Exhaled nitric oxide in children with asthma:

1) Outdoor- versus indoor-generated PM

2) Short term PM exposure

Therese Mar, Ryan Allen, Karen Jansen, Jane Koenig, Timothy Larson, Thomas Lumley, Sally Liu

University of Washington

Background

- Exhaled nitric oxide (eNO) is a ubiquitous molecule in the body and is a non-invasive marker of airway inflammation
- eNO is known to be elevated in individuals with asthma, is increased when a subject is having an asthma attack, and is decreased in those individuals using corticosteroid medication
- eNO has been compared with other techniques for measuring inflammation (ex. breath condensate, induced sputum)

Subject Characteristics

- 19 subjects: 14 male, 5 female
- Ages 6-13
- Medication use:

  10 inhaled corticosteroid (ICS) users

  9 ICS nonusers
- FEV1%: 67-100%

Data Collection

$PM_{2.5}$

- Local outdoor (HI)
- Local indoor (HI)
- Personal (HPEM)
- Average of 3 central sites: Kent, Lynnwood, and Lake Forest Park (TEOM)

Health Endpoint

- Daily concentration of eNO (ppb)

Estimating Exposure to Ambient and Non-ambient PM

Source-Specific Exposure Model

$$E_t = E_a + E_{ig} + \text{“personal cloud”}$$

$E_{ig} = (1\text{-}y)(C_{ig})$

$E_a = [y + (1\text{-}y)(F_{inf})]C_a$

α = “attenuation factor”

E_t = HPEM or pDR

y = fraction of time spent outdoors

C_a = ambient (outdoor) concentration (HI or neph)

C_{ig} = indoor-generated concentration = $C_i - C_a(F_{inf})$

C_i = indoor concentration (HI or neph)

Results

- Associations between various measured PM metrics and exhaled NO
- Associations between estimated concentrations of outdoor- and indoor-generated PM2.5 and eNO

Results ICS nonusers
eNO, ppb (95% CI)

For a10 ug/m^3 increase in $PM_{2.5}$, eNO increase

- Personal: 4.5 (1.02, 7.9)
- Indoor: 4.2 (1.02, 7.4)
- Outdoor : 4.3 (1.4, 7.2)
- Central: 4.2 (1.2, 6.4)
- EIG: -3.3 (-1.1, 7.7)
- EAG: 5.0 (0.3,9.7)
  - No effects were seen in ICS users

Previous findings

- Exhaled NO is a feasible, non-invasive technique for measuring airway inflammation
- Various measures of $PM_{2.5}$ were associated with a marker of airway inflammation in children with asthma
- Inhaled corticosteroid use attenuated the association between eNO and PM2.5
- Other panel studies have reported associations between PM2.5 and eNO. (Adamkiewicz et al, 2004; Jansen et al, 2004)

Short term analysis

- **Objectives:**
- To determine the effect of short term PM exposure (hourly lags) on exhaled nitric oxide

Methods

- Polynomial distributed lag model
- Hourly lags of PM up to 48 hours
- Model controlled for temperature, relative humidity, ambient NO concentrations and medication use

Polynomial distributed lag model

$$E[Y] = B_0 + b_i + B_1(Z1_{ids} - \overline{Z1}_{is}) + B_2 med_i + B_3 med_i * (Z1_{ids} - \overline{Z1}_{is})$$

$$+ B_4(Z2_{ids} - \overline{Z2}_{is}) + B_5 med_i * (Z2_{ids} - \overline{Z2}_{is}) + B_6(Z3_{ids} - \overline{Z3}_{is})$$
$$+ B_7 med_i * (Z3_{ids} - \overline{Z3}_{is}) + B_8(Z4_{ids} - \overline{Z4}_{is}) + B_9 med_i * (Z4_{ids} - \overline{Z4}_{is})$$

$$+ B_{10}(W_{ids} - \overline{W}_{is}) + B_{11} age + B_{12} rh + B_{13} temp$$

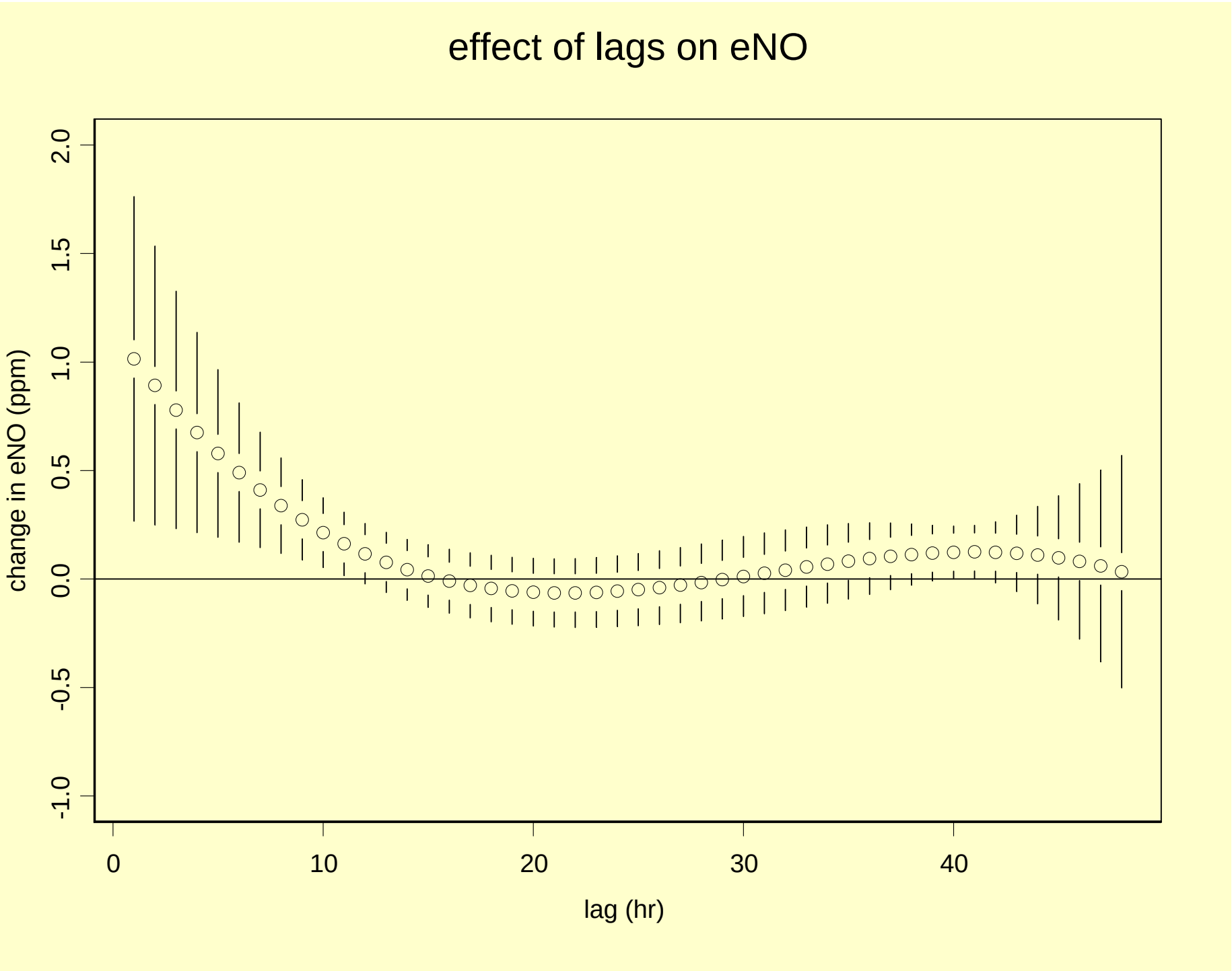
where

$$Z1 = \sum_{n=1}^{24} PMlag_n \quad , \quad Z2 = \sum_{n=1}^{24} n * PMlag_n \quad , \quad Z3 = \sum_{n=1}^{24} n^2 * PMlag_n \quad \text{and} \quad Z4 = \sum_{n=1}^{24} n^3 * PMlag_n$$

W is the ambient NO concentration

Averaged PM effect

PM	change in eNO per 10 μg/m3 PM	95% Lower CI	95% Upper CI
lag 1 hour	7.16	3.72	10.59
lag 4 hour	6.39	2.85	9.93
lag 8 hour	0.56	-1.07	2.20
PM 2.5 averaged from 7pm to 4 am	1.61	0.15	3.07
PM 10 averaged from 7 pm to 4 am	2.27	0.78	3.77



Conclusions

- eNO is associated with PM exposure up to 11 hours prior to eNO measurement
- An association between eNO and PM averaged during high wood smoke hours (7 pm to 4 am) was observed