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
  - Gut microbiome
  - Built environment through its role in exercise and food consumption
  - In utero 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

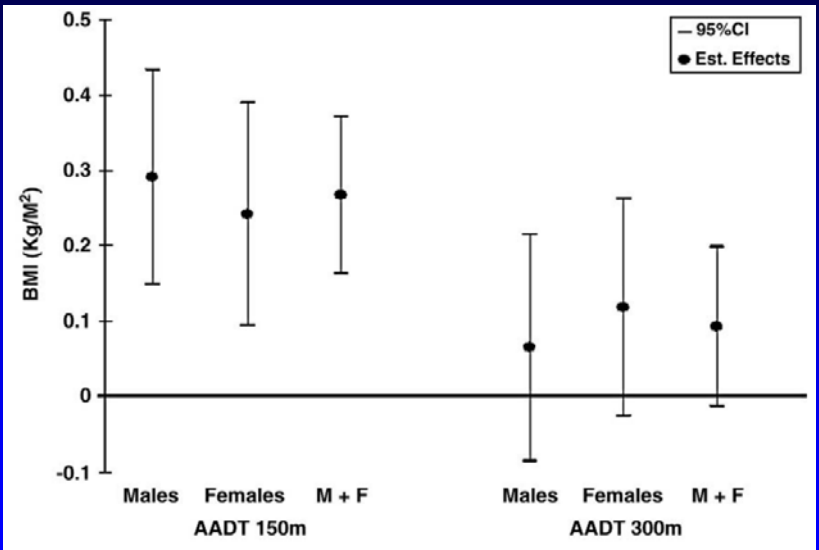
Exposure

- 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 ia Children's Center

Near-Roadway Obesity Associations

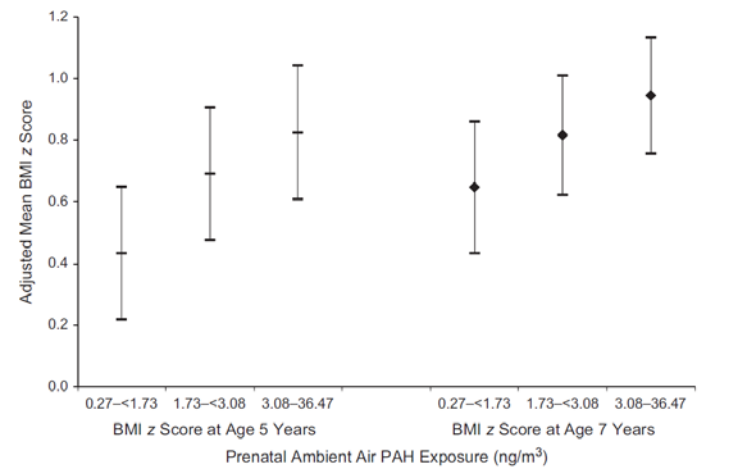
- Near-roadway air pollution (NRAP) associated with obesity or increased body mass index trajectory
  - Jerrett M, McConnell R, et. al. Prev Med 2010; 50 Suppl 1: S50-8
  - Rundle A, Hoepner L. et. al. American J Epidemiol 2012; 175:1163-72
  - Jerrett M, McConnell R, et. al. Environ Health 2014;13: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

BMI Association with Traffic Density



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

BMI Association with Prenatal Polyaromatic Hydrocarbon (PAH) Exposure



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

BMI Association with Dispersion-modeled Near-roadway Air Pollution

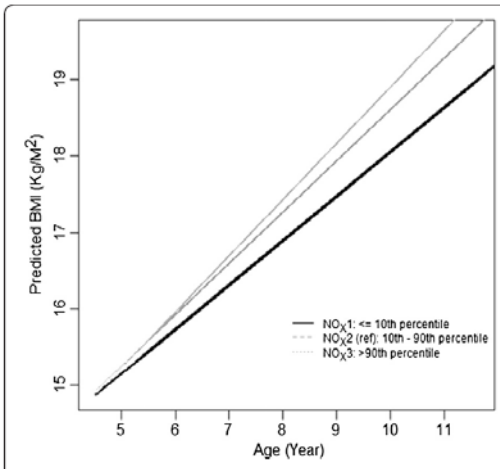
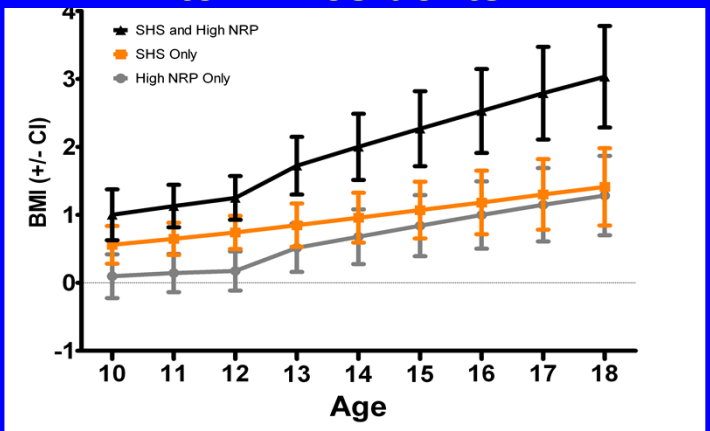


Figure 3 Predicted BMI. Plot of predicted BMI comparing children in the 10th and the 90th percentiles with the 10-90th percentile exposure contrast shown for reference.

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

Main and Synergistic Effects of SHS and Pollution 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

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

Air Pollution and Diabetes

Table 4. Sensitivity analyses and heterogeneity measures.

Analyses	Population	NO_2 OR (95% CI)	Heterogeneity measures [I^2 (%); *p*-value; Tau^2]	$PM_{2.5}$ OR (95% CI)	Heterogeneity measures [I^2 (%); *p*-value; Tau^2]
Main model (random effects)	Males	0.99 (0.93, 1.07)	0; 0.744; 0	1.04 (0.93, 1.17)	0; 0.486; 0
	Females	1.15 (1.05, 1.27)	46.1; 0.135; 0.0042	1.14 (1.03, 1.26)	0; 0.405; 0
	Overall	1.08 (1.00, 1.17)	58.4; 0.025; 0.0063	1.10 (1.02, 1.18)	0; 0.473; 0
Studies assessing air pollution before DM diagnosis	Males	1.02 (0.92, 1.13)	NA; NA; 0	1.04 (0.93, 1.17)	0; 0.486; 0
	Females	1.20 (1.10, 1.30)	12.5; 0.285; 0.0006	1.13 (1.02, 1.25)	0; 0.344; 0
	Overall	1.12 (1.05, 1.19)	69.8; 0.036; 0.008	1.09 (1.01, 1.18)	0; 0.489; 0
Studies including both men and women	Males	0.99 (0.93, 1.07)	0; 0.744; 0	1.04 (0.93, 1.17)	0; 0.486; 0
	Females	1.11 (1.01, 1.23)	30.2; 0.238; 0.0023	1.13 (1.02, 1.25)	0; 0.344; 0
	Overall	1.05 (0.98, 1.12)	34.9; 0.175; 0.0024	1.09 (1.01, 1.18)	0; 0.489; 0
Only longitudinal studies	Males	1.02 (0.92, 1.13)	NA; NA; 0	1.04 (0.93, 1.17)	0; 0.486; 0
	Females	1.20 (1.10, 1.30)	12.5; 0.285; 0.0006	1.14 (1.03, 1.26)	0; 0.405; 0
	Overall	1.12 (1.05, 1.19)	69.8; 0.036; 0.008	1.10 (1.02, 1.18)	0; 0.473; 0
Meta-analysis using fixed-effects model	Males	1.00 (0.93, 1.07)	0; 0.744	1.04 (0.93, 1.17)	0; 0.486
	Females	1.15 (1.07, 1.23)	46.1; 0.135	1.14 (1.03, 1.26)	0; 0.405
	Overall	1.07 (1.02, 1.13)	58.4; 0.025	1.10 (1.02, 1.18)	0; 0.473

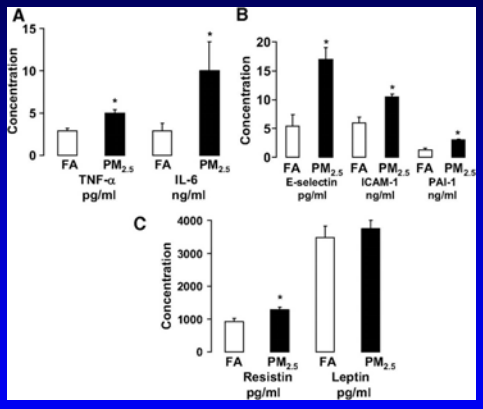
NA, not applicable. I^2 is the proportion of total variability explained by heterogeneity. Tau^2 is a measure of among-study variance.

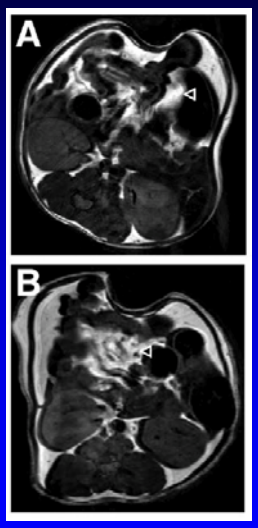
Eze IC, et. al. *Environ Health Perspect.* 2015;123:381-389

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





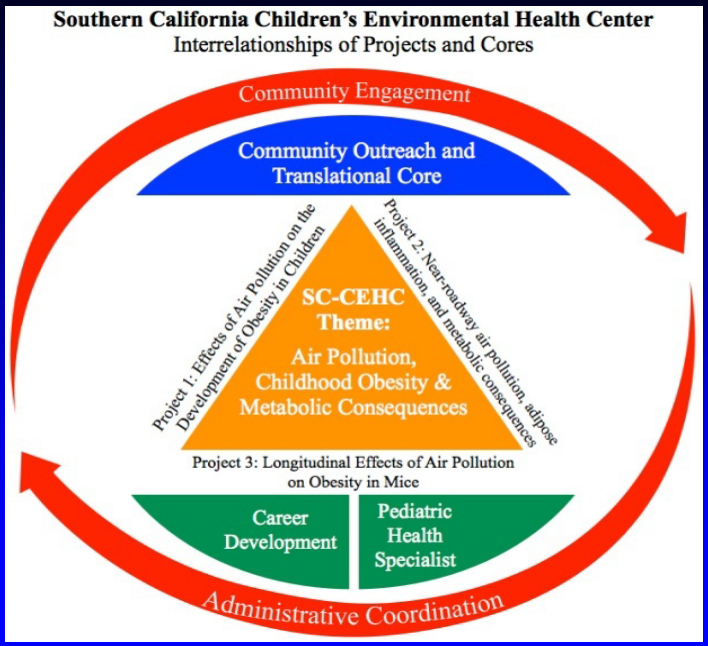
- **$PM_{2.5}$ also induced:**
  - **Larger adipocytes**
  - **Macrophage infiltration**
  - **Insulin resistance**

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

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

Open Questions

- Does air pollution cause obesity?
- Are there different effects of near-roadway and regional pollutant mixtures?
- What is the mechanism(s) for these effects?
- How do environmental obesogens interact with diet and physical activity?



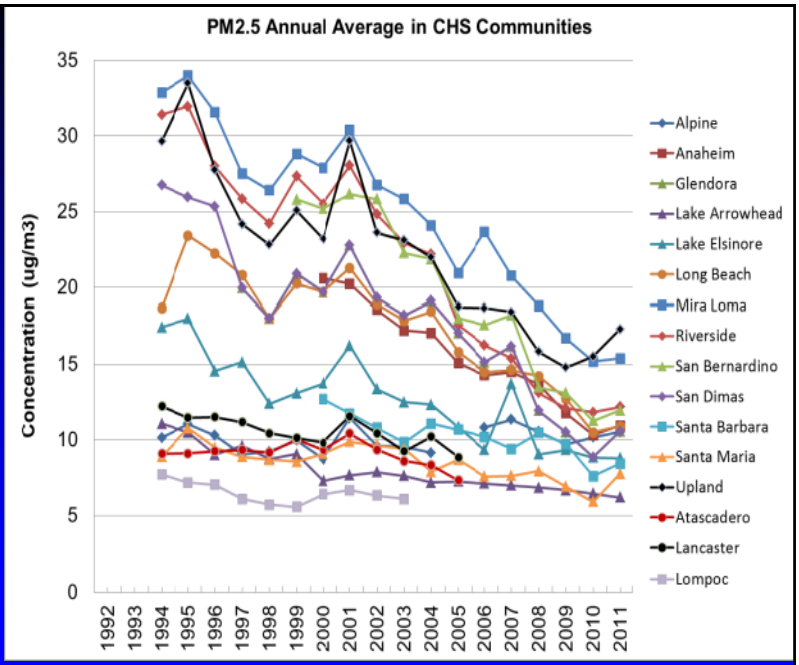
Potential for Harm Reduction?

- Good public policy to reduce ambient levels

  Lurmann F, et. al. *Journal of the Air & Waste Management Association.* 2015;65:324-335
- Outdoor activity <u>not</u> 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?
- Park siting, zoning restrictions near freeways
- ?Filters
- ??Chemoprevention, eg antioxidants

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

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



Lurmann F, et. al. *Journal of the Air & Waste Management Association.* 2015;65:324-335

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Questions?

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