Comparison of biomarkers for use in assessing woodsmoke exposure among wildland firefighters

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Exposure and health effects

- 70-80,000 workers involved in wildland firefighting annually (Harrison et al,, 1995)
- Woodsmoke is complex mixture
  - Hundreds of chemicals (PAHs, aldehydes, etc.)

- Possible respiratory health effects (Naeher et al, 2005)
  - Asthma, infections, lung cancer, COPD
- 40% of firefighter medical problems during ‘88 Yellowstone fires respiratory (Naeher et al, 2005)

Woodsmoke exposure assessment

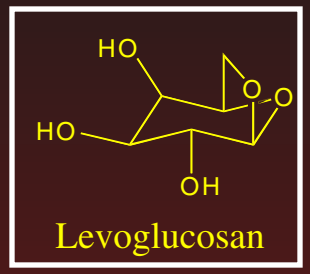
- Difficult among wildland firefighters
  - Highly transient
    - Area level personal exposure
  - Spatial/temporal variation
  - Irregular shifts, conditions
- Previous air measurements
  - Particulate matter (PM_{10}, $PM_{3.5}$) (Reinhardt and Ottmar, 2004)
  - Carbon monoxide (CO) (Reinhardt and Ottmar, 2004)
  - Methoxyphenols (MPs) (Dills et al, 2006; Dills et al, 2001)
  - Levoglucosan (LG) (Simpson et al, 2004; Lee et al, 2005)

Levoglucosan and methoxyphenols

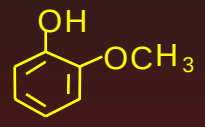
- LG is pyrolysis product of wood polymer cellulose; particulate in air
  - Most abundant organic compound in wildland woodsmoke particles (Lee et al, 2005)
  - More specific for woodsmoke than PM, CO?
    - Less likely to come from non-woodsmoke sources
- $PM_{2.5}$, LG levels related to urinary MPs in controlled exposures (Dills et al, 2005)
  - Pyrolysis products of wood lignin
  - Vapor and particulate in air

Selected markers for biomass combustion

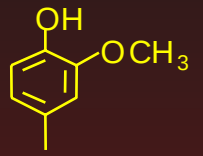
MP level proportions, presence vary depending on type of wood



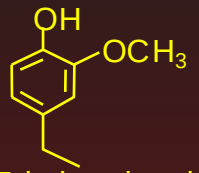
Levoglucosan



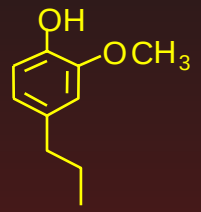
Guaiacol



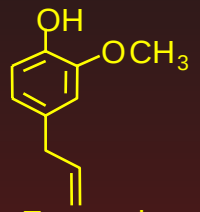
Methylguaiacol



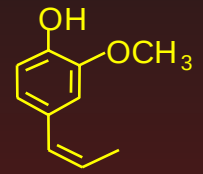
Ethylguaiacol



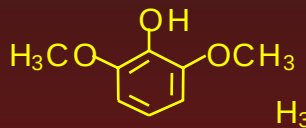
Propylguaiacol



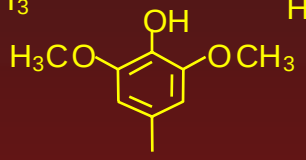
Eugenol



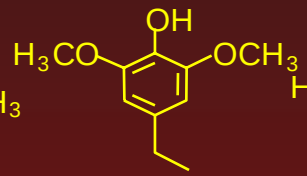
cis-Isoeugenol



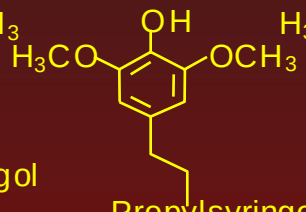
Syringol



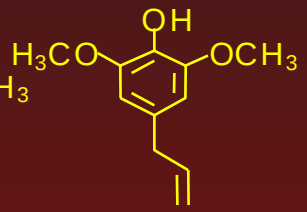
Methylsyringol



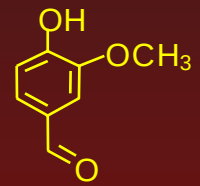
Ethylsyringol



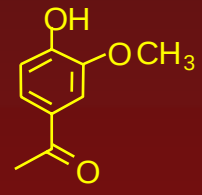
Propylsyringol



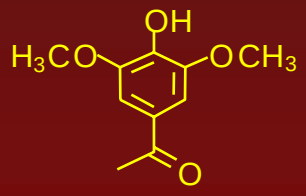
Allylsyringol



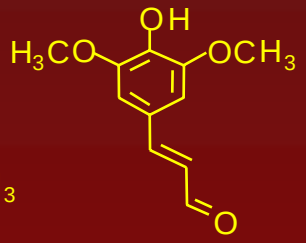
Vanillin



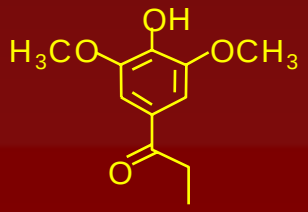
Acetovanillone



Acetosyringone

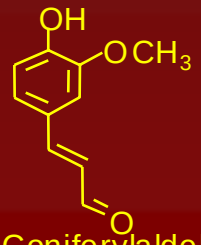


Sinapylaldehyde

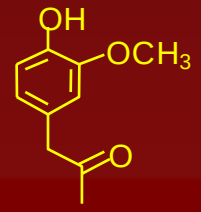


Propylsyringone

Syringaldehyde



Coniferylaldehyde



Guaiacylacetone

Guaiacols = single methoxy group on ring, syringols = two; other groups at position 4

Biological monitoring review

- Advantages
  - Measure of internal dose
  - Integrates exposure from multiple routes (e.g. ingestion, inhalation)
  - PPE, personal activities accounted for in dose
- Disadvantages
  - Potential for confounding from other sources
  - Requires additional subject-specific info
  - Inter-subject variability in uptake, metabolism

Current study

- Biomarkers may be more accurate measure of woodsmoke exposure than air samples
  - Evaluate relationships between $PM_{2.5}$, CO, and LG woodsmoke exposure and urinary MPs
- Hypotheses:
  1. $PM_{2.5}$, CO, LG levels will be highly correlated
  2. $PM_{2.5}$, CO, LG concentrations will be highly correlated with cross-shift urinary MP changes

Study data

- 20 shifts worked by 13 firefighters
  - Part of dataset collected by UGA, CDC
  - Chosen to cover range of $PM_{2.5}$ exposures
- Personal TWA levels of CO, $PM_{2.5}$, LG + qxr
  - CO measured via datalogging monitor
  - $PM_{2.5}$, LG from single filter
  - Smoked/grilled foods, smoking
- Pre- /post-shift urine samples
  - 22 MPs + creatinine

Methods

- Problem:
  - Urinary MP levels represent full-shift exposure
  - CO monitors all ran for full-shift
  - PM/LG sample pumps often failed during shift
    - Failure times, later exposure recorded in field notes
- Solution: data divided into three subsets
  - Full-shift exposure measurements
  - Measurement length >60% of full-shift
  - All measurements

Methods

- Invalid or non-detect (ND) data for 22 MPs
  - Some compounds available in all measures; some absent in nearly all measures
    - Mean 19.7% ND, 22.5% invalid for any reason
    - Invalid/ND data excluded unless noted
- Questionnaire results (shift + 48 hrs prior):
  - MPs not sig. different after smoking; no subjects removed from analysis
  - Syringol MPs sig. different after smoked/grilled food; 2 subjects removed from syringol analyses

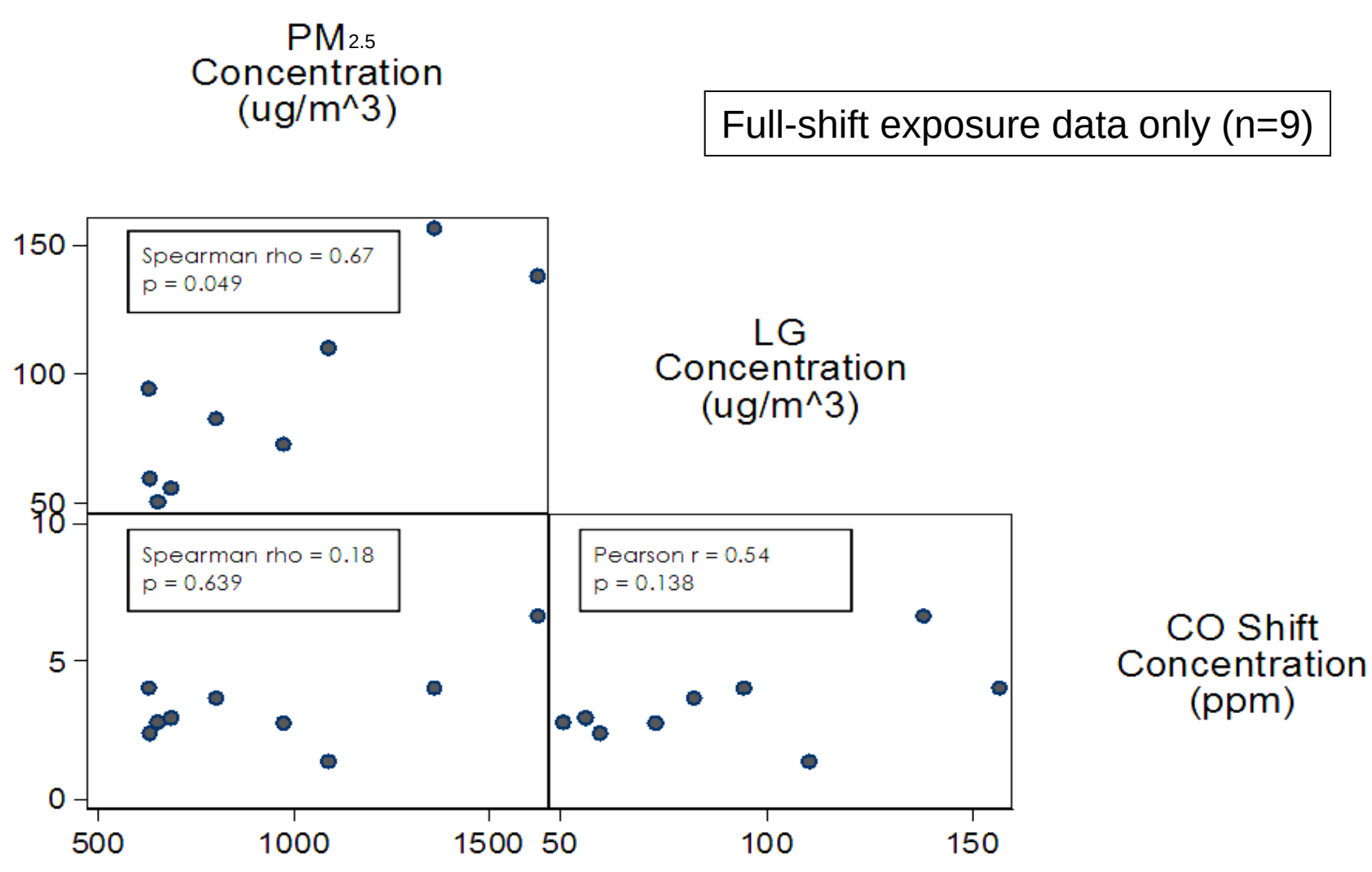
Methods

- CO and LG levels normally distributed
- $PM_{2.5}$ levels log-normally distributed
  - Not transformed; non-parametric analyses
  - 2 $PM_{2.5}$ samples with very low (<0.2%) LG:$PM_{2.5}$ ratio and low CO:$PM_{2.5}$ ratio removed
- Urinary MP levels
  - Pre-/post-shift MP levels normalized to creatinine levels before analysis (Dills et al, 2005)
    - Correct for temporal variations in urine concentration

Significant creatinine-adjusted urinary MP correlations

- Most abundant MPs; all vapor phase
  - Four guaiacol-type MPs
    - Guaiacol, methylguaiacol, ethylguaiacol and propylguaiacol (Pearson $r > 0.6$, $p < 0.01$)
  - Three syringol-type MPs
    - Syringol, methylsyringol, and ethylsyringol (Pearson $r > 0.6$, $p < 0.01$)
- Levels for these MPs combined into summed guaiacol and syringol variables
  - Summed variables *only*: ND assigned LOD/2

Correlations: $PM_{2.5}$, CO, and LG exposures



Correlations: *full-shift* exposures vs. creatinine-adjusted guaiacols

Agent	Parameter	Guaiacol	Methyl-guaiacol	Ethyl-guaiacol	Propyl-guaiacol	Summed guaiacols
CO	r	0.781	0.879	0.614	0.734	0.794
(n=20)	p	0.0001	<0.0001	0.004	0.001	0.0004
	n	19	19	20	16	15
LG	r	0.231	0.277	0.339	0.290	0.160
(n=9)	p	0.550	0.506	0.372	0.449	0.704
	n	9	9	9	9	9
$PM_{2.5}$	r	0.033	0.000	0.150	-0.050	-0.228
(n=9)	p	0.932	1	0.700	0.898	0.587
	n	9	9	9	9	9

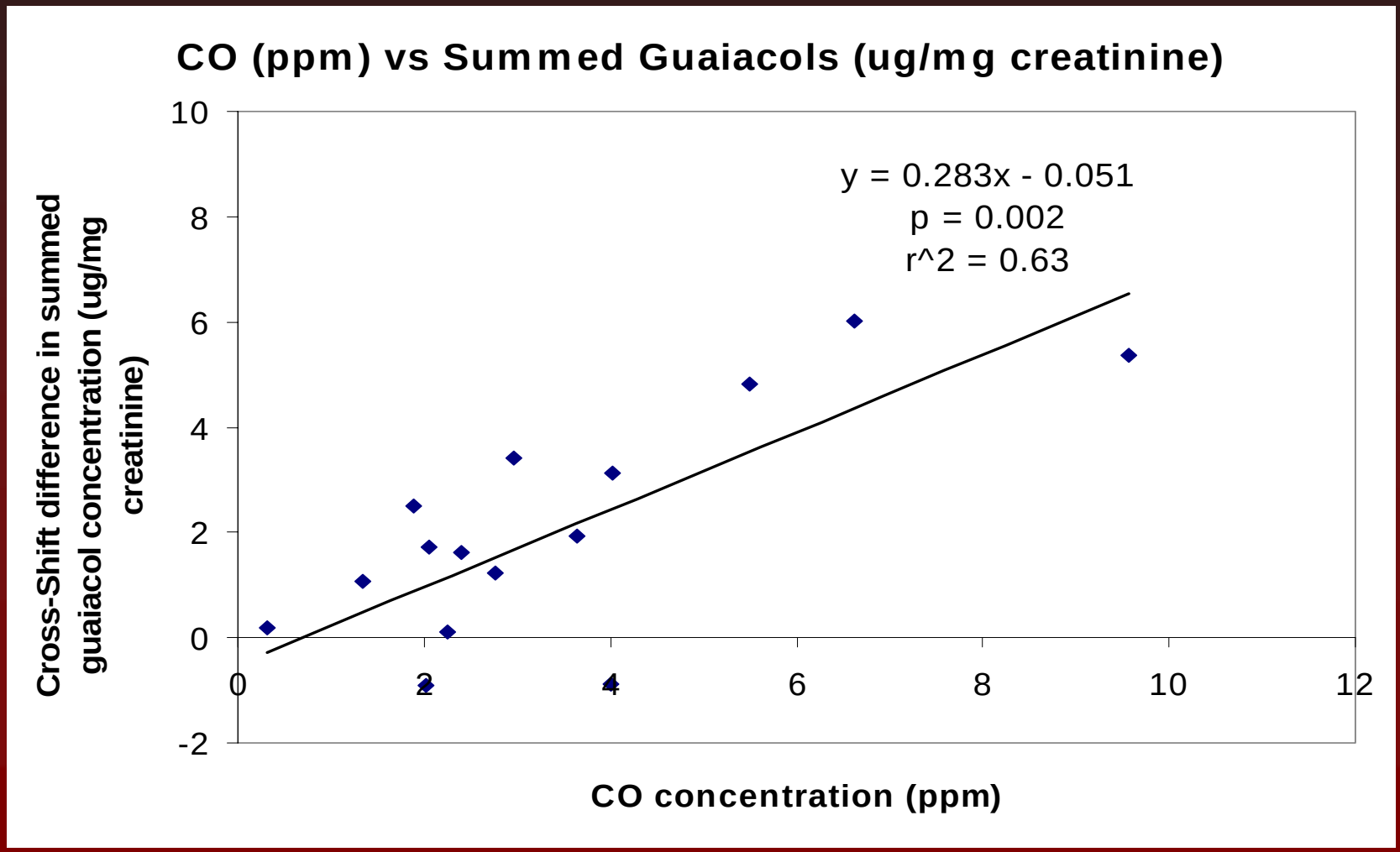
Syringols not significantly correlated with full-shift $PM_{2.5}$, CO, or LG

Correlations: *all* exposures vs. creatinine-adjusted guaiacols

Agent	Parameter	Guaiacol	Methyl-guaiacol	Ethyl-guaiacol	Propyl-guaiacol	Summed guaiacols
CO	r	0.781	0.879	0.614	0.734	0.794
(n=20)	p	0.0001	<0.0001	0.004	0.001	0.0004
	n	19	19	20	16	15
LG	r	0.423	0.718	0.702	0.605	0.334
(n=19)	p	0.116	0.003	0.003	0.022	0.289
	n	15	15	16	14	12
$PM_{2.5}$	r	0.278	0.443	0.409	0.303	0.131
(n=16)	p	0.315	0.098	0.116	0.293	0.686
	n	15	15	16	14	12

Syringols not significantly correlated with $PM_{2.5}$, CO, or LG

CO vs. change in creatinine-adjusted summed guaiacols



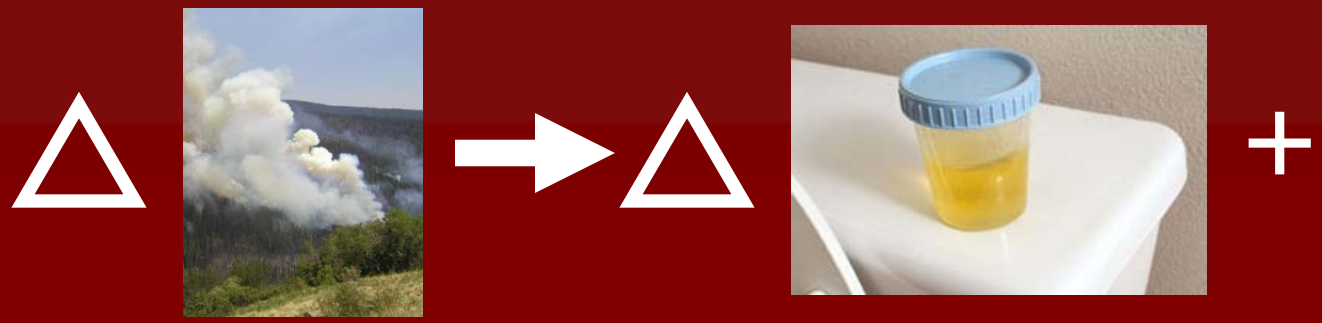
Other model r^2: LG vs guaiacols, 0.03; CO+LG vs. guaiacols, 0.79

Conclusions: exposure levels (hypothesis 1)

- LG and $PM_{2.5}$ significantly correlated
- LG and CO variably correlated
  - Insignificant correlation among full-shift samples
  - Significant correlation among all samples
- $PM_{2.5}$ and CO correlation poor to negligible
  - Literature generally shows strong correlation between $PM_{2.5}$ and CO for firefighters
  - Lack of correlation here possibly due to small n

Conclusions: urinary MPs vs. exposure levels (hypothesis 2)

- Significant cross-shift changes in 14 of 22 urinary MPs
- Exposures vs. MPs
  - Individual and summed creatinine-adjusted guaiacols highly associated with CO levels
  - Smaller association with LG; none with $PM_{2.5}$
  - CO explains most variance in MPs



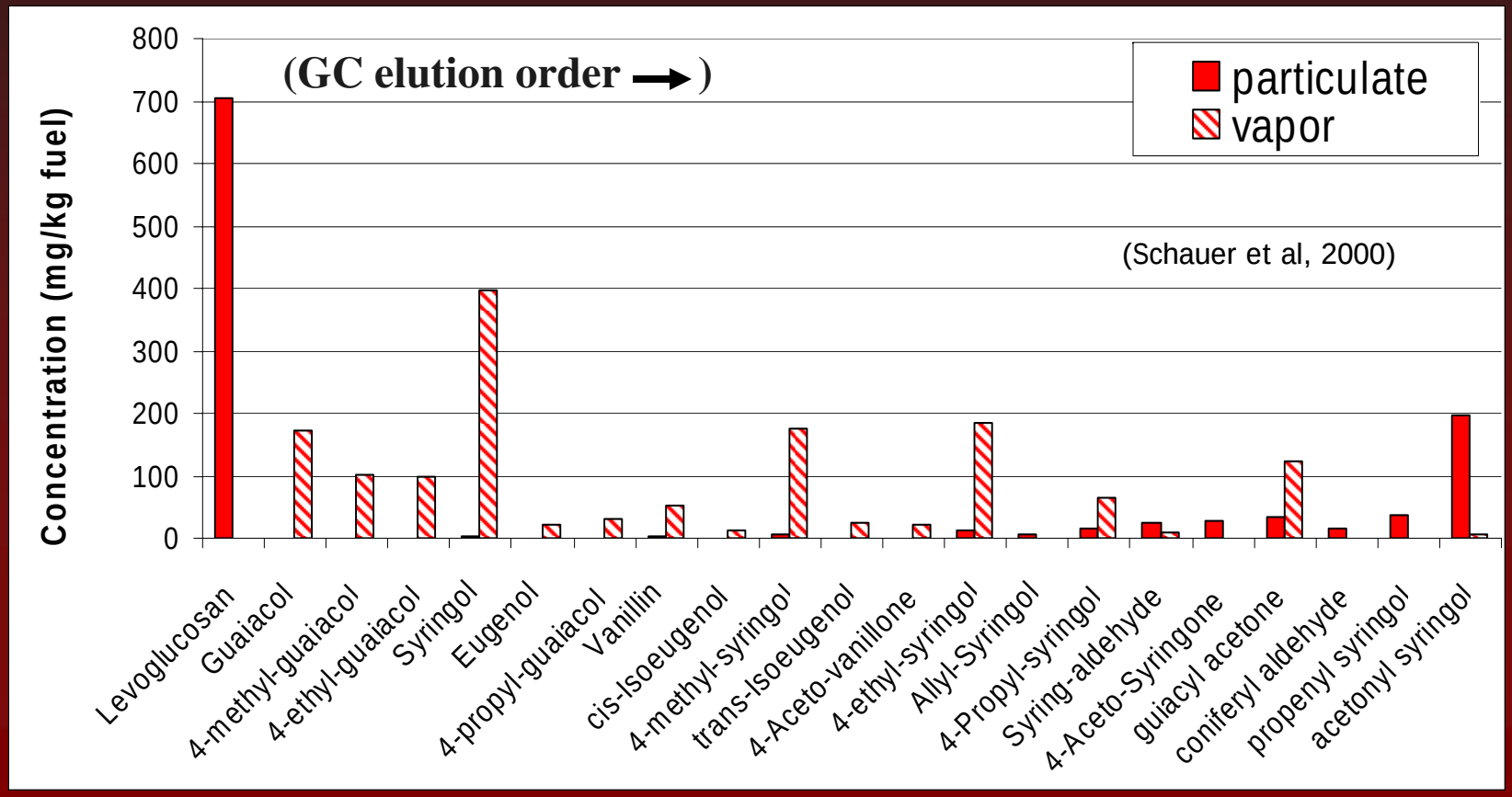
Future directions and acknowledgements

- Examine exposure and urinary MP relationship in full UGA/CDC dataset
  - Focus on urinary MPs from current study
  - Stratify analysis by forest type, activity, etc
- Thanks to:
  - Chris Simpson and Mike Paulsen, UW
  - Luke Naeher, UGA
  - Kevin Dunn, Alison Stock, Dana Barr, CDC
  - Participating firefighters
- Funded in part by:
  - Northwest Center for Particulate Air Pollution and Health (U.S. EPA grant #CR827355) and NIOSH (#R03-OH007656)

Additional: key features for a woodsmoke biomarker

- Relatively abundant in woodsmoke
- Ideally, should be particle-associated
- Should be stable in the atmosphere
- Should not be appreciably metabolized
- Must have low abundance in urine from subjects with low exposures to woodsmoke

Additional: abundance of molecular markers in smoke from oak combustion



LG exists only in particle phase; MPs primarily in vapor phase

Additional: MP analysis

- MPs with simple alkyl substituents at 4 position on ring primarily excreted as phase 2 conjugates
  - Conjugates of glucuronide and sulfate
  - Guaiacol, methyl guaiacol, ethyl guaiacol, etc.
- Analysis: conjugates hydrolyzed, reform original MP
- Compounds with complex sidechains undergo more extensive metabolism (usually side chain oxidation)
  - Eugenol, vanillin, etc.
- Only tried to measure parent compounds (not oxidized metabolites)
  - So don't see much of a biomarker signal for complex MPs

Additional results: regression models, full-shift exposure vs. creatinine-adjusted guaiacols

		Cross-shift difference in summed guaiacols (ug/mg creatinine)				
Model	**Model variables**	**N**	**Coeff.**	**95% CI**	**Coeff. P-value**	**Model R^2**
1	CO (ppm)	15	0.283	0.167 - 0.400	0.0002	0.63
2	LG (ug/m3)	9	0.003	-0.018 - 0.024	0.701	0.03
3	CO (ppm)	9	0.425	0.221 - 0.629	0.002	0.79
	LG (ug/m3)		-0.008	-0.021 - 0.004	0.151	

- Models for other data subsets displayed similar trends