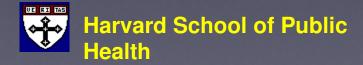
# Particles and Health Policy Relevant Science

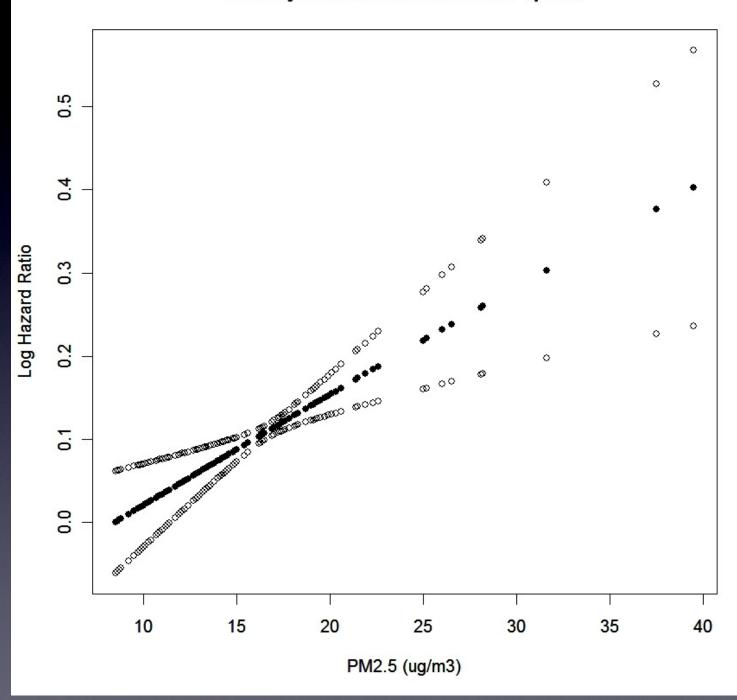
Joel Schwartz



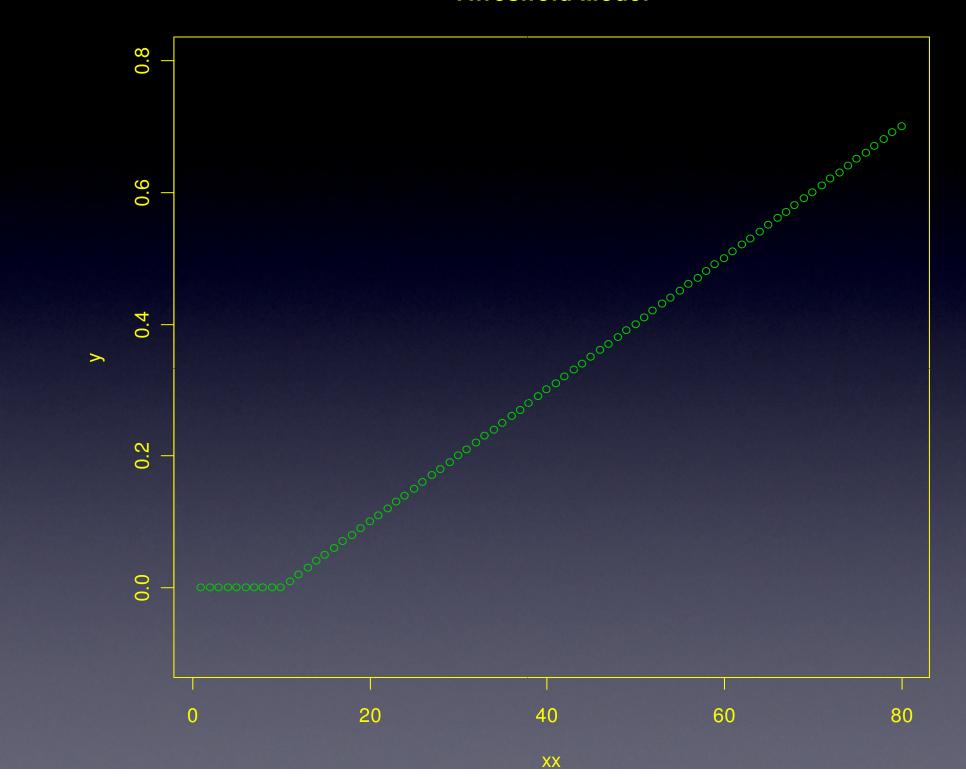
## Policy Questions

- Dose Response below 15 μg/m³?
- Does Health Really Improve when you Change Particle Concentrations?
- Are there Biologically Plausible Mechanisms?
- •New Outcomes/Mechanisms?

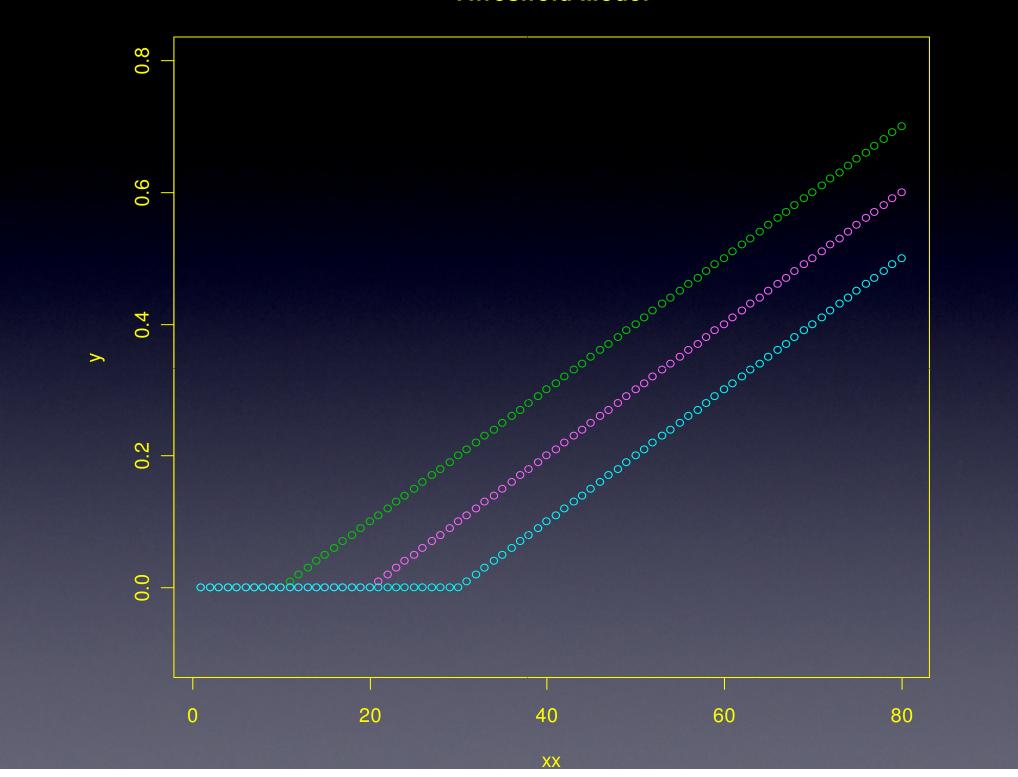
#### Six City Cohort with Penalized Spline



#### **Threshold Model**

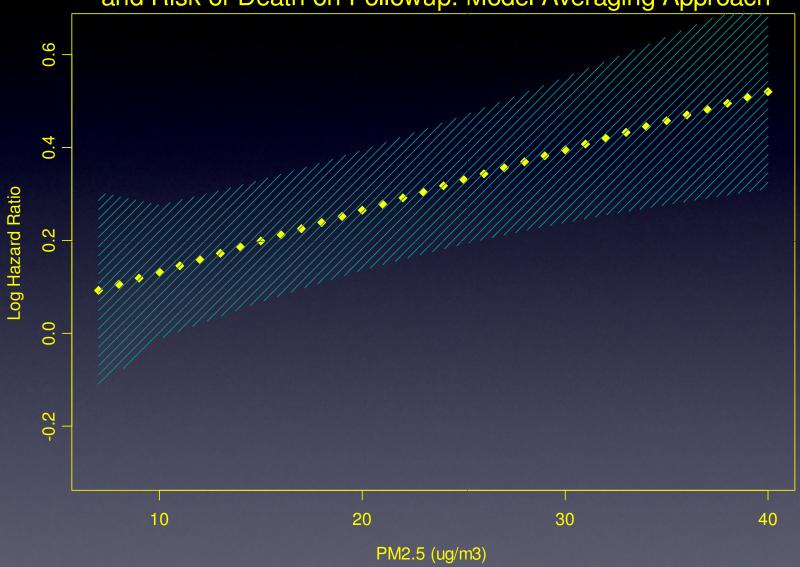


#### **Threshold Model**



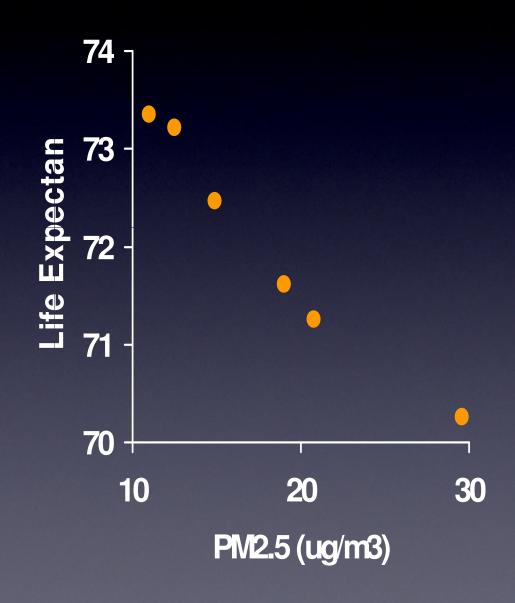
#### Six City Cohort Study

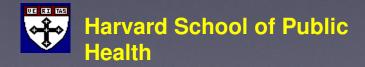
Concentration-Response Relation between PM2.5 and Risk of Death on Followup: Model Averaging Approach



### Harvard Six Cities Mortality

- Survival Analysis
- -Adjustment
- •Age, Sex
- Cigarette Smoking
- Occupation
- Education
- Obesity
- Chronic Disease

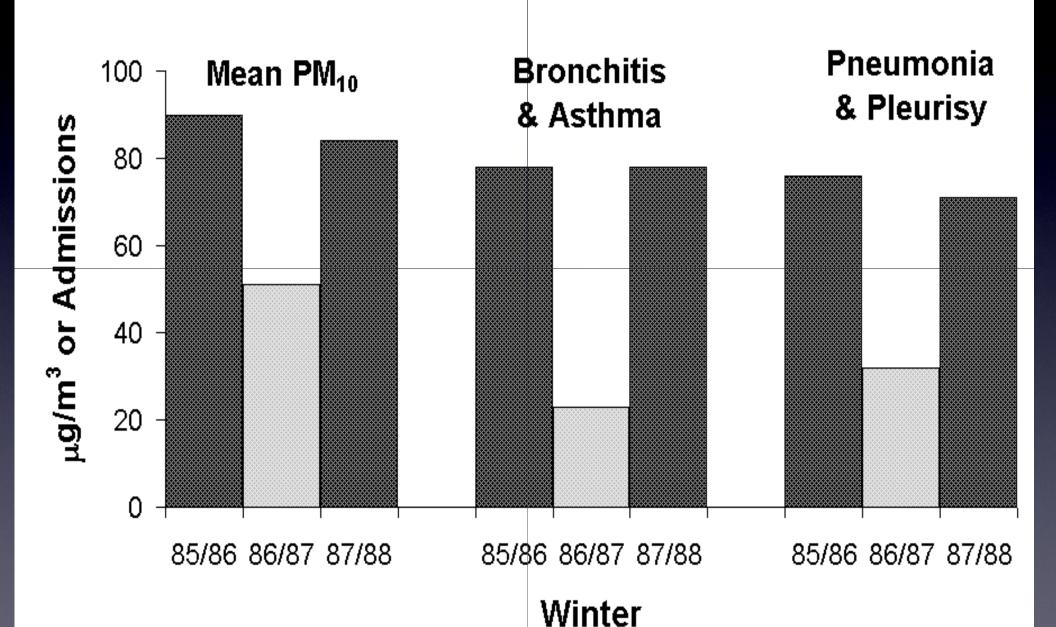




### What happens if we Improve Air Quality?



## Utah Hospital Admissions Children 0-17 Year

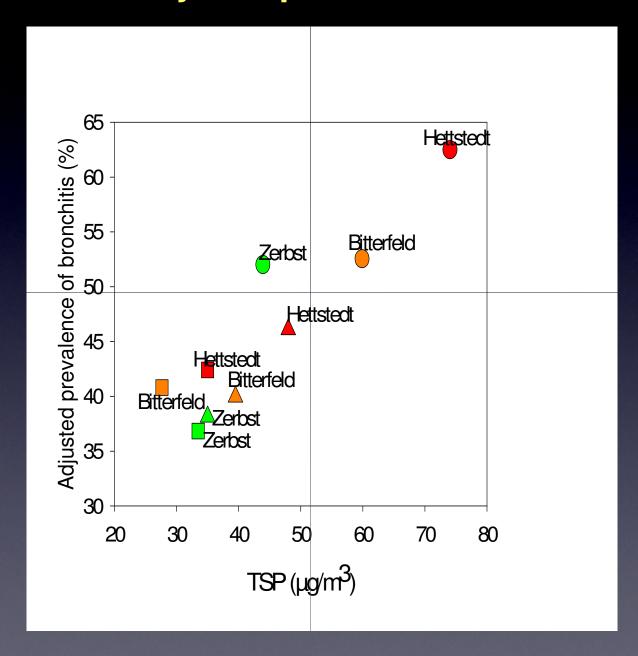


Pope, Amer J Public Health 1989; 79: 623

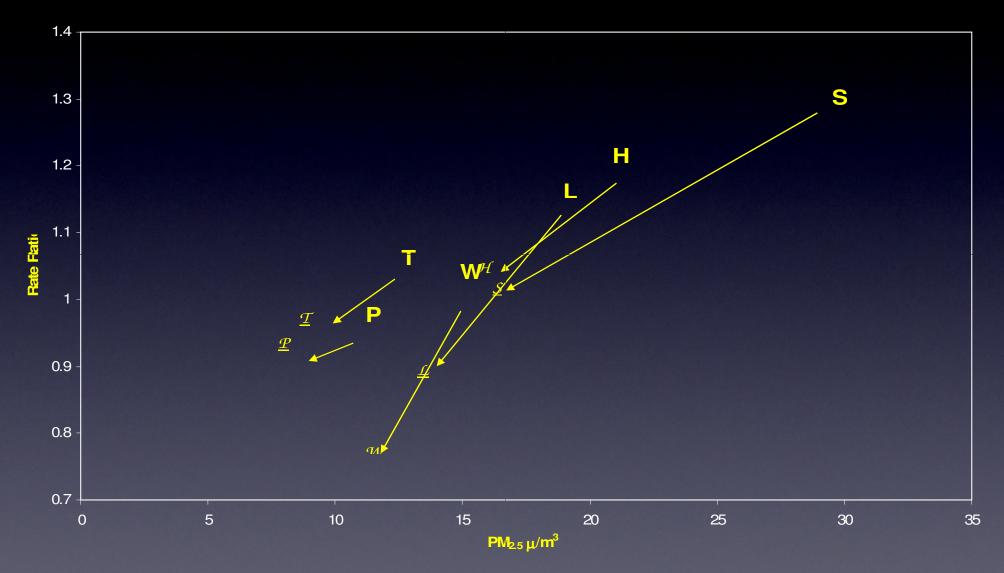
## Pope Smelter Strike

- •Smelter Strike Reduced Sulfates in U.S. Southwest by ~60%
- •2.5 ug/m³ decrease in Sulfates
- •2.5% Reduction in Mortality
- Avol Lung Function Growth in Southern California
   Children's Cohort
- —Children who moved to more polluted areas had slower growth
- —Children who moved to less polluted areas had faster growth

## Adjusted prevalence of bronchitis in children and annual TSP two years prior to the examination



## Relative Risk of Death in Six US Cities during Two Follow-up Periods

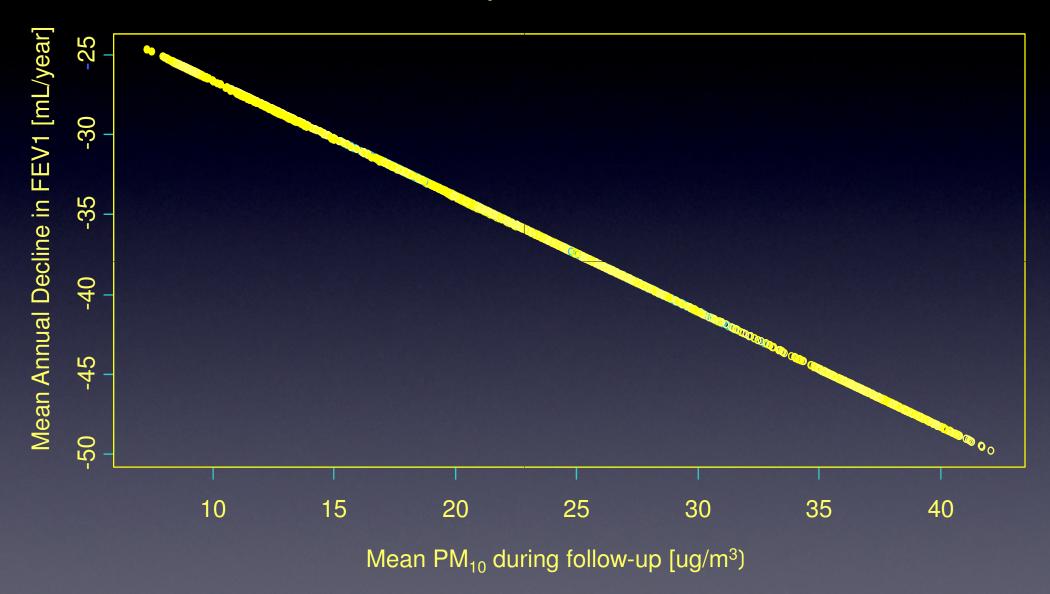




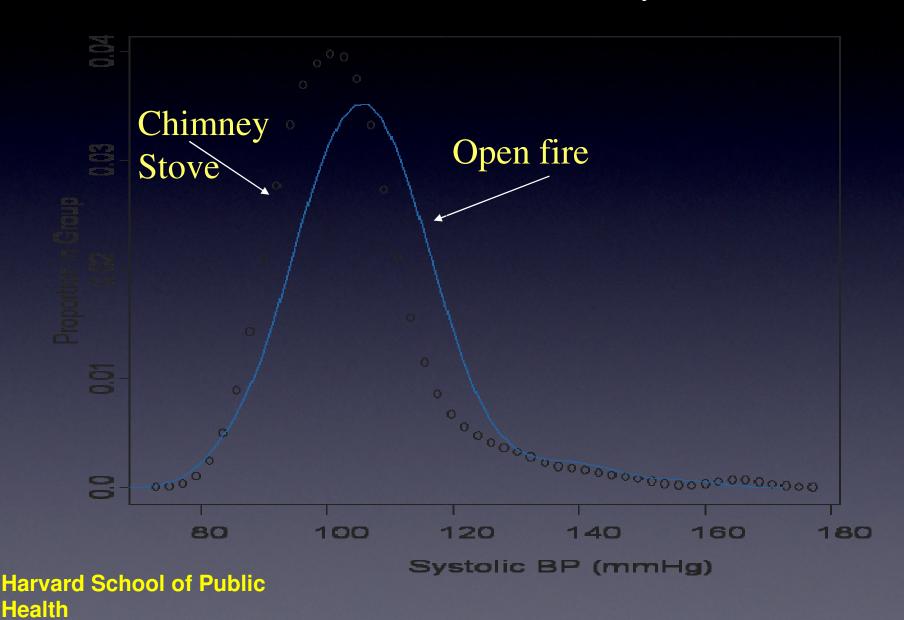
### Lung Function Change

- •Avol (2001) looked at children in Southern California Children's Study Cohort
- who moved
- —If moved to less polluted area, growth accelerated
- —If moved to more polluted area, it slowed
- Downs (2007) looked at adults
- —Drop in pollution at their address over 10 years predicted slower decline in lung function

## Annual Decline In Lung Function Vs PM in Interval: 11 Year Followup of SAPALDIA Cohort

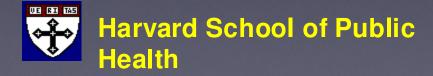


#### Randomized Trial: Effect of Stove on Distribution of Systolic Blood Pressure



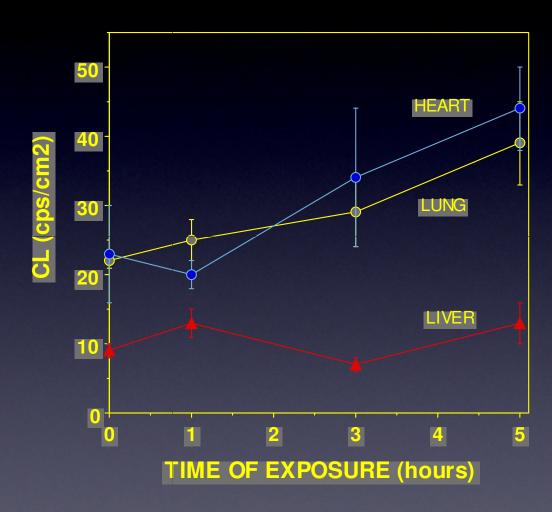
## Mechanism

Oxidative Stress



#### Particles Induce oxidants in the Heart and Lung

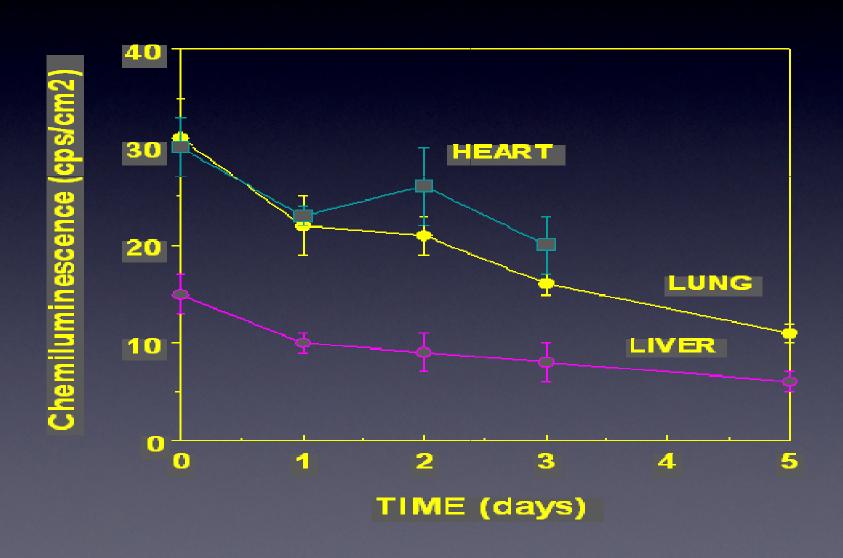
—Gurguera et al EHP 2003)



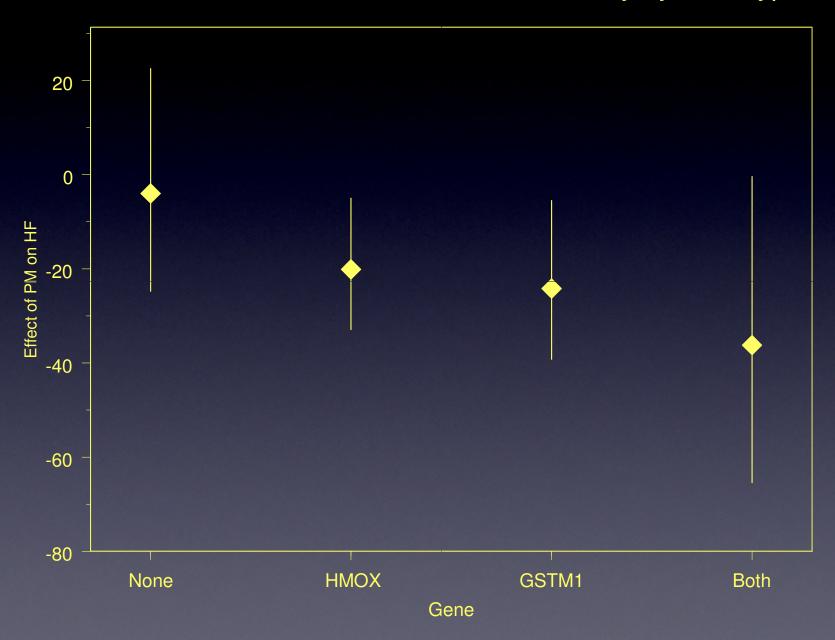


Chemiluminescence (CL) of lung, heart, and liver after various durations of Particle exposure.

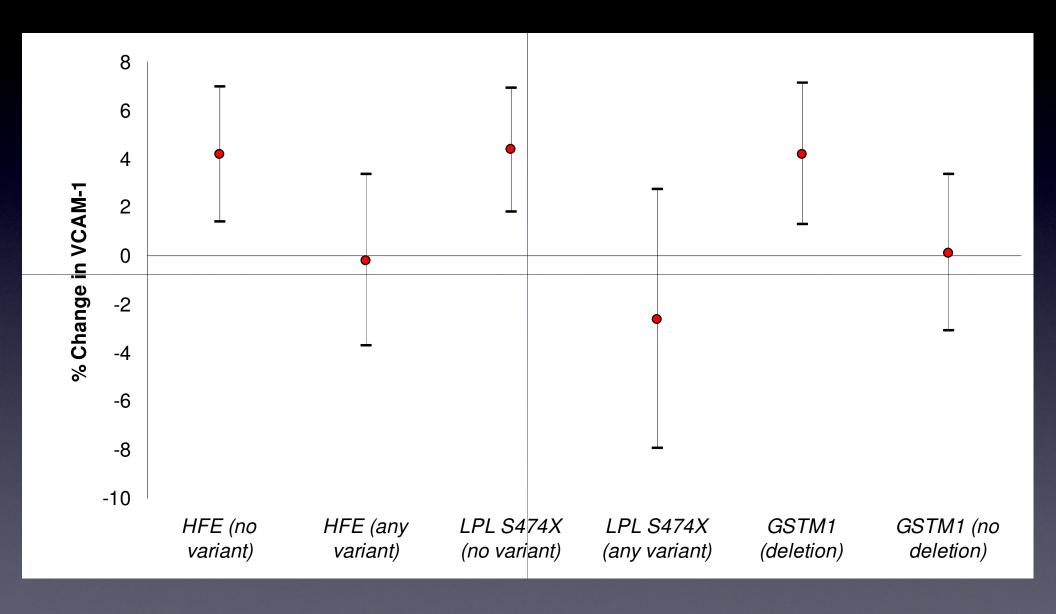
Removal of Particles from the air results in a decrease in the level of oxidants in the Body (Evelson & Gonzalez-Flecha, Biochim Biophys Acta, 2000)



#### Effect of Particles on Heart Rate Variability by Genotype



## Effect of Particles on VCAM-1 by Genotype

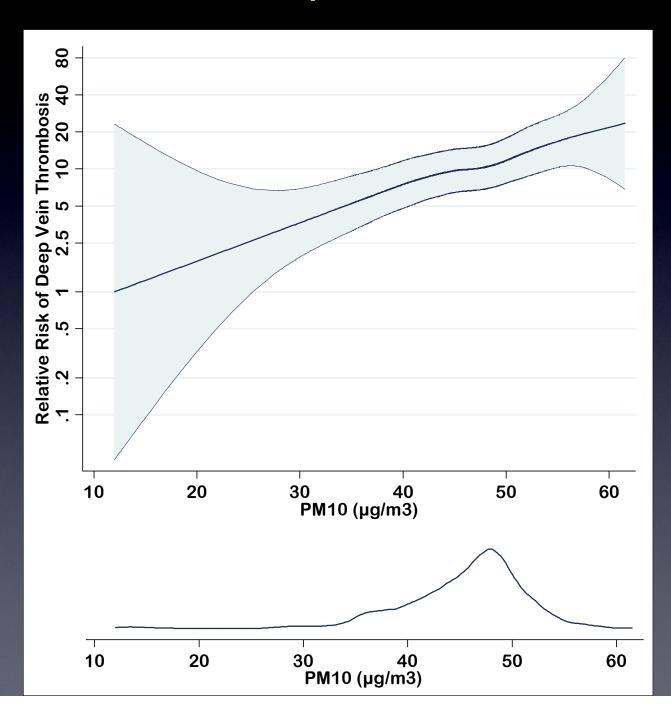


## Mechanism

Thrombosis



### Particles and Deep Vein Thrombosis



### **New Outcomes**

- Cognitive Effects
- Epigenetic Effects

## Association of Traffic Particles with Children's Cognitive Performance

	Vocabulary		Matrices		Composite	
	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI
		-5.3,		-7.7, -		-6.6, -
BC (adjust demographics)	-2.0	1.3	-4.2	0.7*	-3.4	0.3*
BC (adjust above + UTS		-5.3,		-7.5, -		-6.4, -
+SHS)	-2.0	1.4	-4.0	0.4*	-3.3	0.1*
		-5.4,		-7.6, -		-6.5, -
BC (adjust above + BW)	-2.0	1.3	-4.0	0.5*	-3.3	0.2*
		-5.5,		-7.6, -		-6.6, -
BC (adjust above + BLL)	-2.2	1.1	-4.0	0.5*	-3.4	0.3*

Above models adjusted for standard control variables: age, gender primary language spoken at home and mothers education

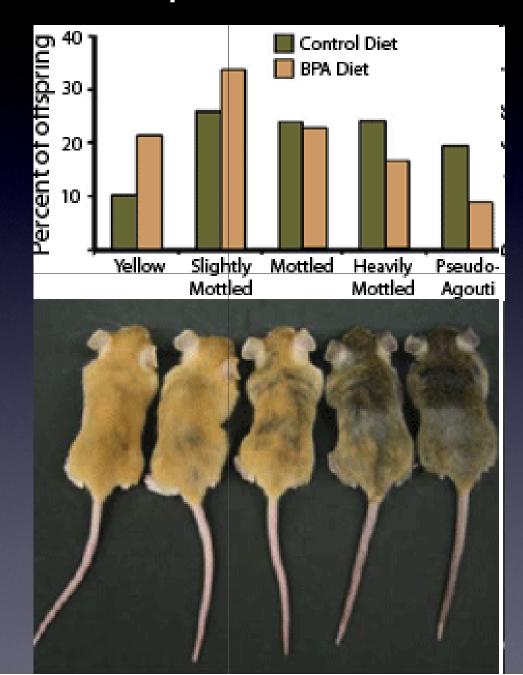
BC=black carbon; UTS=In-Utero tobacco smoke exposure; SHS=Second Hand Smoke;

BW=birthweight; BLL=blood lead level; IQR=inter quartile range

## Genetically Identical!



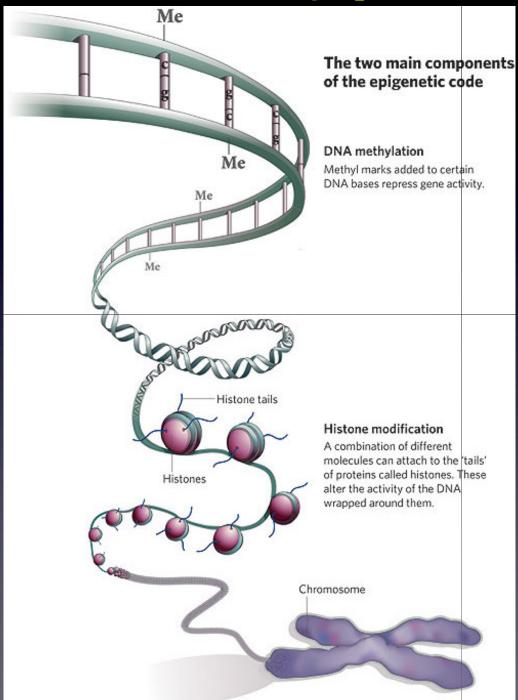
## Bisphenol A

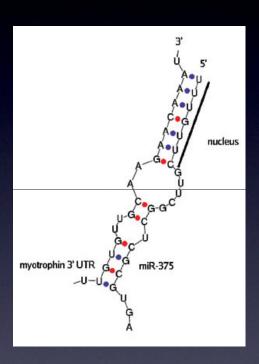


## The Sins of the Mothers are Visited on their Children unto Seven Generations

Sperm Motility Reductions Passed by Female Line to Multiple Generations of Exposed Mice Epigenetic, not Genetic

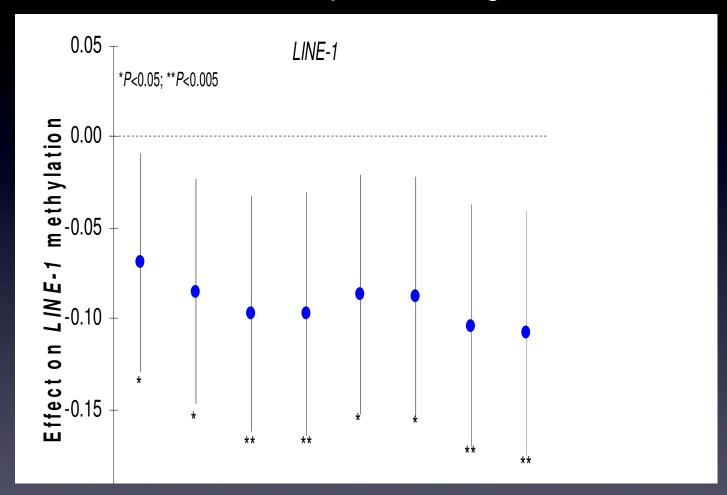
## **Epigenetic Marks**





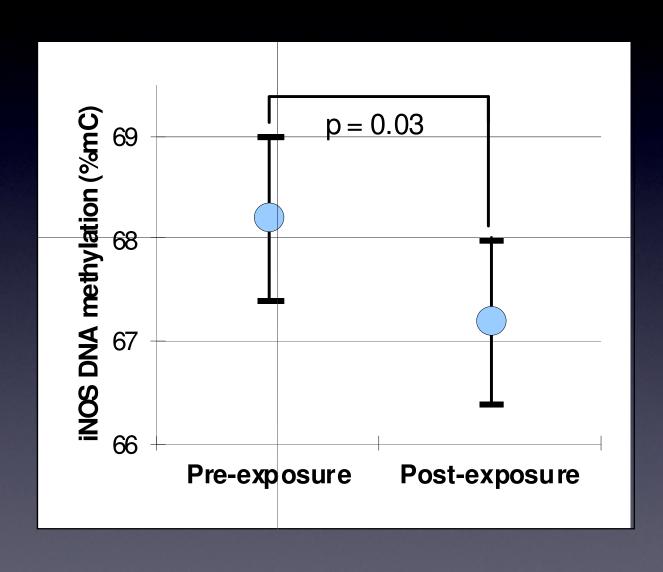
microRNAs (snRNAs)

#### Effect of black carbon exposure on global DNA methylation



Black carbon effect is reported as standardized coefficients (circles) and 95% CIs (bars) from multivariable models adjusted for age, BMI, smoking, pack-years, statin use, fasting glycemia, diabetes, % lymphocytes and neutrophils in blood count, day of the week, season, temperature

## Tarantini, 2008



### **Particles**

- Kill people at concentrations below the NAAQS
- Reducing Exposure Leads to a Rapid Increase in Life Expectancy
- There are Biologically Plausible Pathways
- Things Could be Worse than we Think