DOES AIR POLLUTION CAUSE CHILDHOOD OBESITY?

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Overview of Presentation

- Findings from the Southern California Children's Health Study (CHS)
- Other influential epidemiological studies
- Biological plausibility
- Air pollution, diabetes and metabolic outcomes

Risk Factors for Childhood Obesity

- Major risk factors: family history, increased caloric density and decreased physical activity
- Other factors may promote development of obesity
  - Absorption
  - Basal metabolism
  - Adipose deposition
- Environmental obesogens
  - Dietary composition
  - Built environment through its role in exercise and food consumption
  - Gut microbiome
  - In utero and childhood chemical exposures

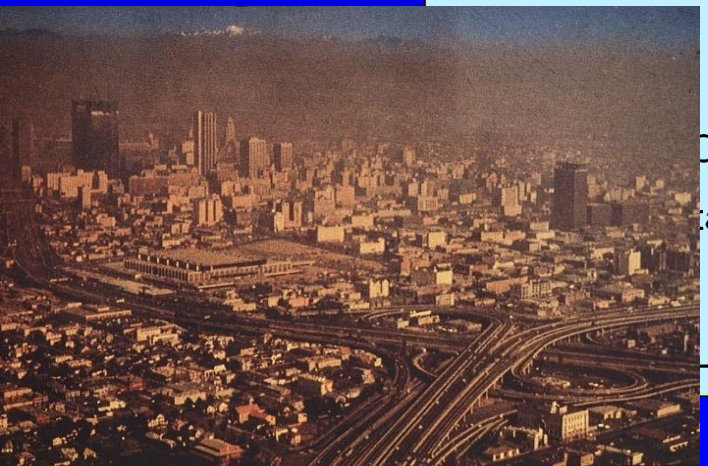
Sharma Am J Epidemiol. 2008; Trasande, JAMA 2012, Valvi EHP 2012, Verhulst EHP 2009,

Environmental Risk Factors for Childhood Obesity

- **Chemical exposures are implicated**
  - **Organochlorines (PCBs, DDT, HCB)**
  - **Bisphenol A**
  - **Cigarette smoke (nicotine?)**
  - **Air pollution?**

Sharma Am J Epidemiol. 2008; Trasande, JAMA 2012, Valvi EHP 2012, Verhulst EHP 2009,

Children's Health Study Communities



MAIN OUTCOMES

- **Currently**
  - Asthma
  - Respiratory symptoms (eg. bronchitis)
  - Lung function (spirometry)
  - Exhaled nitric oxide
  - Respiratory school absences
  - Carotid intima medial thickness, arterial stiffness, blood pressure
  - **Obesity/BMI trajectory**
  - Epigenetic marks
- **With Southern California Children's Environmental Health Center (SC-CEHC) support**
  - Metabolic outcomes
  - Fat distribution
  - Fat tissue phenotype

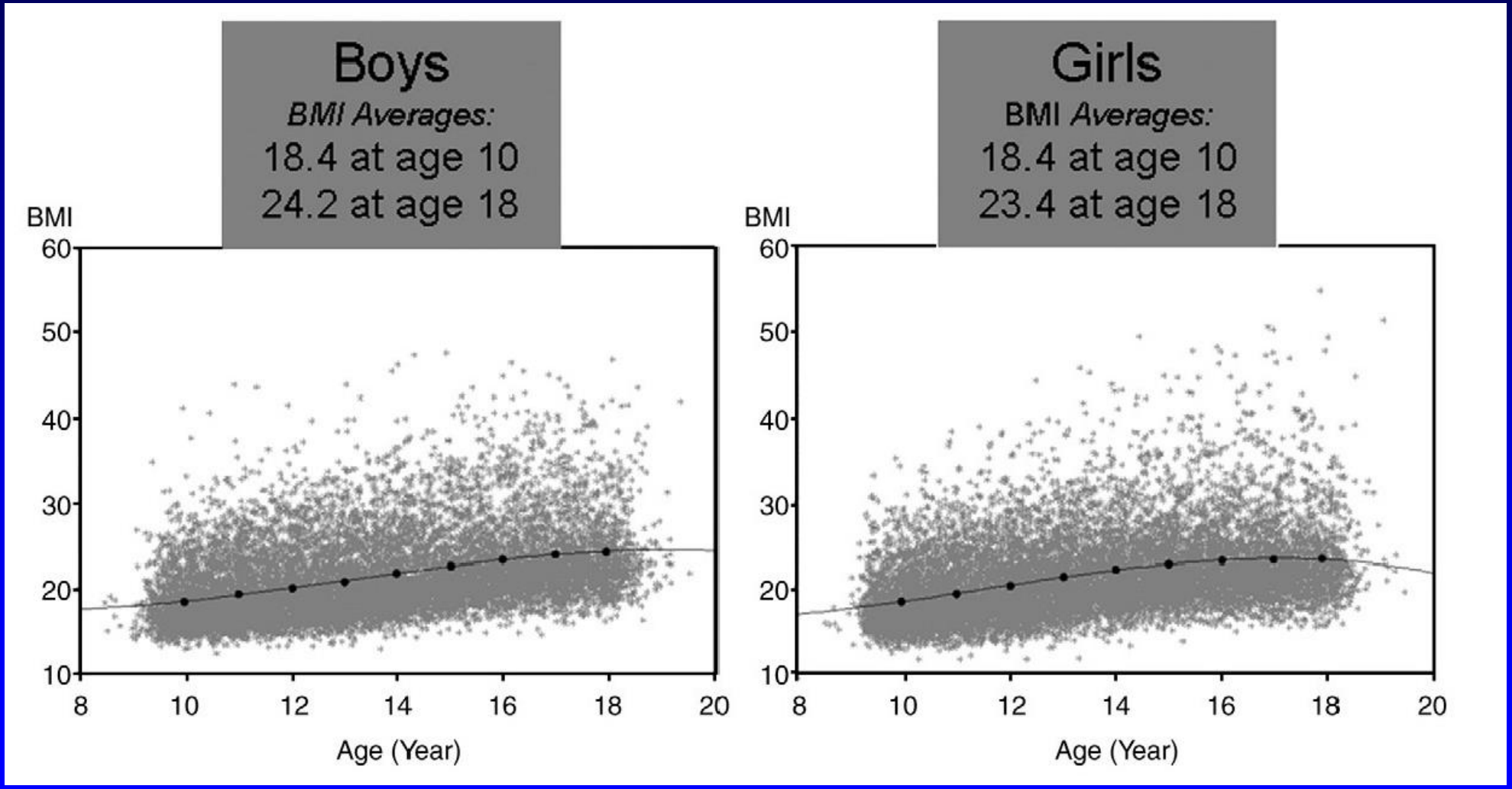
Exposure

- Age 5+
  - Regional pollutants
  - Near-roadway Air Pollution (NRAP)
    - Traffic proximity
    - Traffic density
    - Estimated from land use regression and dispersion modeled NO_x
- Extending back to birth as part of Children's Center

Near-Roadway Obesity Associations

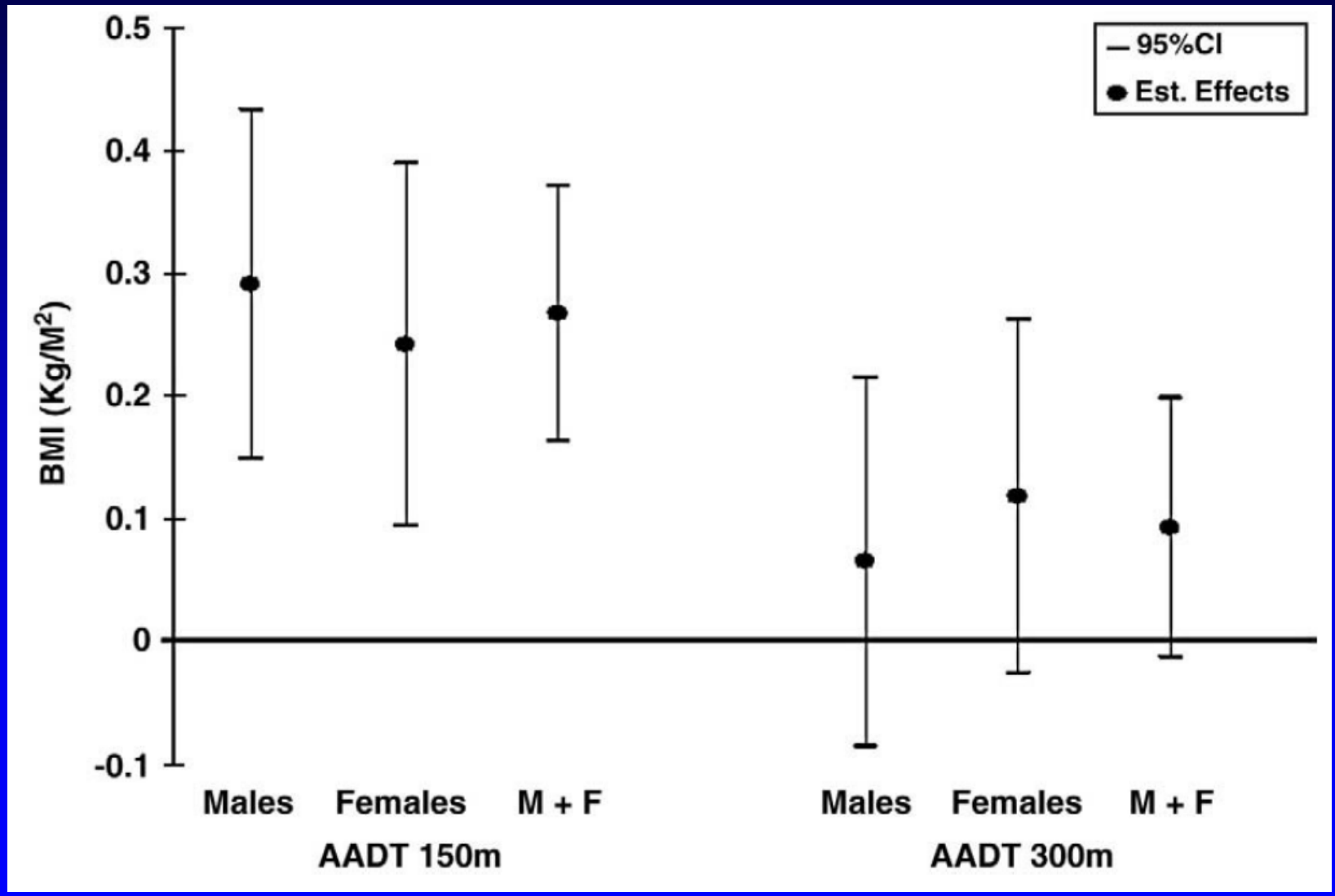
- Near-roadway air pollution (NRAP) associated with obesity or increased body mass index trajectory
  - Jerrett M, McConnell R, et. al. Prev Med 2010; 50 Suppl 1: S50-8
  - Rundle A, Hoepner L. et. al. American J Epidemiol 2012; 175:1163-72
  - Jerrett M, McConnell R, et. al. Environ Health 2014;13: 49.
  - McConnell R, Shen E, et. al. Environ Health Perspectives 2015;123: 360-6

Trajectory of BMI Growth over Adolescence



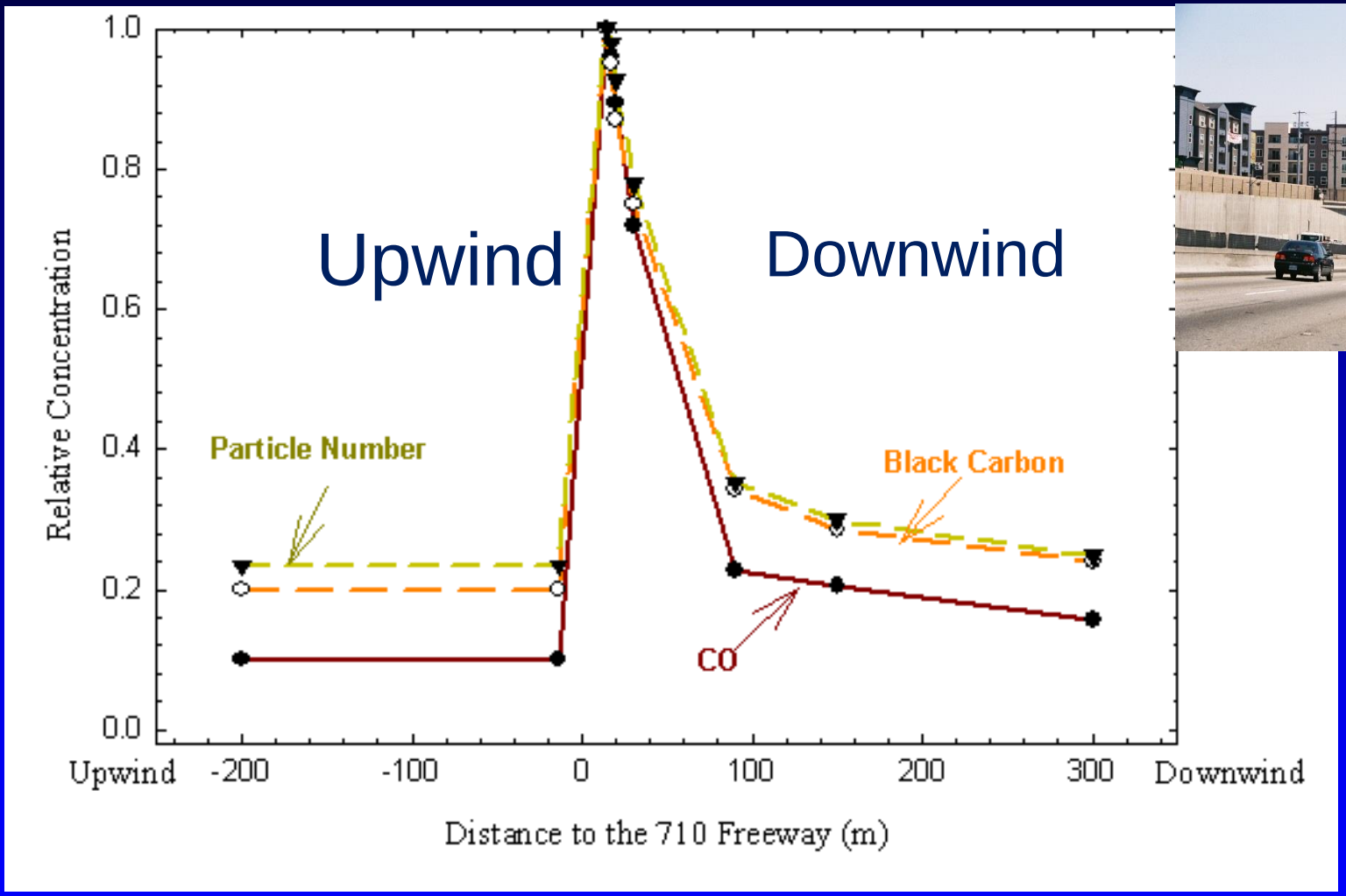
Jerrett M, et. al. *Prev Med.* 2010;50 Suppl 1:S50-58

BMI Association with Traffic Density



Jerrett M, et. al. *Prev Med.* 2010;50 Suppl 1:S50-58

Air Quality is Worse Near a Freeway



Zhu Y, et. al. *J Air Waste Manag Assoc* 2002;52:1032-1042

Zhu Y, et. al. *Environ Sci Technol* 2006;40:2531-2536

BMI Association with Dispersion-modeled Near-roadway Air Pollution

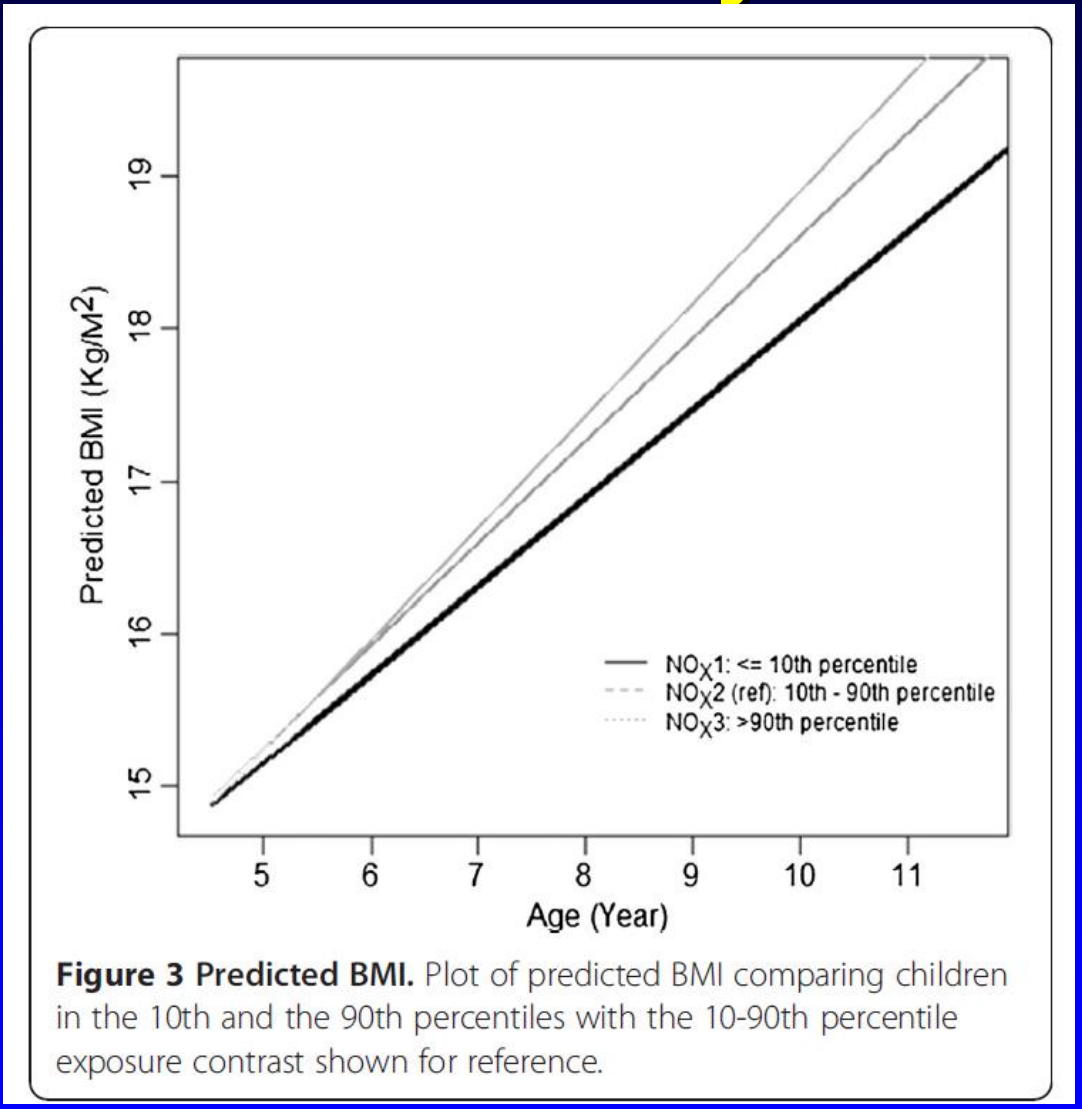
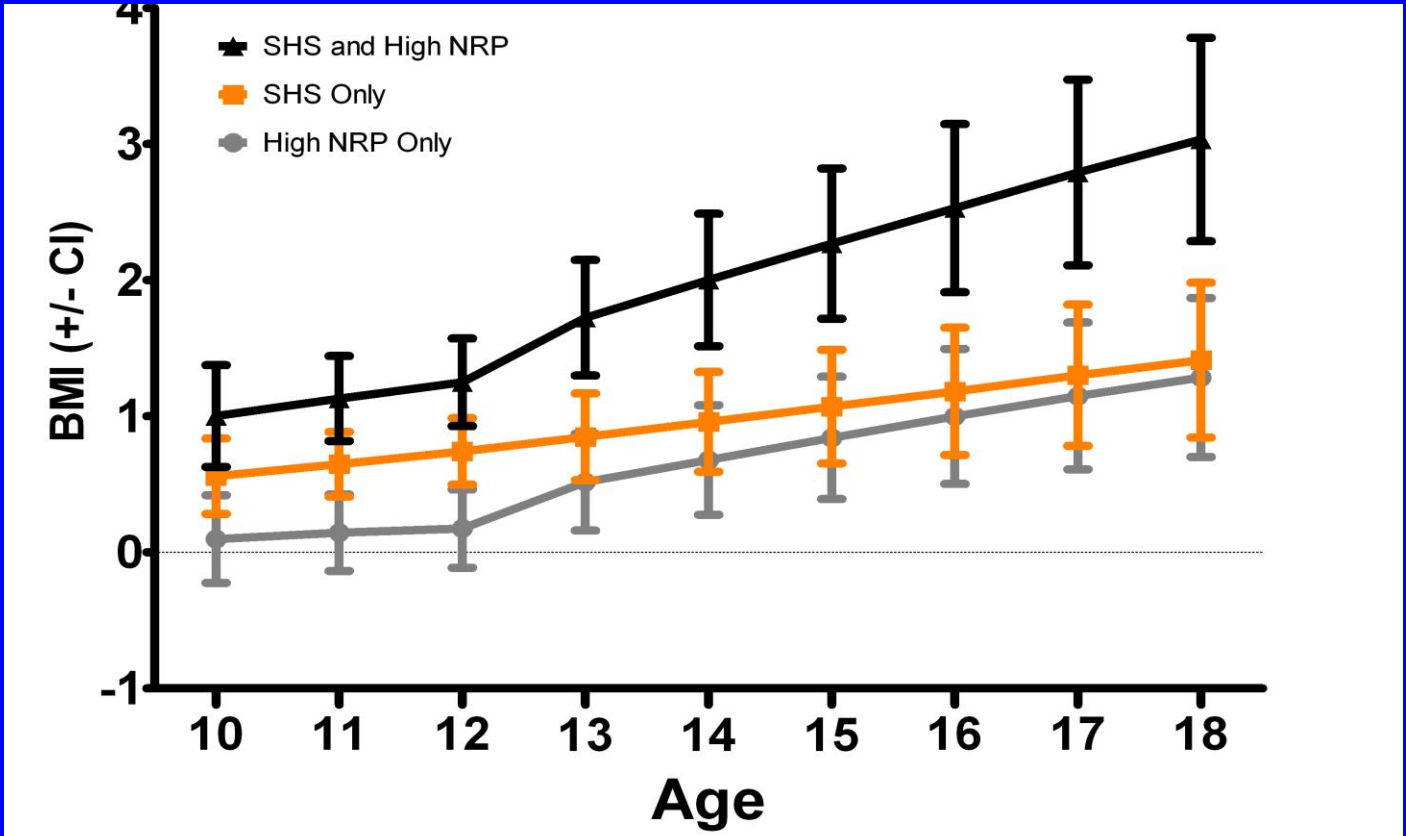


Figure 3 Predicted BMI. Plot of predicted BMI comparing children in the 10th and the 90th percentiles with the 10-90th percentile exposure contrast shown for reference.

Jerrett M, et. al. *Environ Health.* 2014;13:49

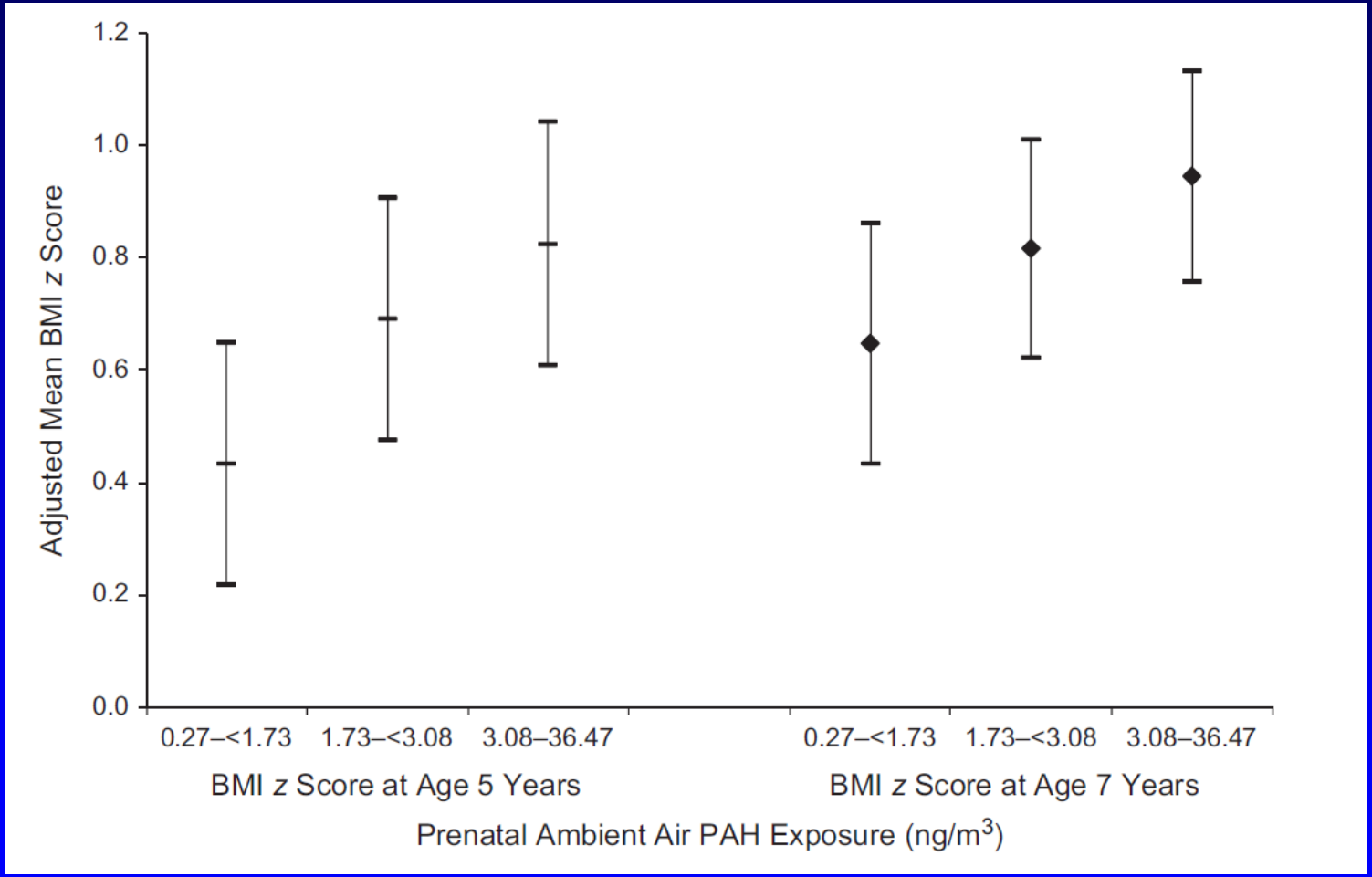
Main and Synergistic Effects of SHS and Pollution on Attained BMI by Age Among Long-term Residents



Difference in mean BMI (95% confidence intervals) at each age was compared with reference exposure category of children with neither exposure (X-axis).

McConnell, et. al. *Environ Health Perspect* 2015;123:360-366

BMI Association with Prenatal Polyaromatic Hydrocarbon (PAH) Exposure



Rundle A, et. al. *Am J Epidemiol.* 2012;175:1163-1172

Implications

- **These are big effects, if causal**
  - **Potentially large public health implications**
- **No nicotine in near-roadway air pollution**
  - **Are there complementary or overlapping pathways that account for SHS effects?**

What Might Cause These Effects?

- **Near-roadway pollution composition is a complex mixture…**
  - **Fresh particle and gaseous combustion products**
  - **Debris from tires and brake wear**
  - **Metals from engine wear**

Tox Studies

- **Prenatal diesel exhaust exposure resulted in increased weight in males in early life and primed female adults for weight gain on high fat diet**
- **Possible mechanism through damage diesel exhaust did to feeding centers in the hypothalamus or to anxiety-associated eating?**

Bolton JL, et. al. Faseb J. 2012; 26: 4743-54.
Bolton JL, et al. *Environ Health Perspect.* 2013;121:1075-1082.
Bolton JL, et. al. *Behav Immun.* 2014;37:30-44

Potential Mechanisms

- **Changes in basal metabolism**
  - **Polyaromatic hydrocarbons inhibit catecholamine-induced lipolysis**
  - **Mitochondrial damage from early life urban particle exposure**
  - **Reduced methylation and increased expression of PPARγ induced by early life particle exposure**
  - **Estrogenic effects of urban particles**
  - **Increased visceral adipose tissue (AT) and AT inflammation resulting from *in utero* PM exposure**

McConnell R, et. al. Peds Obesity 2015

What Characteristics of Fat Predict the Development of Diabetes?

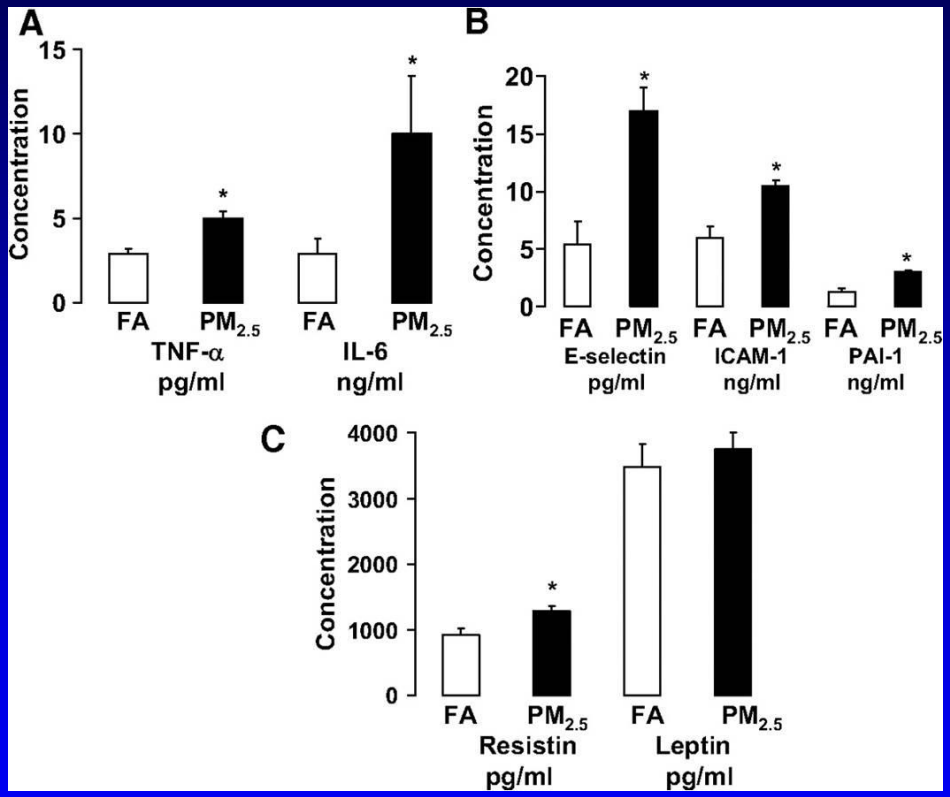
- **Lots of obese people, a relatively small proportion get diabetes…**
  - **Visceral fat (hence waist circumference better predictor than BMI)**
  - **"Ectopic" fat (eg in liver, pancreas…)**
  - **Inflammation**
  - **Insulin resistance**

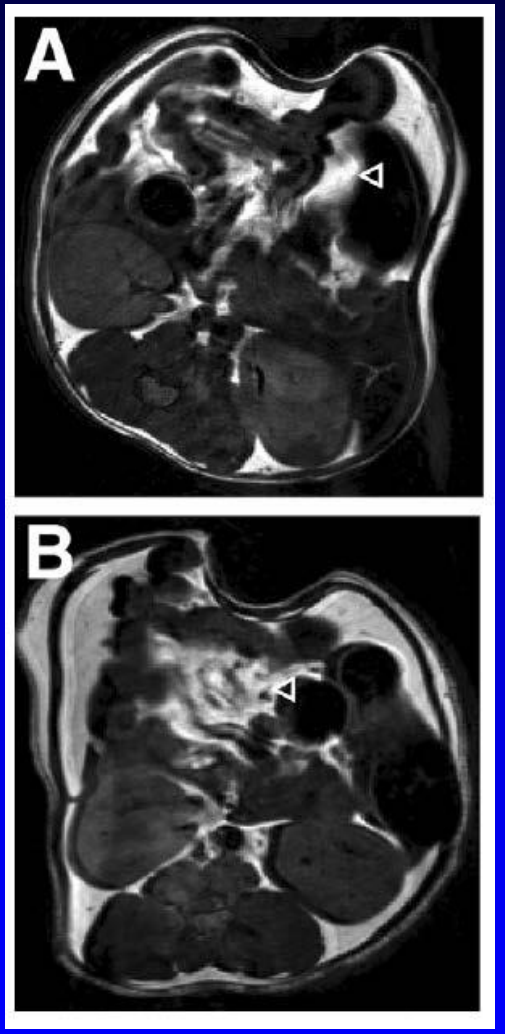
Kolak M, et al. *Diabetes*. 2007;56(8):1960-1968.
Olefsky JM, et. al. *Annu Rev Physiol*. 2010;72:219-246.
Apovian CM, et al. *Arterioscler Thromb Vasc Biol*. 2008;28(9):1654-1659.

Ambient Air Pollution Exaggerates Adipose Inflammation and Insulin Resistance in a Mouse Model of Diet-Induced Obesity

Sun Q. Circulation 2009

Increased systemic adipokines and inflammatory biomarkers



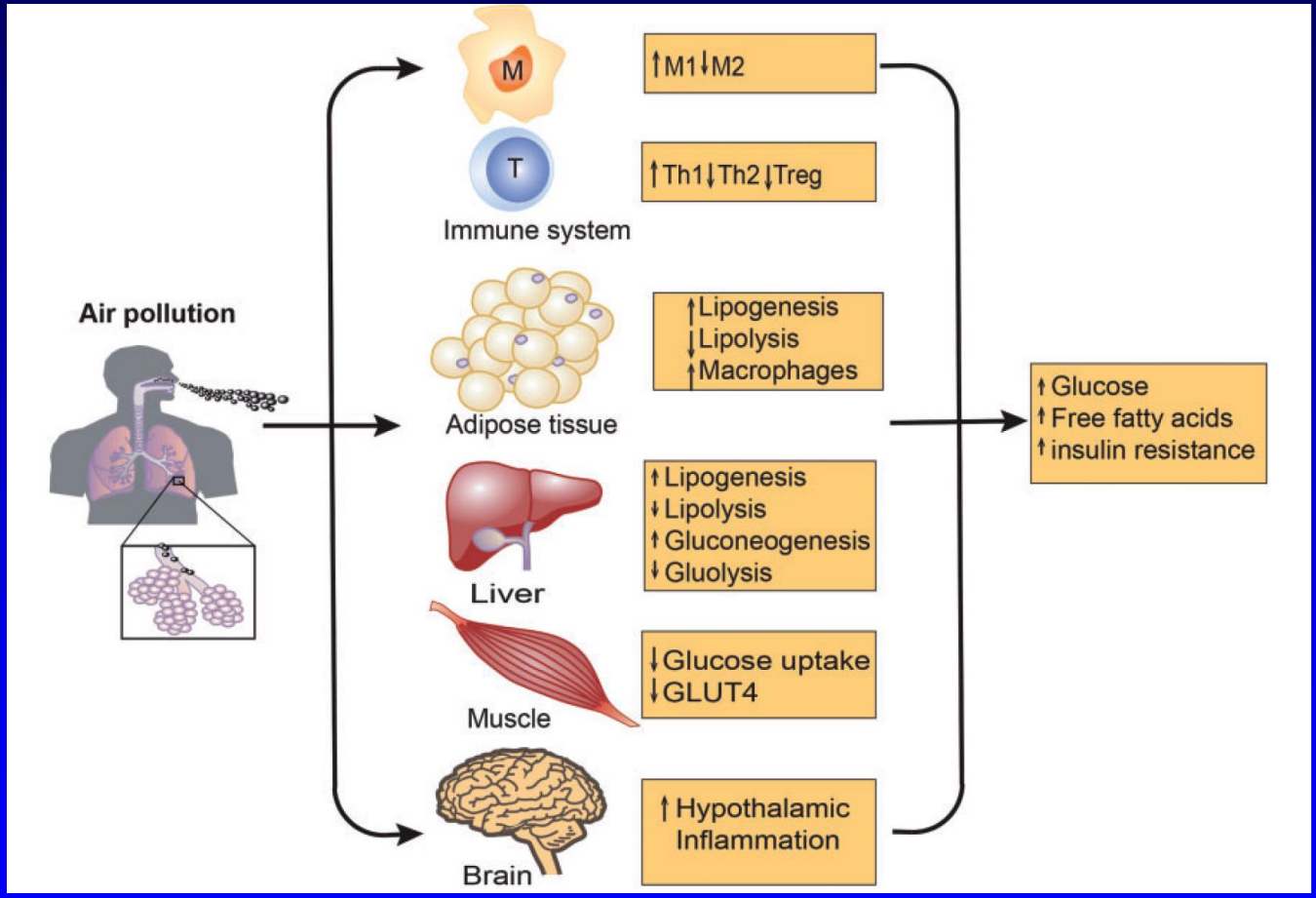


- **$PM_{2.5}$ also induced:**
  - **Larger adipocytes**
  - **Macrophage infiltration**
  - **Insulin resistance**

Rao X, et. al. *Toxicol Sci.* 2015;143:231-241

Sun Q, et. al. *Circulation.* 2009;119:538-54

Mechanisms for Development of Metabolic Outcomes



Rao X, et. al. *Toxicol Sci.* 2015;143(2):231-241.

CHILDREN'S CENTER RESEARCH QUESTIONS

- Does *in utero* and childhood near-roadway air pollution (NRAP) exposure cause childhood obesity? If so, what are the mechanisms?
- Does NRAP affect fat distribution, ectopic fat and adipose tissue inflammation?
- Does NRAP affect glucose homeostasis, lipid profile, systemic inflammation and the metabolic syndrome?
- Are effects of NRAP on metabolic and inflammatory outcomes the result of changes in fat distribution and/or adipose tissue inflammation?

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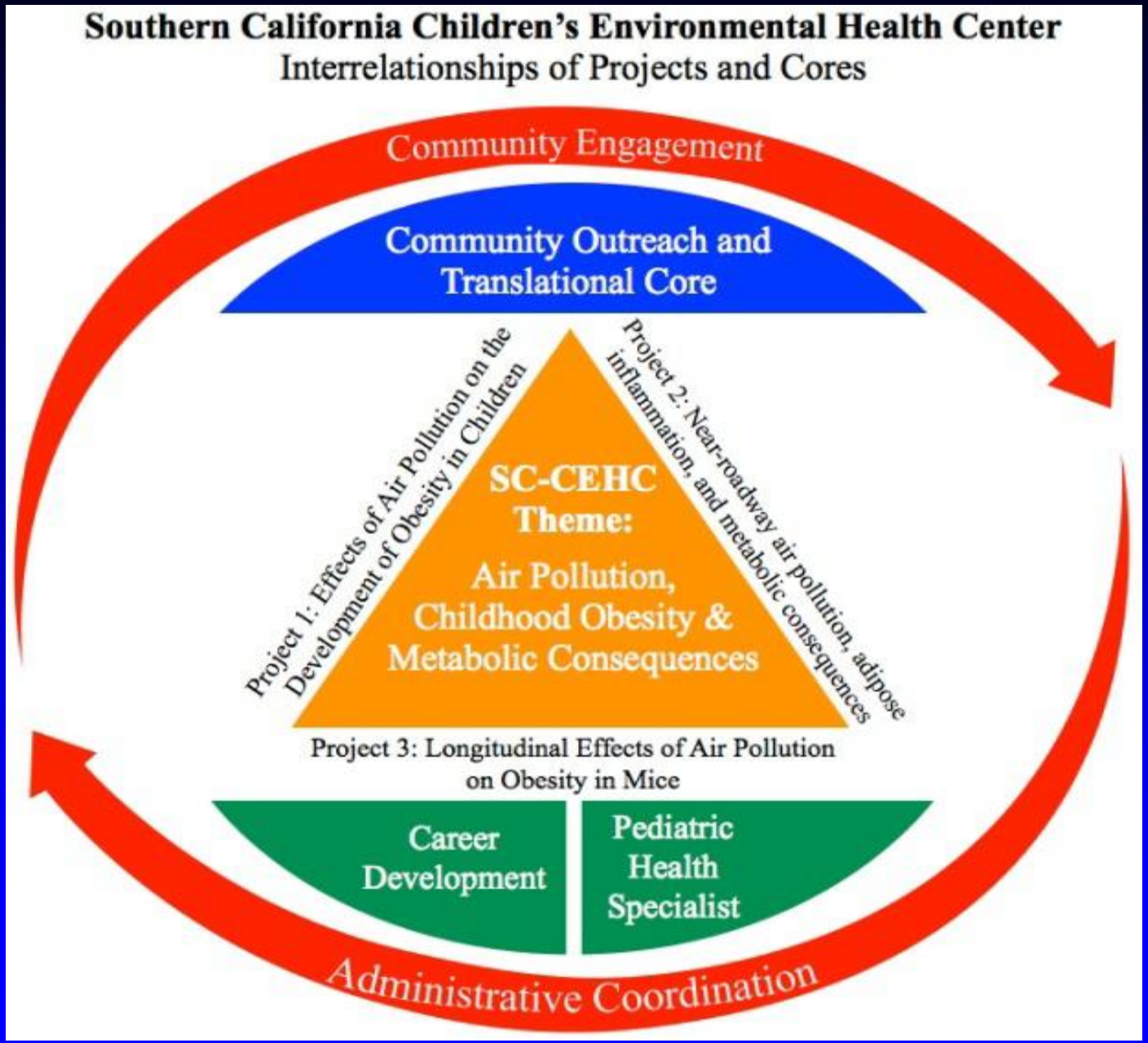
Interrelationships of Projects and Cores



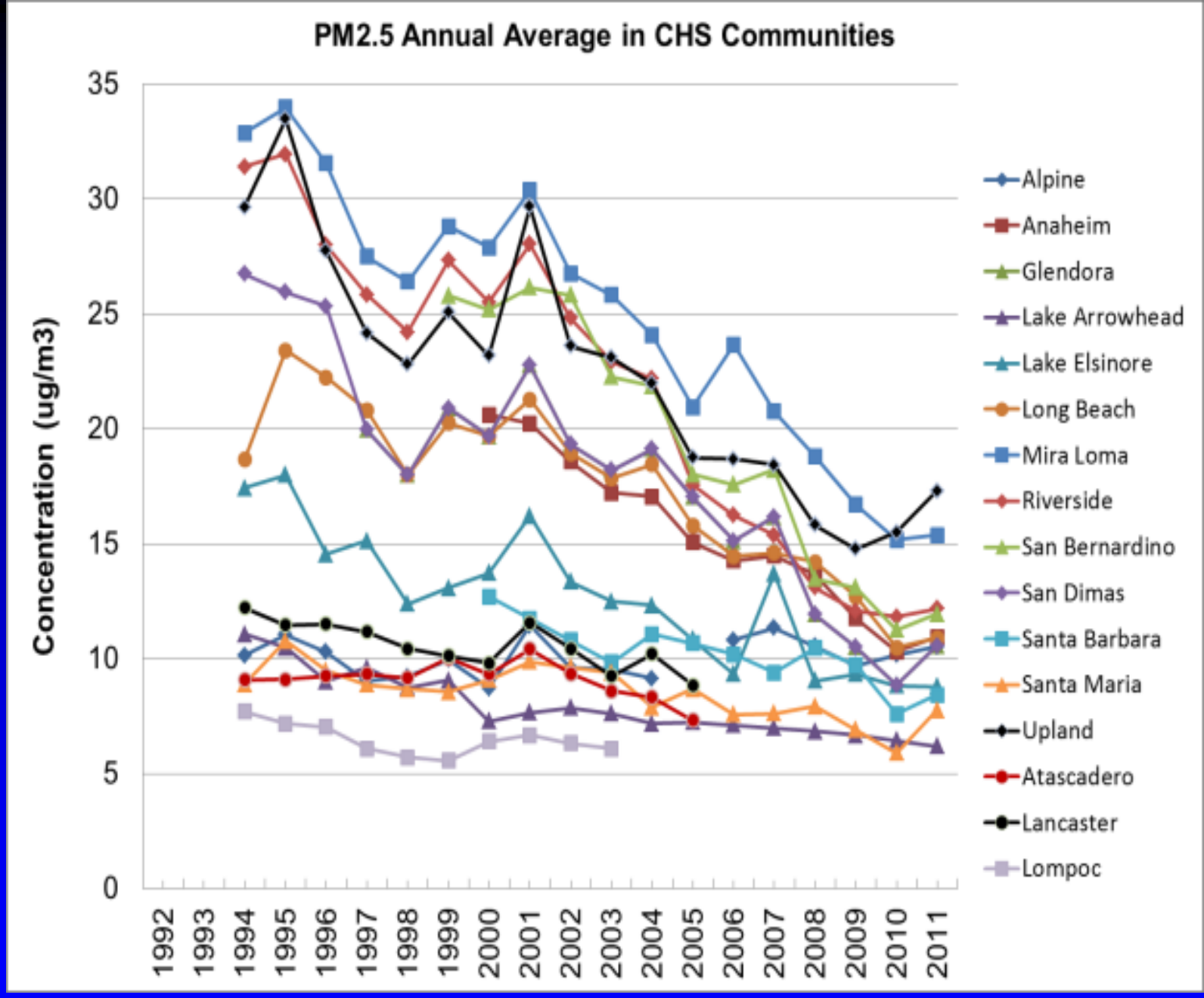
Potential for Harm Reduction?

- **Good public policy to reduce ambient levels**

  Lurmann F, et. al. *Journal of the Air & Waste Management Association.* 2015;65:324-335
- **Park siting, zoning restrictions near freeways**
- **Outdoor activity not coincident with pollution**
  - **Exercise! …but not next to a freeway or busy road, or during high pollution times (eg. ozone in mid-day, PM in early morning)**
  - **Unintended negative consequences from reduced physical activity?**
- **?Filters**
- **?Chemoprevention, eg antioxidants**

Laumbach R, et. al. *Journal of thoracic disease* 2015;7:96-107

Average Levels of Particles ($PM_{2.5}$) ***declined*** **13% to 54%**



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Questions?

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