>
<tr>
<td>East Asian</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>9.7% (-13.5%, 32.0%)</td>
<td>5.0% (-9.9%, 19.7%)</td>
<td>-0.3% (-7.9%, 1.3%)</td>
<td>-1.8% (-6.4%, -2.7%)</td>
</tr>
<tr>
<td>Adjusteda</td>
<td>6.1% (-18.3%, 31.0%)</td>
<td>2.6% (-12.2%, 17.3%)</td>
<td>0.1% (-1.2%, 1.4%)</td>
<td>-0.06% (-5.4%, 4.2%)</td>
</tr>
</tbody>
</table>

a Adjusted for age, sex, continuous BMI, smoking status and education.
Adjustment for confounders, especially BMI, improves linearity
Metabolome analysis
>8000 molecules identified

“UFP is associated with antioxidant pathways, in vivo generation of reactive oxygen species and processes critical to endothelial functions”

Cluster 1: TNF-RII
- Tryptophan metabolism ($p=7.6e-5$)
- Metabolism of xenobiotics by CYP P450 ($p=1.5e-4$)
- Pentose and glucuronate interconversions ($p=3.6e-4$)
- Lysine degradation ($p=0.002$)
- One carbon pool by folate ($p=0.01$)

Cluster 2: Fibrinogen
- Arginine and proline metabolism ($p=6.1e-5$)
- Glycine, serine and threonine metabolism ($p=0.01$)

Cluster 3: IL-6
- Caffeine metabolism ($p=0.002$)
- Glyoxylate and dicarboxylate metabolism ($p=0.01$)

Cluster 4: CRP
- Glycine, serine and threonine metabolism ($p=4.1e-5$)
- Beta-alanine metabolism ($p=0.007$)

Pearson $r$
-0.75 0 0.75

Plasma protein biomarkers
$C_{18}$ w/negative ESI HRM
HIILC w/positive ESI HRM
Additional studies find associations between long-term ultrafine particles and health.

Three longitudinal studies have reported associations of long-term exposure to PNC with cardiovascular risk factors and mortality and reported findings that are broadly consistent with CAFEH analyses.

- **Ostro et al., 2015.** In California a statewide study found significant associations of UFP and their chemical constituents with death from S/IHD as well as total cardiovascular mortality.

- **Aguilera et al., 2016.** A multi-city cohort study in Switzerland observed an association of long-term exposure to UFP with subclinical atherosclerosis, measured by carotid intima-media thickness.

- **Viehmann et al., 2015.** A cohort study in Germany studied blood inflammatory and coagulation markers in a cohort study findings association of PNC with fibrinogen.
**Strengths:**
- Monitoring, model building and exposure assessment
- Objective health outcome measures
- Ability to control for many potential confounders
- Have data on other pollutants
- Random, reasonably representative sample

**Limitations:**
- Monitoring, model building and exposure assessment
- Cross sectional
- Main analysis is not actual development of disease
- Single pollutant models
- Small N
Conclusions:

We generated some evidence for UFP association with health

Came out about the same time as some other UFP epidemiology

But finer grain, near roadway exposure assignment

Need for larger, longitudinal studies

We will publish on a larger, longitudinal cohort soon
Time activity patterns differed by working and non-working.