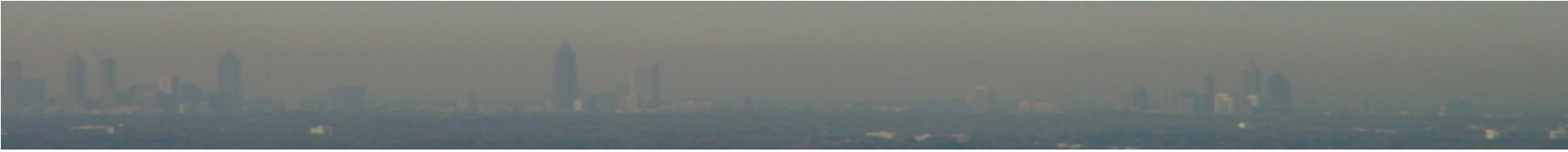


DEVELOPING STRATEGIES TO ADVANCE MULTI-POLLUTANT EPIDEMIOLOGIC RESEARCH

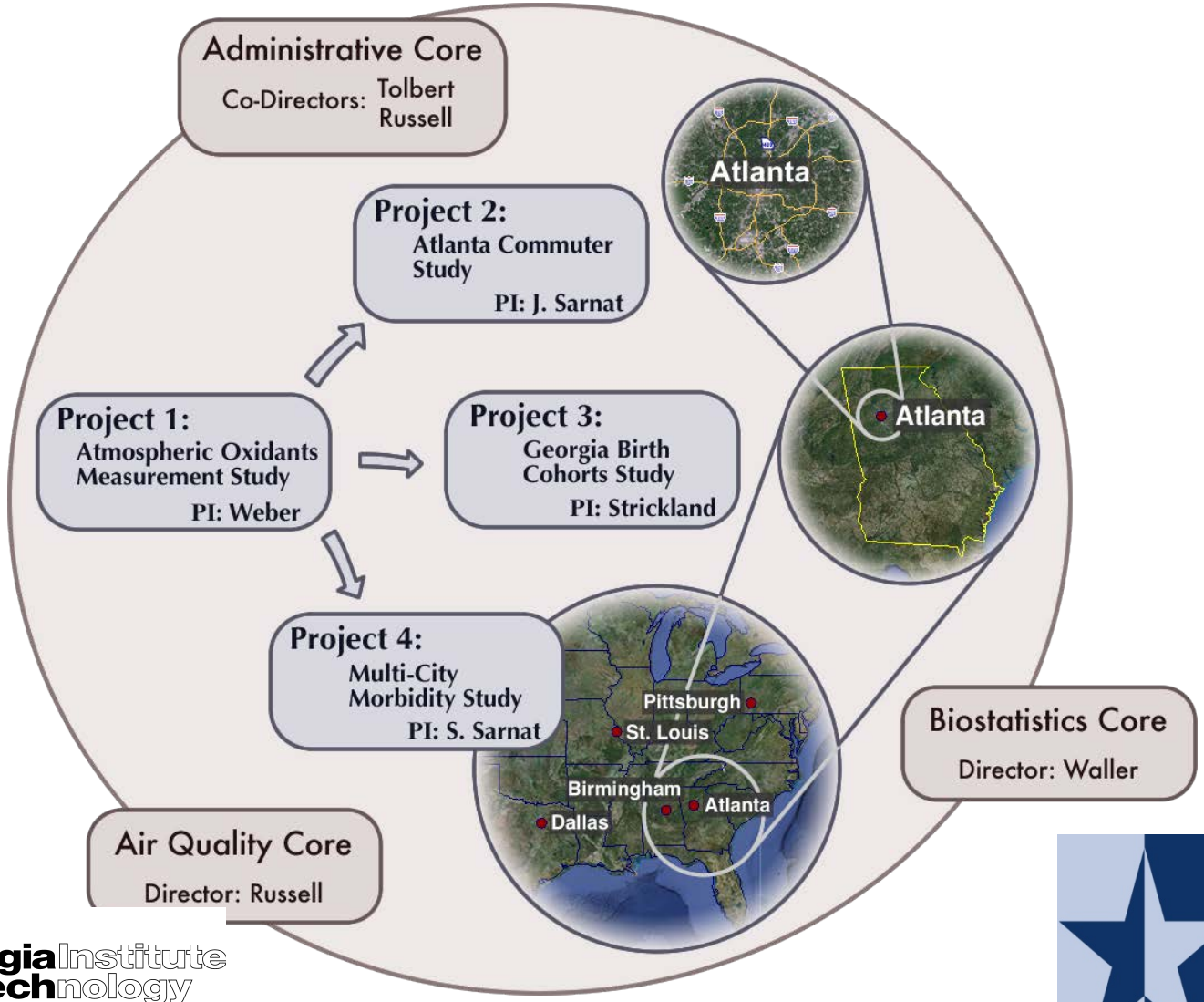
Paige Tolbert, Ph.D.

NIEHS Workshop: Advancing Research on Mixtures: New Perspectives and Approaches for Predicting Adverse Human Health Effects, Chapel Hill 9/26-27/11

Southeastern Center for Air Pollution and Epidemiology (SCAPE)

U.S.E.P.A. Clean Air Research Center

Co-Directors: Paige Tolbert, Emory, and Armistead (Ted) Russell, Georgia Tech



ROLLINS SCHOOL OF PUBLIC HEALTH EMORY

Georgia Institute of Technology

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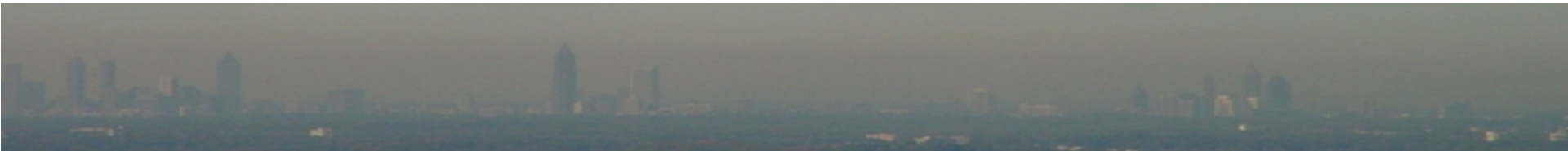
Center Approach to Mixture Characterization

- Perspectives
  - *evidence-based perspective*
    - **focus on vehicular emissions and near-roadway impacts, as accumulating evidence supports a major role for traffic emissions**
  - *biologically-based perspective*
    - **assess the role of reactive oxygen species (ROS) and other oxidants as a group with potential biological activity relevant to oxidative stress-mediated responses**
  - *environmental management perspective*
    - **use state-of-the-art methods of source apportionment to better understand roles of groups of agents co-emitted from specific sources and their transformation products**
  - *empirical perspective*
    - **apply data-based approaches to sort species and group them according to their associations with health endpoints of interest.**



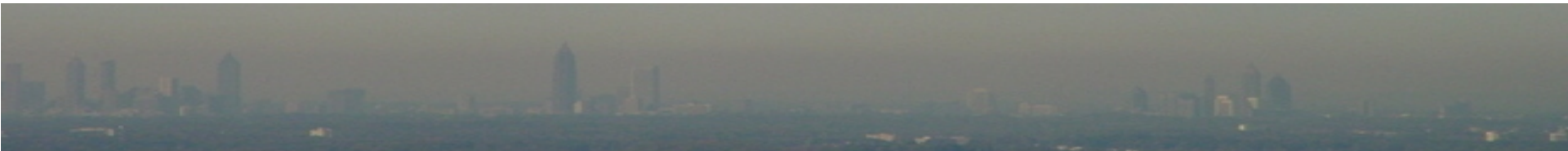
Variety of Goals in Multi-Pollutant Research

- "…estimating the total health effect associated with the exposure to multiple pollutants."

  [Dominici et al, Epidemiology, 2010]

- "…to model complex air pollution mixture effects more explicitly to gain better insight into the features of an air pollution mix that are most toxic."

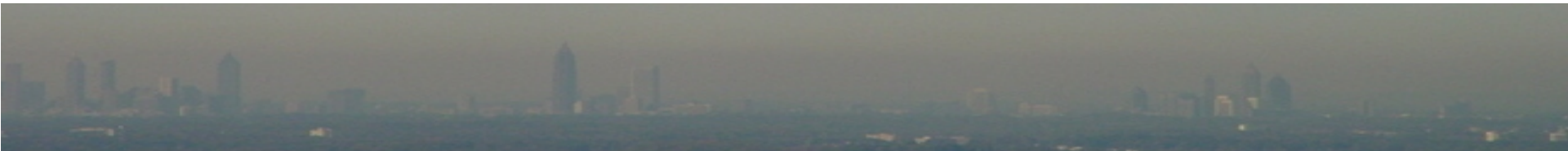
  [Vedal & Kaufman, Am J Resp Crit Care Med, 2011]



Conceptual Issues

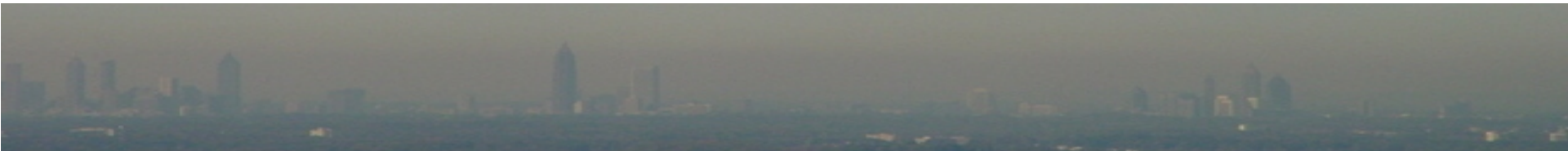
- Clarify conceptual issues, statistical issues follow
  - Covariation
  - Interaction
  - Joint effects
  - Disentangling effects

[Klein et al, manuscript in preparation]



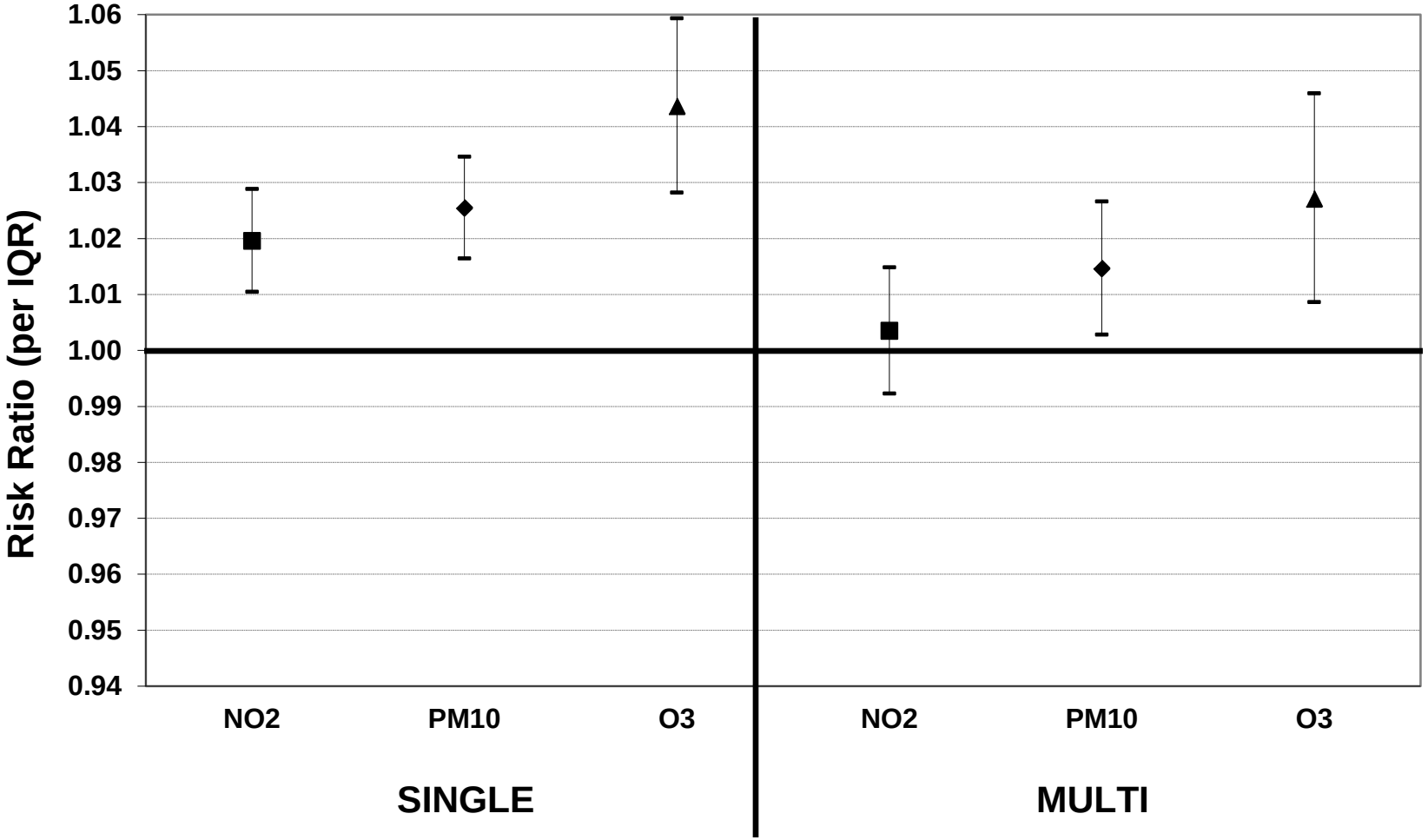
Covariation

- Many pollutants covary temporally and spatially as a result of co-emission or common atmospheric processes
- Typically, this is why multi-pollutant models have been used – to estimate effects of a single pollutant controlling for effects of others



Atlanta Example

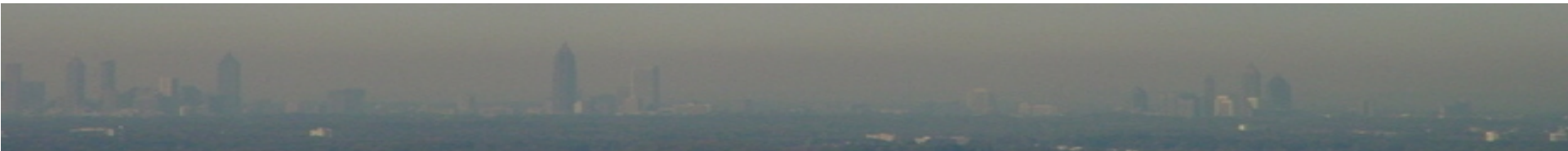
Single- and Multi-Pollutant Models: Respiratory ED Visits



[Tolbert et al, J Exp Sci Environ Epidemiol, 2007]

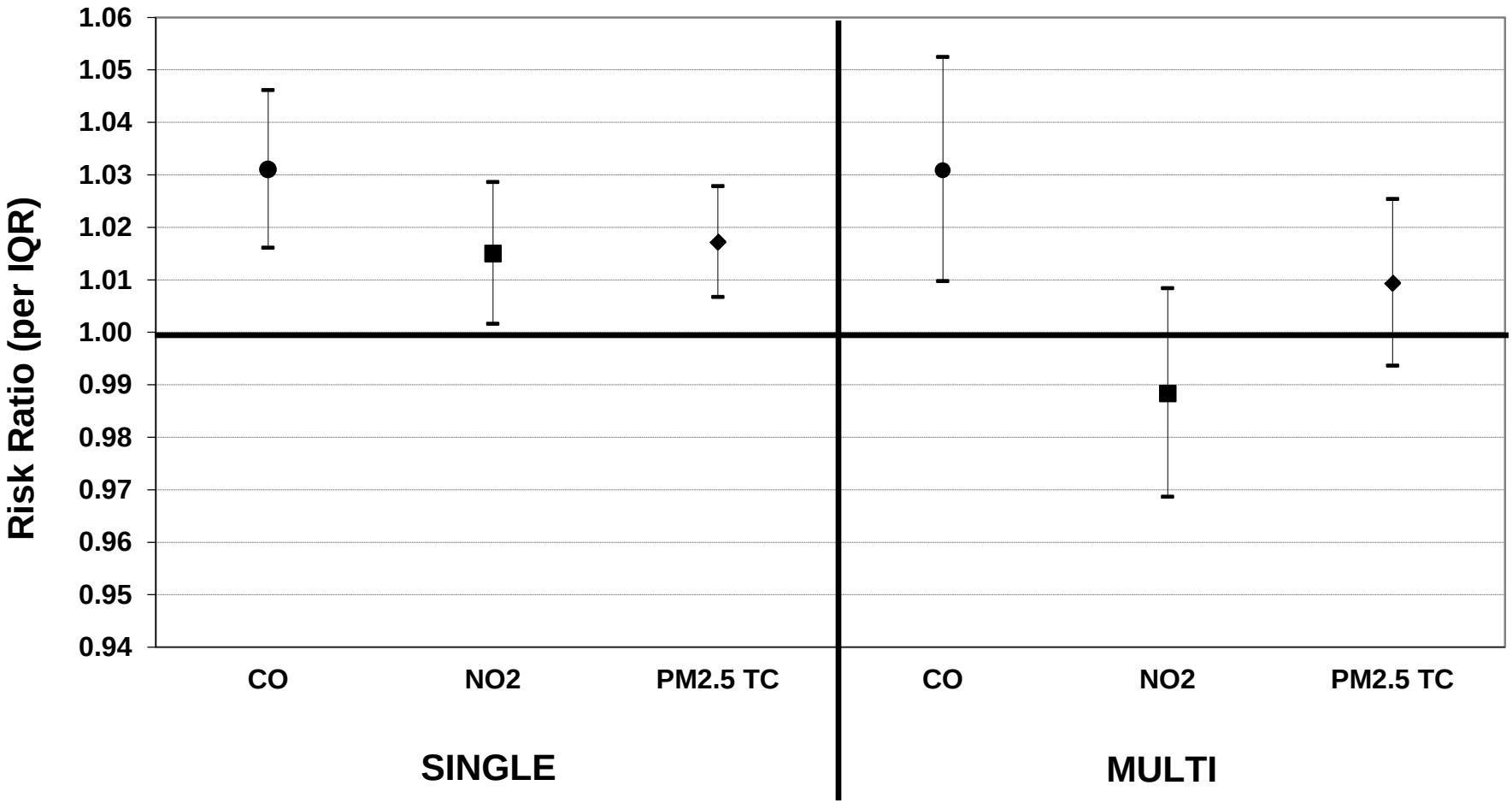
Covariation (cont'd)

- But:
  - Too tightly correlated? Power problem
  - Differing levels of measurement error across pollutants?
  - Surrogate issue – if etiologically important pollutant not measured or poorly measured, other pollutant may act as surrogate



Atlanta Example

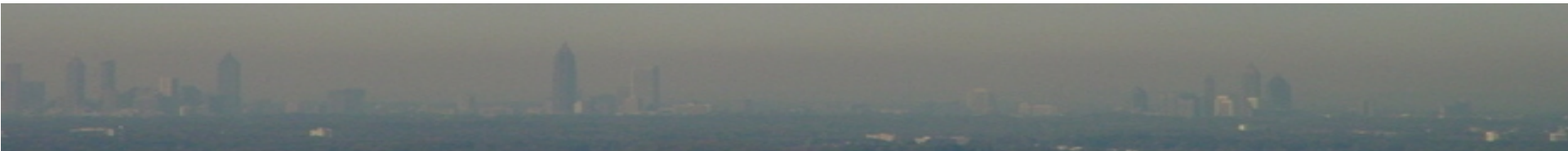
Single- and Multi-Pollutant Models: CVD ED Visits



[Tolbert et al, J Exp Sci Environ Epidemiol, 2007]

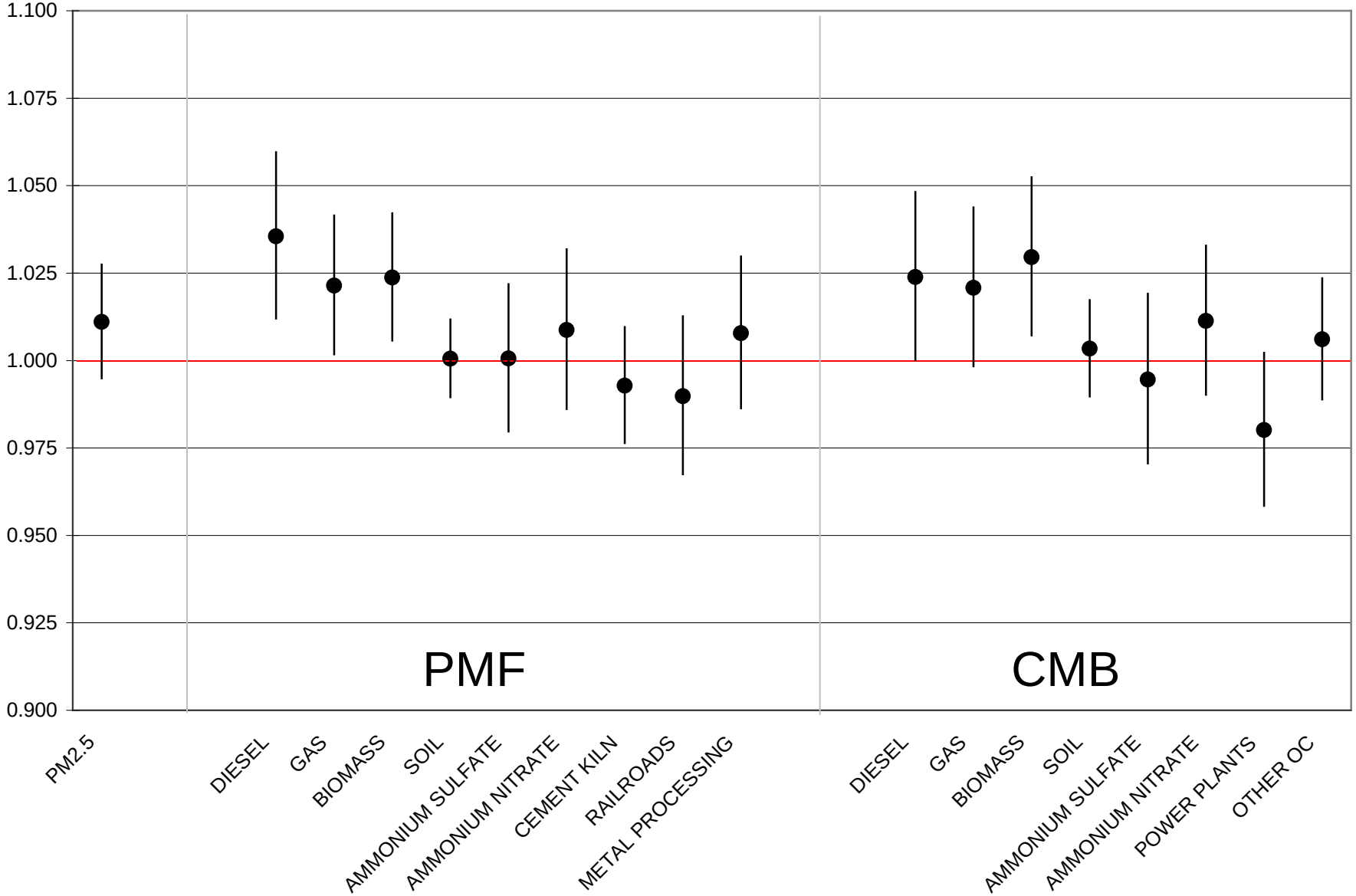
Covariation (cont'd)

- Source apportionment
  - Grouping co-emissions by common source
  - Step forward and backward?
    - Helpful for environmental management
    - Dimension reduction / less correlated
    - But:
      - added layer of uncertainty
      - etiologic agent could be in multiple sources
      - if one source is associated with outcome, will want to know which component(s) important



Atlanta Example

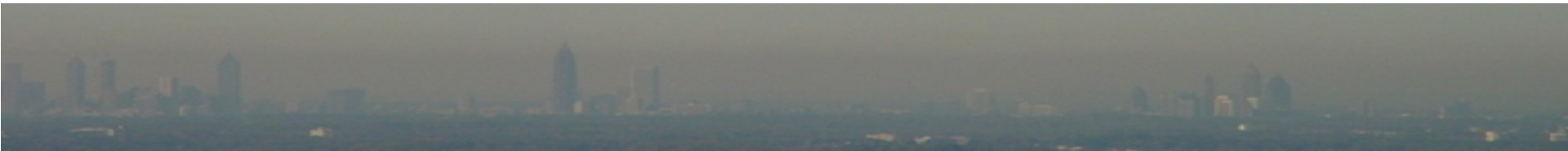
$PM_{2.5}$ Source-Resolved Results: CVD ED Visits (RR per IQR and CI)



[Sarnat et al, EHP, 2008]

Interaction

- Knowledge of separate effects of individual pollutants may be insufficient to predict effects of combination
- Statistical interaction – model-dependent, may reflect biological or chemical interaction
- Not necessarily simultaneous exposure – e.g., ozone may potentiate effects of PM

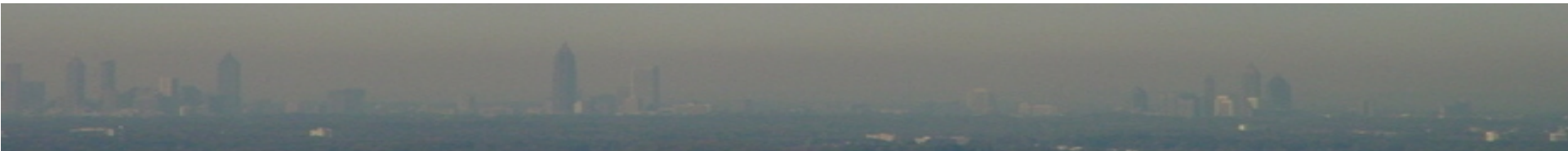


Interaction (cont'd)

- Challenges:
  - Power
  - Unmanageable number of potential combinations (all 2-way, 3-way,…n-way)
    - Multiple comparisons problem
    - How prioritize?
    - A priori selection based on co-occurrence, biological considerations, prior evidence
    - Dimension reduction/model stabilization techniques
      - e.g., LASSO/ridge regression

Joint Effects

- What is total effect of mixture?
- One approach: from multi-pollutant model, add parameter estimates, exponentiate to get RR for simultaneous increase of one unit of each pollutant
  - May include interaction terms
  - Choice of units critical to weighting

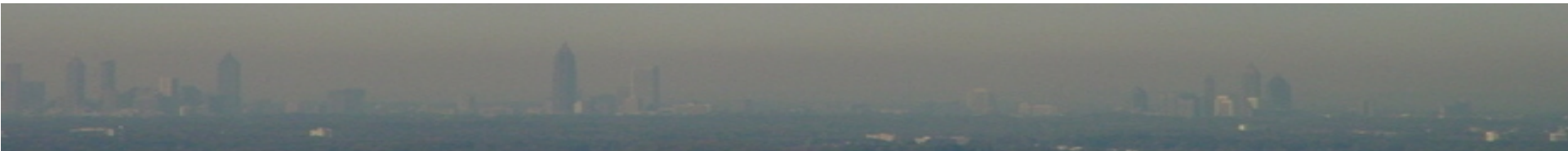


Joint Effects (cont'd)

- Alternative approach:

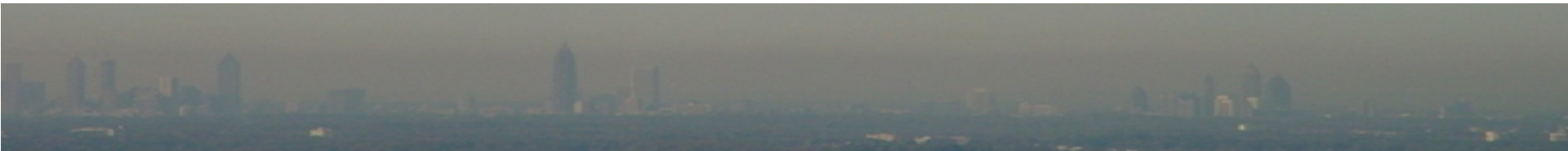
  "One atmosphere" paradigm, estimate risk associated with unit increment of this mixture

  (or other mixtures)
- Leads to question of what is driving association, how does risk vary by composition of mixture?



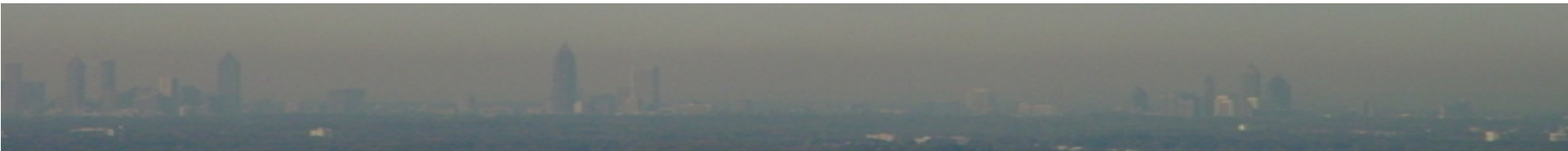
Disentangling Effects

- Deconstruct from joint effect: which components are driving association?
- How group components?
  - Measurement method: e.g., PM2.5, ultrafines, OC
  - Source apportionment
  - Mode of action: e.g., ROS, other mechanistically-relevant property groups
  - Empirically-based techniques: e.g., PCA, CART, random forests, supervised or unsupervised clustering…



Multi-Pollutant Approaches to Air Pollution Mixtures

- Ultimately getting closer to true complexity of etiologic picture involved in real-world exposures
- But need clarity in goals and thoughtful approaches to minimize vulnerability to issues of data mining, multiple comparisons and other pitfalls…



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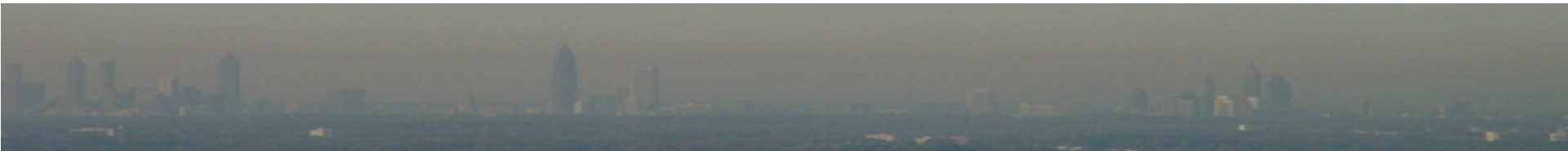
- Mitch Klein
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