

# Pediatric Environmental Health: Why should we care?

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# Disclaimer & Acknowledgment

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- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this presentation
- I receive funding from Meridian Biosciences for a clinical trial unrelated to today's presentation
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# Learning Objectives

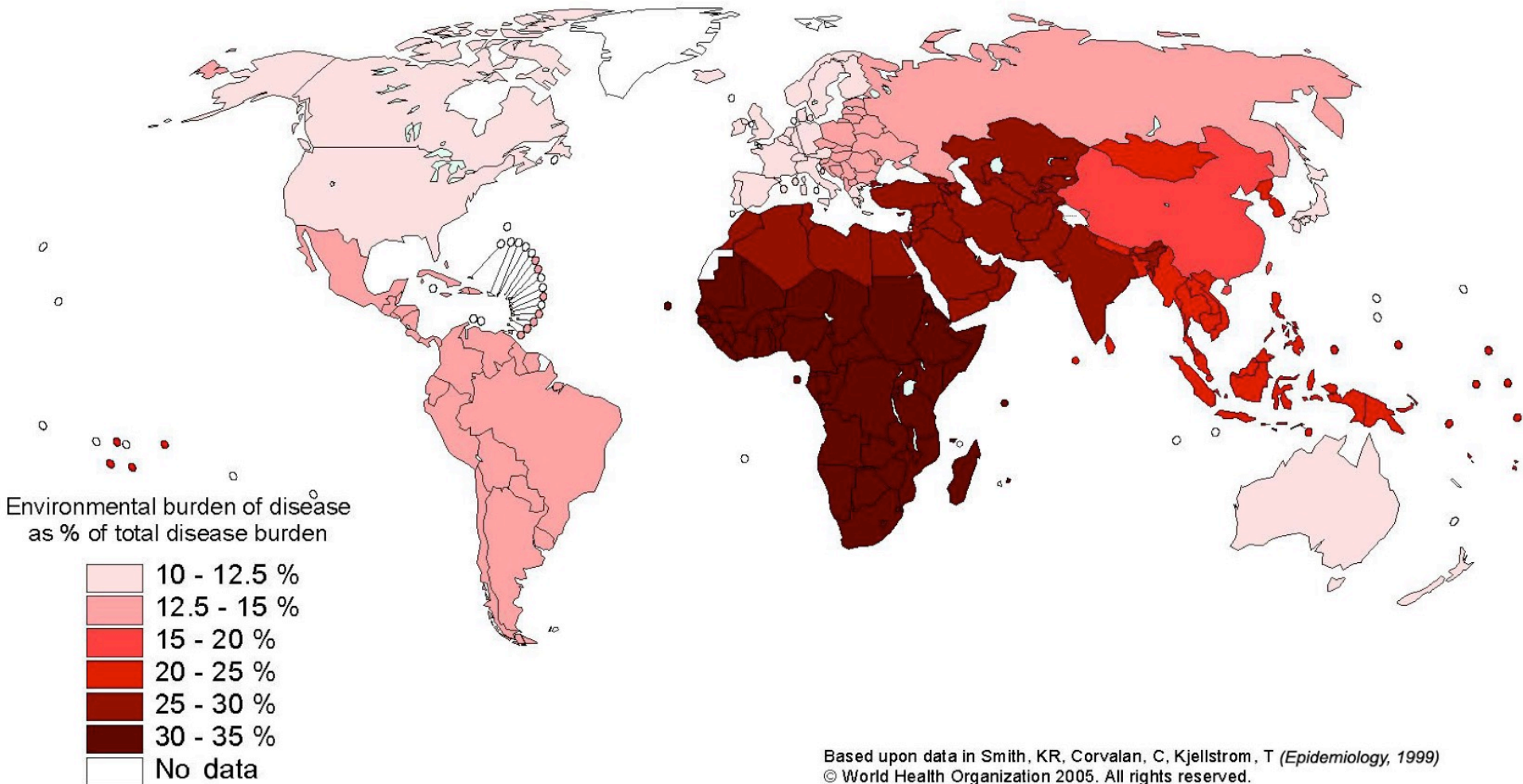
- Introduce concepts of Pediatric Environmental Health
- Explore research regarding two neurodevelopmental toxicants
  - Lead
  - Traffic-Related Air Pollution
- Discuss Pediatric Environmental Health Specialty Units



Francisco Goya  
Saturn devouring  
his son, 1819-1923

# Concepts

# Environmental burden of disease globally





# What is Pediatric Environmental Health (PEH)?

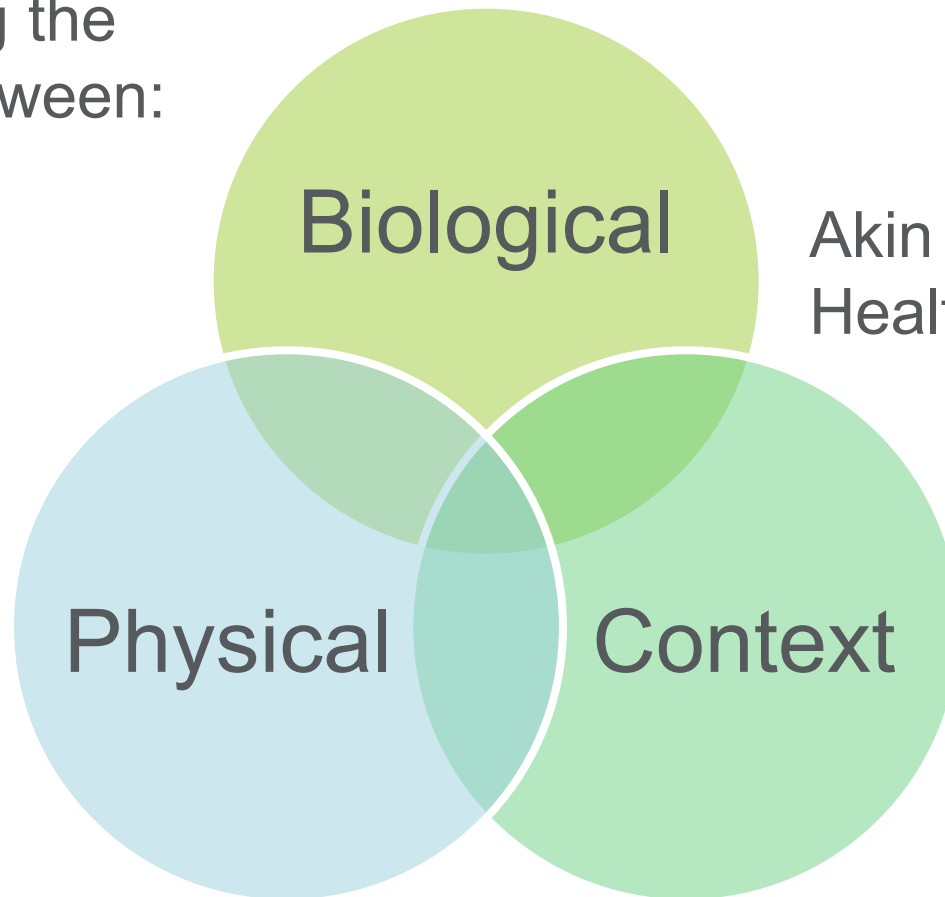
- Pediatric environmental health focuses on the prevention and control of environmental exposures and associated adverse health effects on infants, children, adolescents, and young adults.
- Recognized by American Academy of Pediatrics in 1950's (radioactive fallout)

<http://www.aap.org/healthtopics/environmentalhealth.cfm> (Accessed 07/07/09)



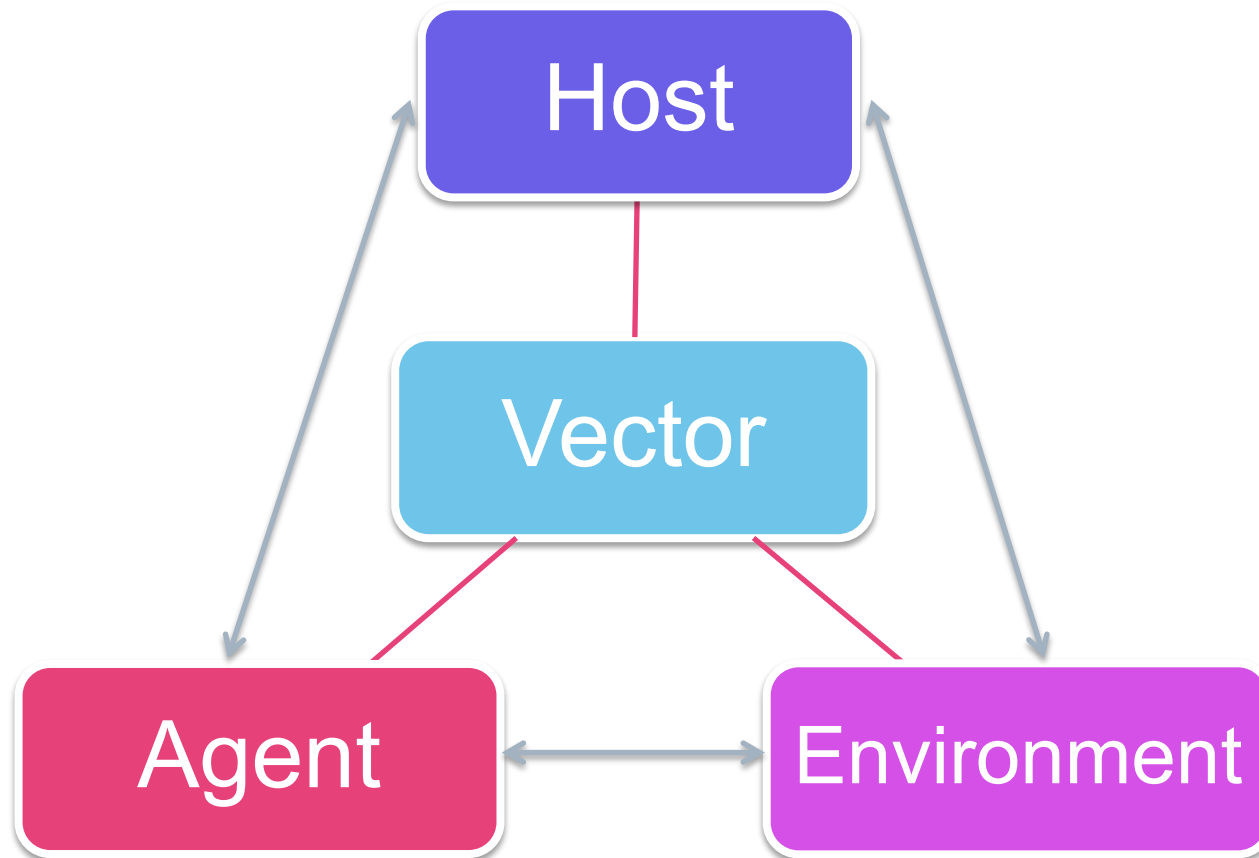
# What is Pediatric Environmental Health?

Understanding the interaction between:



Akin to Occupational Health in adults

# Traditional Epidemiological Triad



# A child's occupation?

- Grow
- Develop
- Explore
- Problem solve
- Learn new things
- Become an adult
  - Happy
  - Healthy

# Children are Different

- Windows of vulnerability
- Breathing zones
- Oxygen, Food & Water consumption
- Hand-Mouth behaviors
- Time

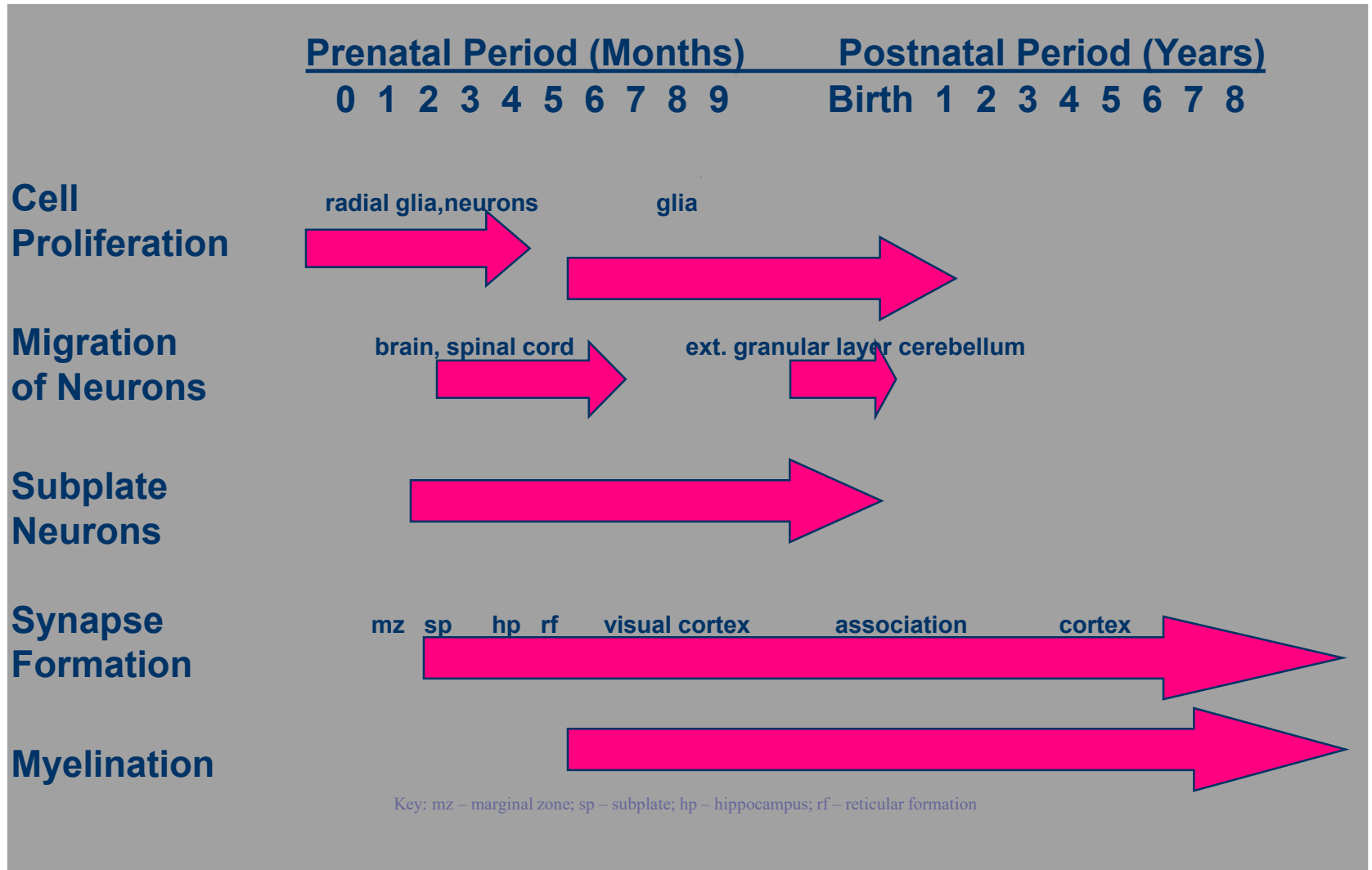


# Windows of Vulnerability

- Children naturally grow and develop
- Effect of exposure based on stage of development
- Multiple exposures at once
- Genetic predisposition to adverse effects

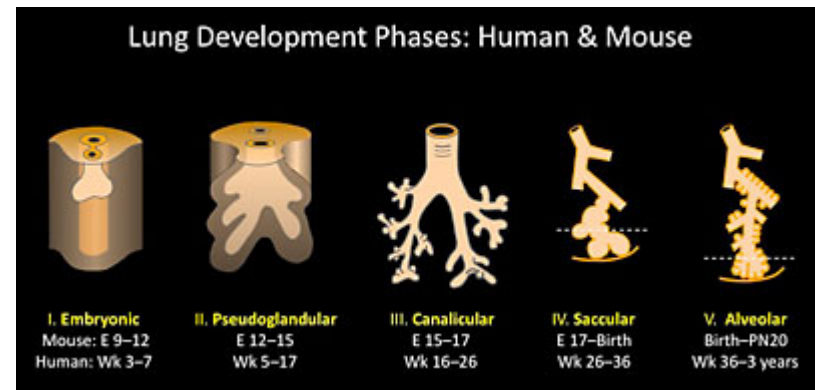


# Brain Development

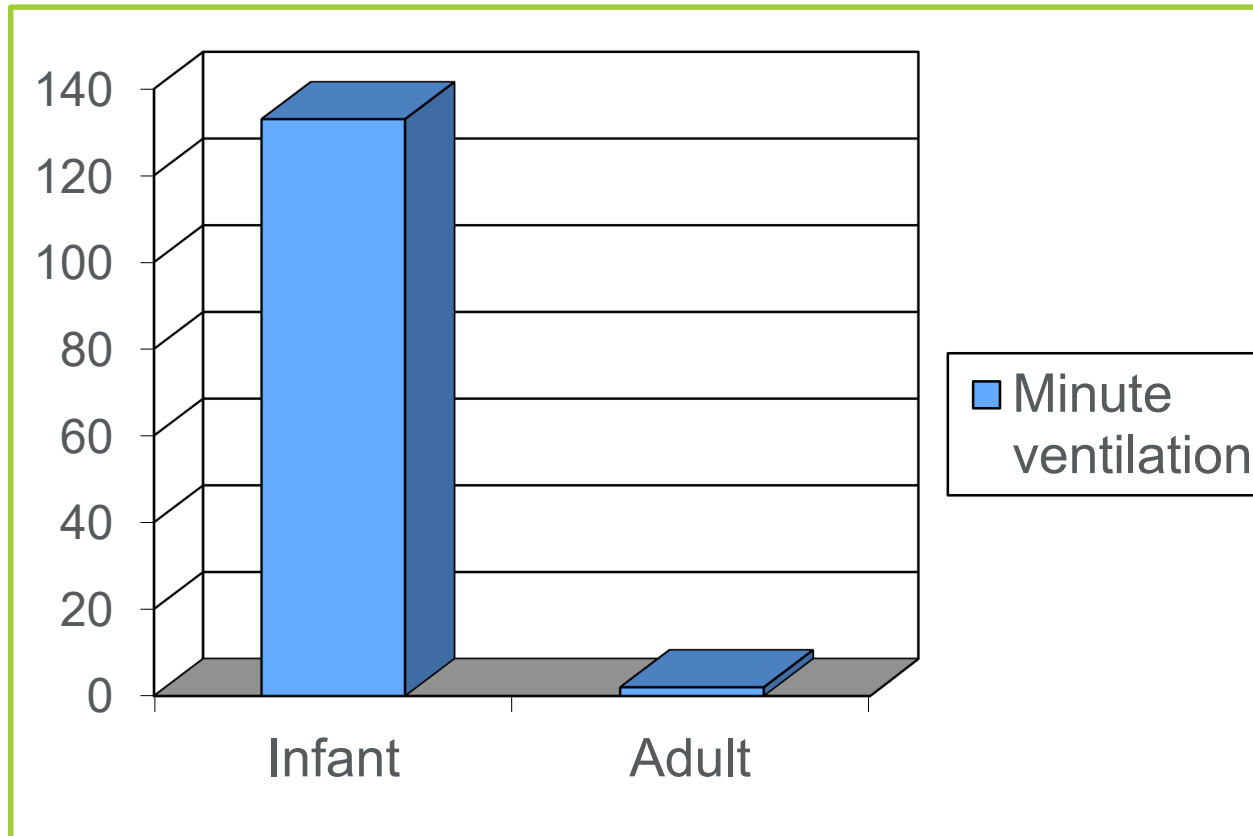


# Lung Development

- Pseudoglandular period (5-17 weeks)
- Canalicular period (16-25 weeks)
- Terminal sac period (24 weeks to birth)
- Alveolar period (late fetal to age 8 years)



# Lung Function



Adapted from Snodgrass in Guzelin, Henry Olin, eds, 1992

Minute ventilation =  
respiratory rate X tidal  
volume

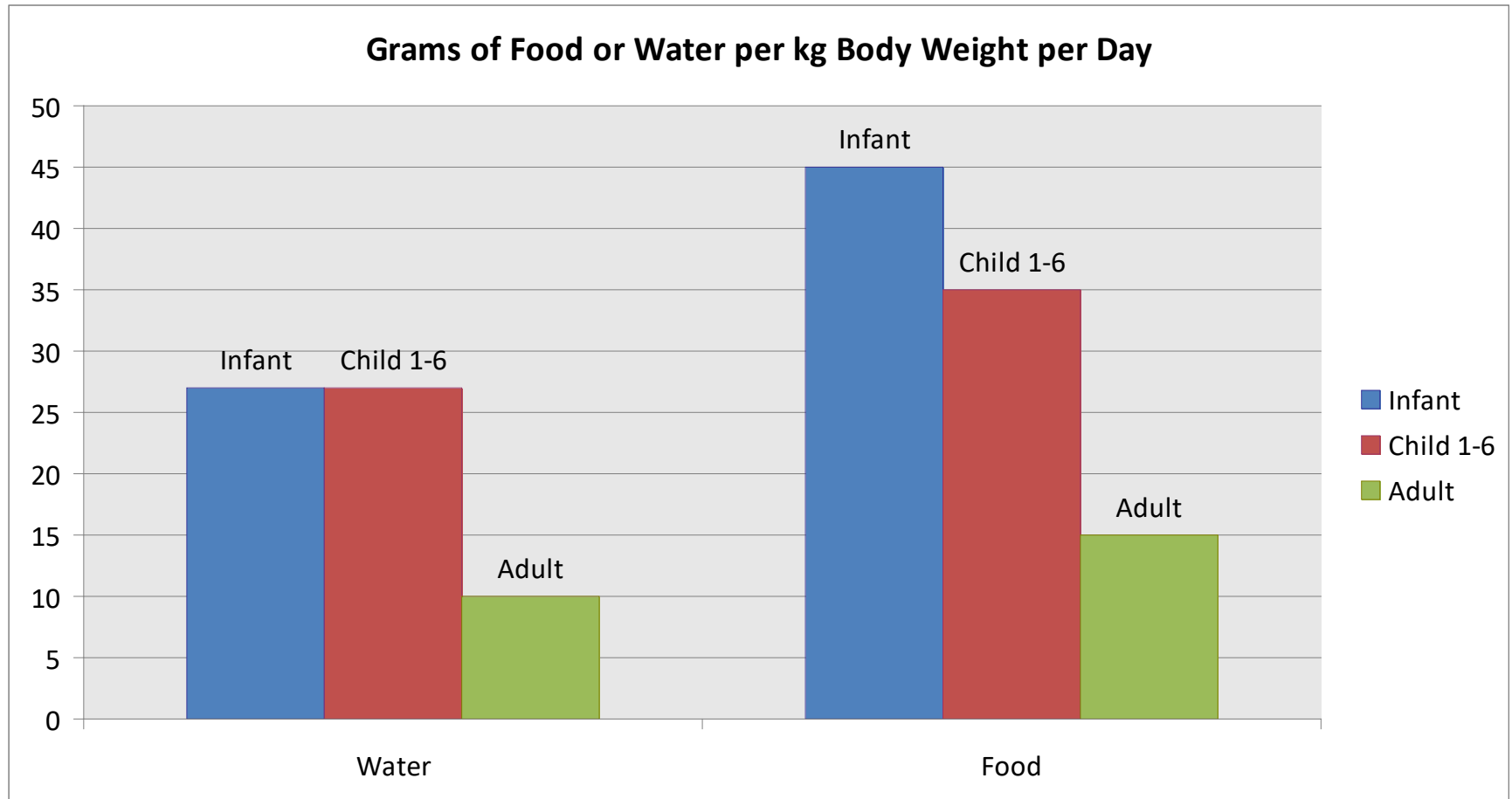


# Breathing zones

- Closer to the ground
  - Closer to dust
  - Heavy than air chemicals accumulate
- Infants tend to be indoors
  - Bedrooms
  - Automobiles
- School-aged children
  - School buses



# Food and Water



Adapted from Plunkett in Guzelin, Henry Olin, eds, 1992

# Differences in diet



- Infants
  - Limited diet: Breast milk or formula
  - Complementary foods
- Toddlers
  - Limited diet
  - Tend to eat off of the floor
  - Non-food items
- Older Children & Adults
  - Varied diet

# Hand to mouth behaviors

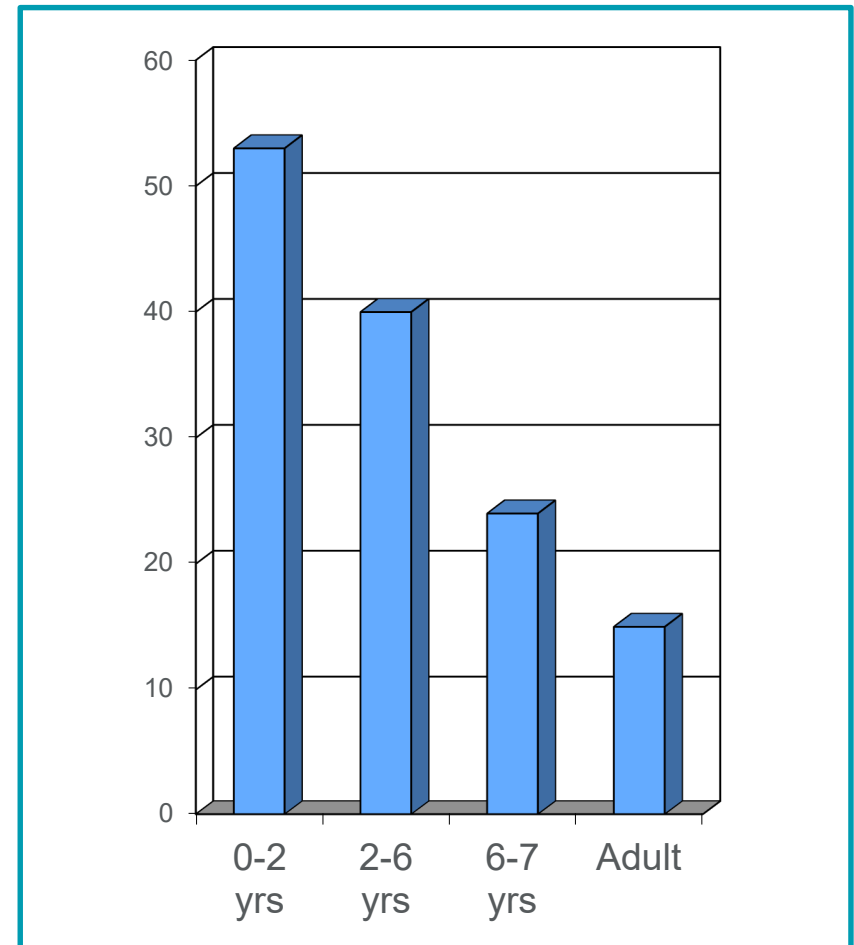
- Young children: stage of oral exploration
  - Lead dust
  - Arsenic on play equipment
  - Pesticides
- Older children: independent
- Adolescence
  - More independent
  - Lack of abstract reasoning



# Differences in GI absorption

- Gastrointestinal absorption of lead decreases with age
- Diet plays a part in changes in absorption
- Higher Pb absorption in Fe-deficient state
- Higher Pb absorption between meals

Adapted from Plunkett in Guzelin, Henry Olin, eds, 1992  
White, et al., *Env Health Perspectives*, 106:6, 1998



# Time

- Latency time
  - Time between exposure and development of disease
  - Decades may pass between radiation exposure and development of cancer
- Females in Hiroshima/Nagasaki Cohort
  - Increased breast cancer
  - Based on exposure at younger age



# Two important toxicants

- Widespread
- Negative impact on children's health
  
- Lead
- Traffic-related air pollution



# Lead - Review

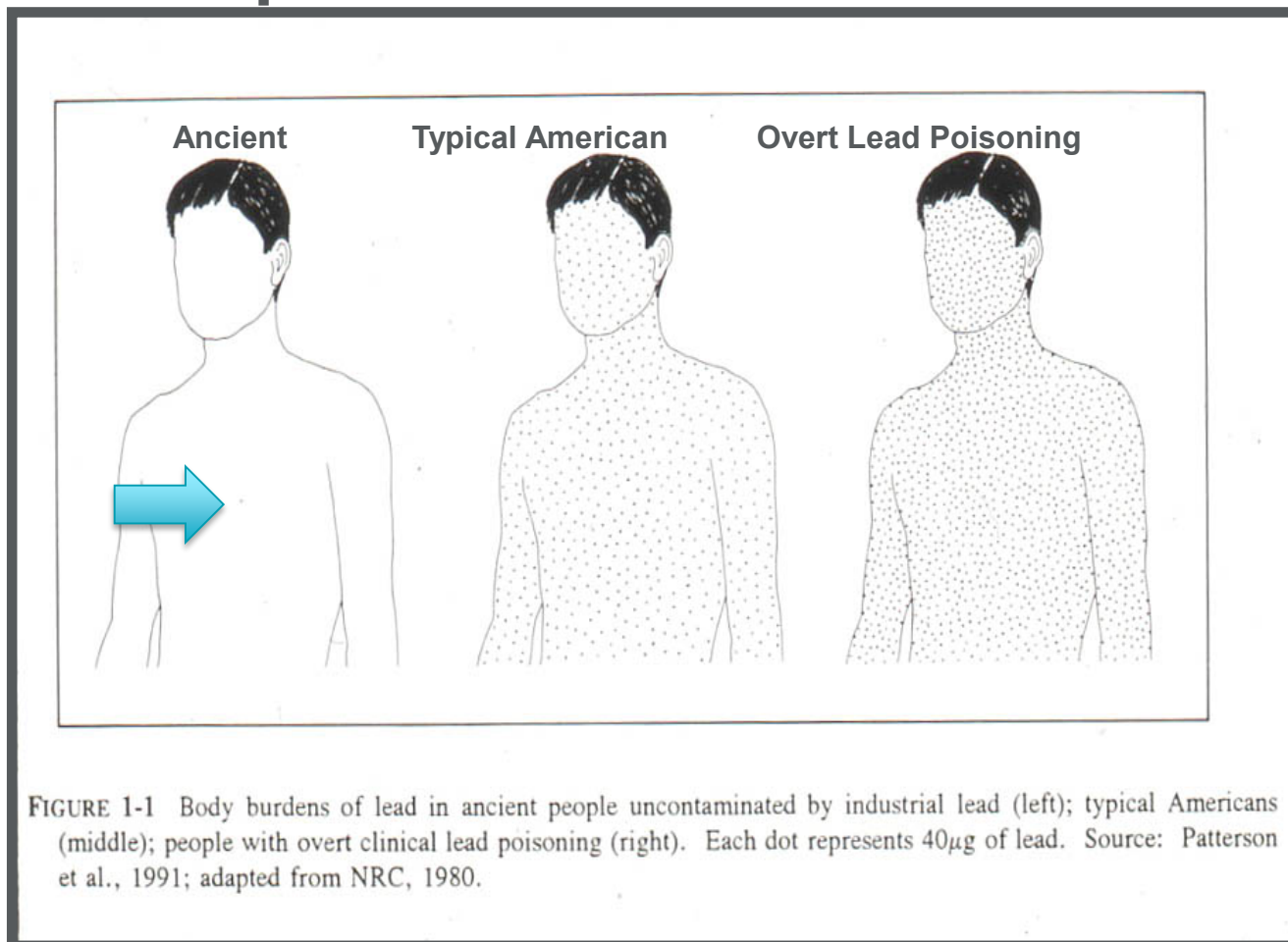
- Malleable, corrosion-resistant metal
- Used by humans since 6500 BCE (Turkey)
- Toxicity described by Greek Physician Nicander in 2<sup>nd</sup> Century BCE
- “The first pollutant”

AAP, Pediatric Environmental Health, 2012; Bennett, et al. Cont Peds, 2015  
NIOSH/CDC, 2019





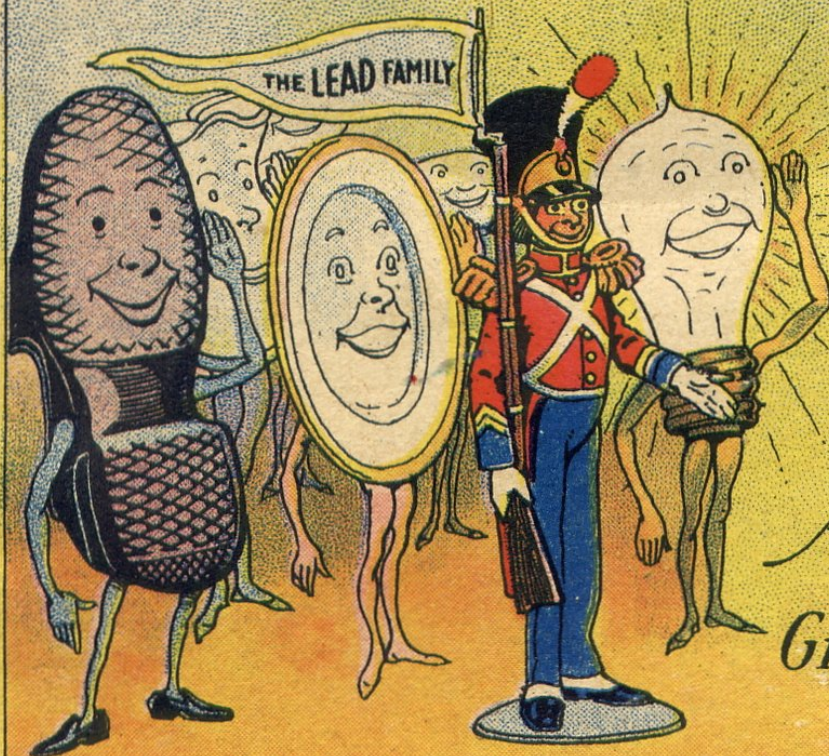
# Historical Perspective on Lead Exposure



# Modern History of Lead Paint

<b>Year</b>	<b>Event</b>
1887	U.S. medical authorities diagnose childhood lead poisoning
1904	Dr. John Lockhart Gibson describes childhood lead poisoning from paint
1909	France, Belgium, and Austria ban white-lead interior paint
1914	Pediatric lead-paint poisoning death from eating crib paint described
1921	National Lead Company admits lead is a poison
1922	League of Nations bans white-lead interior paint; U.S. declines to adopt
1943	Report concludes eating lead paint chips causes physical and neurological disorders, behavior, learning and intelligence problems in children
1971	Lead-Based Paint Poisoning Prevention Act passed
1978	Lead-based house paint banned in U.S.

# THE DUTCH BOY'S LEAD PARTY



*A Paint Book  
for  
Girls and Boys*

With which is bound  
**COLOR HARMONY IN THE HOME**  
A Booklet for the Grown-ups



Electric light bulbs, cut glass, the lenses of cameras, telescopes, microscopes and eye-glasses—in fact all fine glass is made by fusing sand and red-lead together. Red-lead is a fine, orange-red powder. It is a lead oxide, that is, a chemical compound of lead and oxygen. Lead in glass gives brightness and greater power.



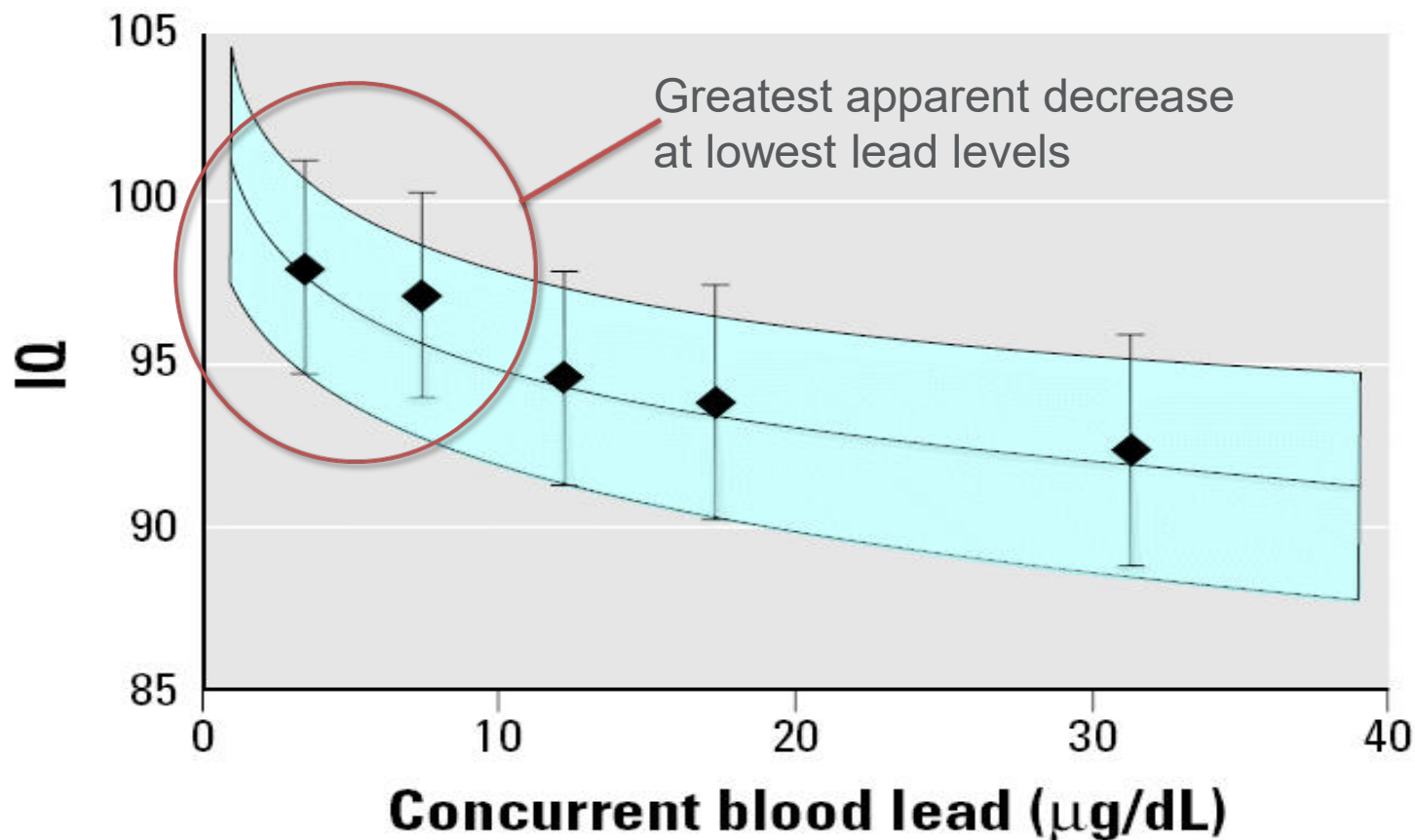
The first one at the party  
Was gay Electric Light.  
He said, "I'm very brilliant,  
I always shine at night!



"No little of my brilliance  
Is due to my glass head,  
Which gives a light much brighter  
Because it's made with lead."

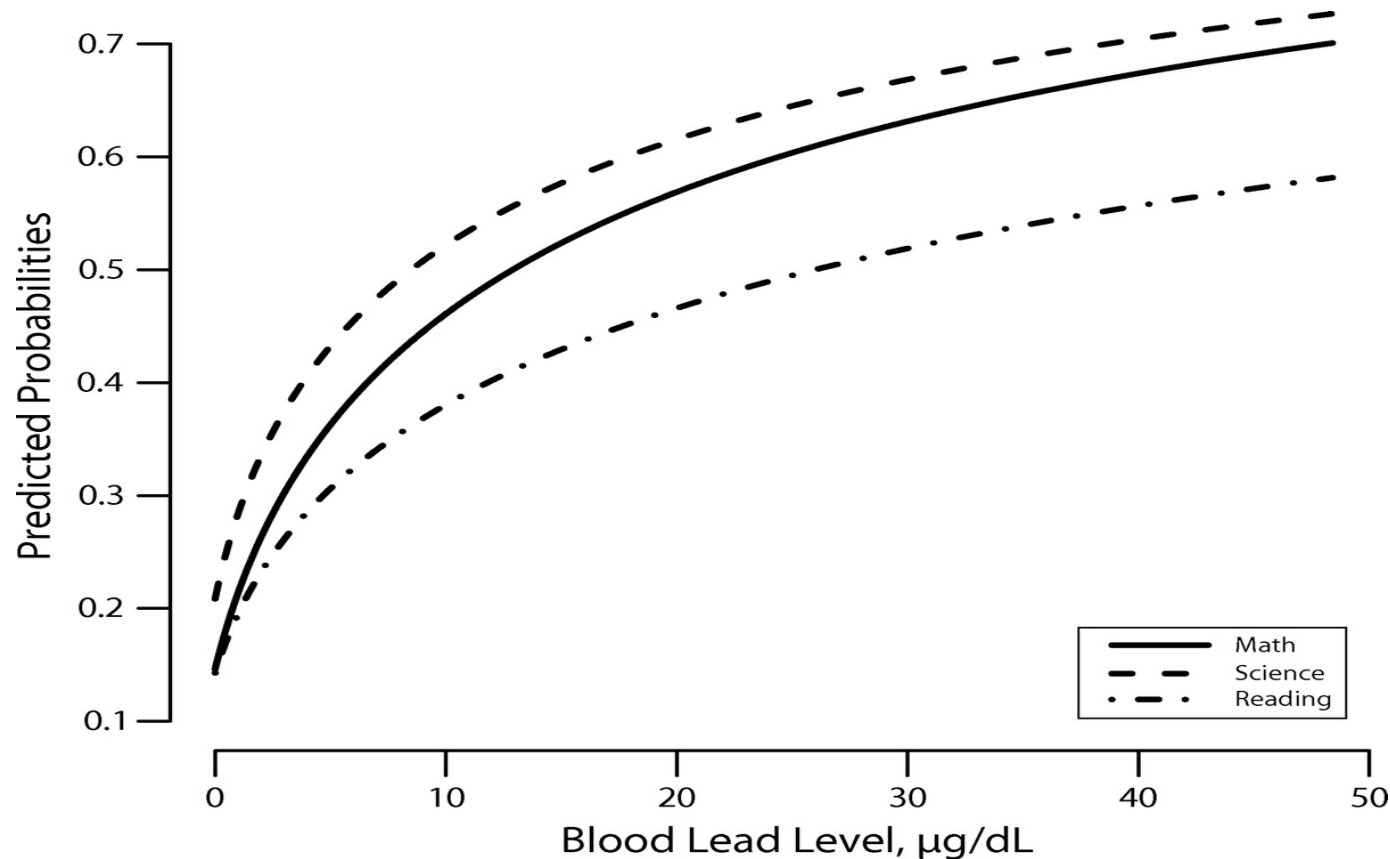
# Implications of lead exposure in children

# Blood Lead Level and IQ



Log-linear model (95% CIs shaded) for concurrent blood lead concentration, adjusted for HOME score, maternal education, maternal IQ, and birth weight. The mean IQ (95% CI) for the intervals < 5  $\mu\text{g/dL}$ , 5–10  $\mu\text{g/dL}$ , 10–15  $\mu\text{g/dL}$ , 15–20  $\mu\text{g/dL}$ , and > 20  $\mu\text{g/dL}$  are shown.

# School Performance



Predicted probabilities of scoring “less than proficient” on 3 tests of the Michigan Educational Assessment Program as a function of blood lead level:  
Detroit Public Schools, MI, 2008–2010



# Behavioral Problems



- Attention Deficit-Hyperactivity Disorder
  - Estimated 25% of ADHD may be attributable to lead exposure (BLL >1.3 mcg/dL)
- Antisocial behavior
- Increased adult criminal behavior & incarceration

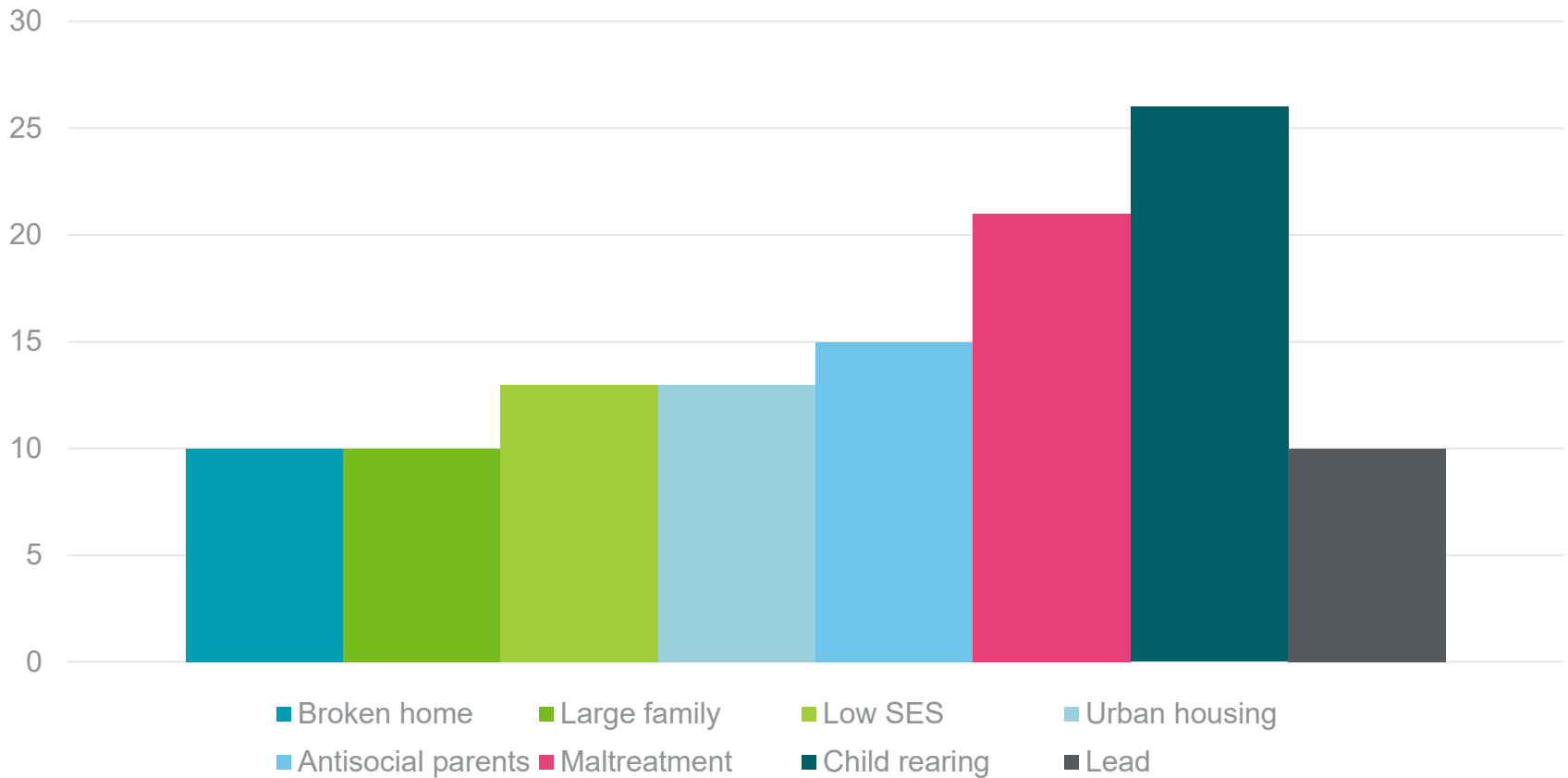
# Economics of Lead exposure



- \$50.9 Billion/year
  - Medical costs
  - Special education
  - Incarceration
  - Lost IQ/productivity
- Cost to Mahoning County, OH \$500K
- ROI for lead poisoning prevention
  - \$1 → \$17-\$221
  - Vaccines \$1 → \$5.30 (direct) \$16.50 (indirect)

# Risk factors for incarceration

Relative contribution of nonbiological risk factors



Farrington, JAMA Pediatrics, 2018

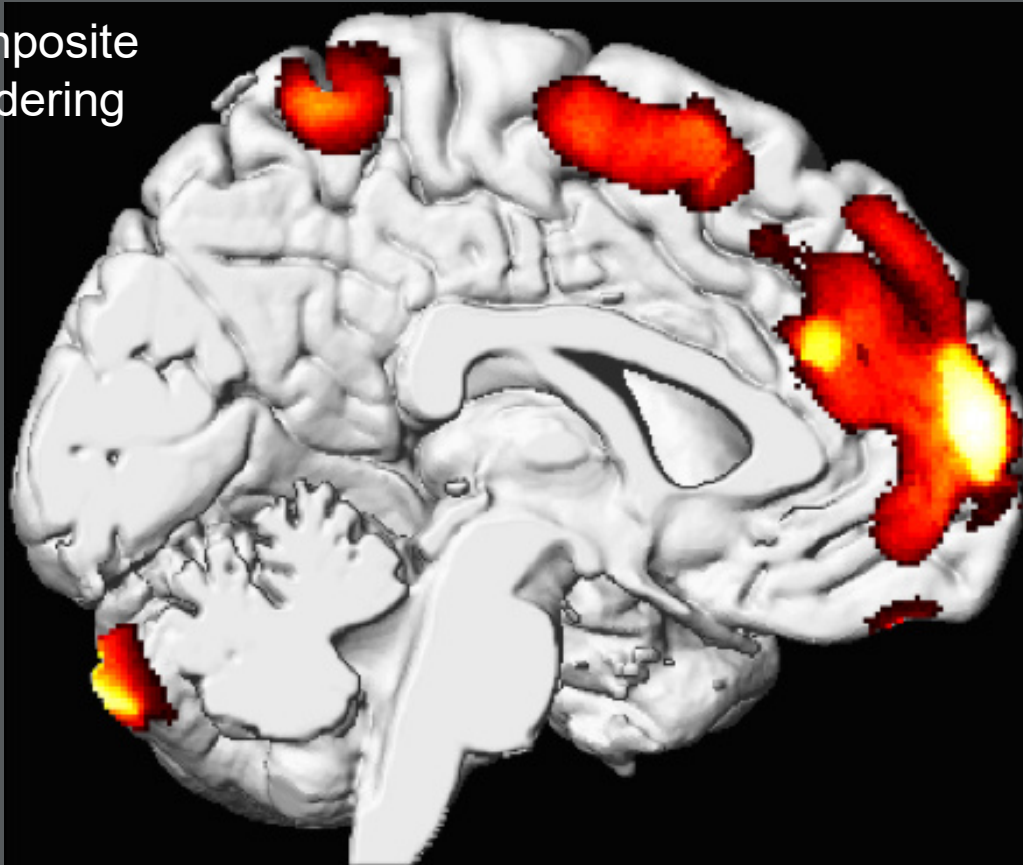
# Numerous uses for lead



- Storage Batteries
- Metallurgy
- Electronics
- Cosmetics
- Home remedies
- Pottery glaze
- Gasoline additive
- Plumbing
- Paint
- Rubber Materials
- Electrical solder
- Munitions
- Art Supplies
- Crayons
- Stabilizer for plastics

# Cortical Gray Matter Loss in Relationship to Postnatal Lead Exposure to Six Years

Composite  
rendering



Single  
voxel  
significance  
more significant



less significant

Map of strength of association between blood lead concentration and population-wide loss of gray matter volume. Single-voxel minimum significance threshold is  $p < 0.001$  (uncorrected), found within a cluster of at least 700 voxels (Cecil, et al)

# Clinical Vignette

# Two children with elevated blood lead levels

- Dad worked at e-waste recycler
  - Operated CRT grinder
  - “I throw the CRTs and all this dust comes out”
  - Wears clothes home from work
- “He comes home covered with dust”
  - Children would run to meet him at the door
  - Played with children at the door
- Average 25” TV tube has 1-2kg of lead

# Course of Events

Clinical Evaluation

Cincinnati Health Dept

NIOSH/OSHA



# Angel-Devil Machine



Huffington Post, 2016, Courtesy of CDC/NIOSH

# Work site investigation

- Dust wipe samples from cathode ray tube area showed high levels of lead
- CRTs are made from leaded glass
- Some employees continued to have detectable lead on their hands despite hand washing
- 12/13 uniforms tested positive for lead

Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report

Weekly / Vol. 64 / No. 27

July 17, 2015

## Investigation of Childhood Lead Poisoning from Parental Take-Home Exposure from an Electronic Scrap Recycling Facility — Ohio, 2012

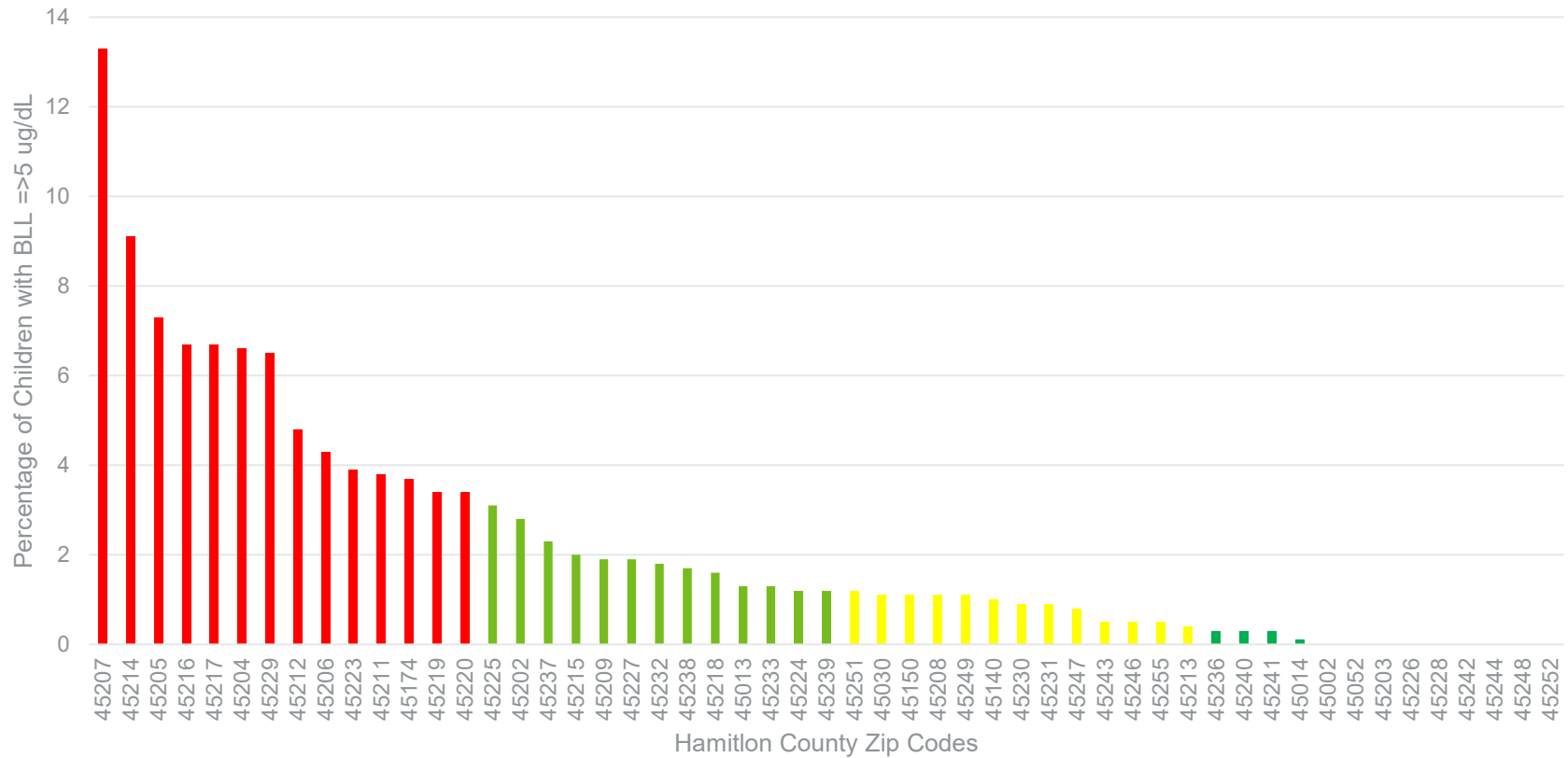
Nick Newman, DO<sup>1</sup>; Camille Jones, MD<sup>2</sup>; Elena Page, MD<sup>3</sup>; Diana Ceballos, PhD<sup>3</sup>; Aalok Oza, MS<sup>3</sup> (Author affiliations at end of text)

Lead affects the developing nervous system of children, and no safe blood lead level (BLL) in children has been identified (1). Elevated BLLs in childhood are associated with hyperactivity, attention problems, conduct problems, and impairment in cognition (2). Young children are at higher risk

father was advised to notify the Occupational Safety and Health Administration of his BLL; it is not known if he did. The father left his job soon after the elevated BLLs were recognized, and the children's BLLs decreased to 8.7  $\mu\text{g}/\text{dL}$  and 7.9  $\mu\text{g}/\text{dL}$ , respectively, over the next 3 months.

# Using data to target outreach

Percentage of Children with BLL =>5 by Zip Code





**Title:** The Midnight Mass

**Artist:** Edward Timothy Hurley (American, b.1869, d.1950), painter

**Date:** 1911

**Place:** Cincinnati/Ohio/United States

**Courtesy:** Cincinnati Art Museum

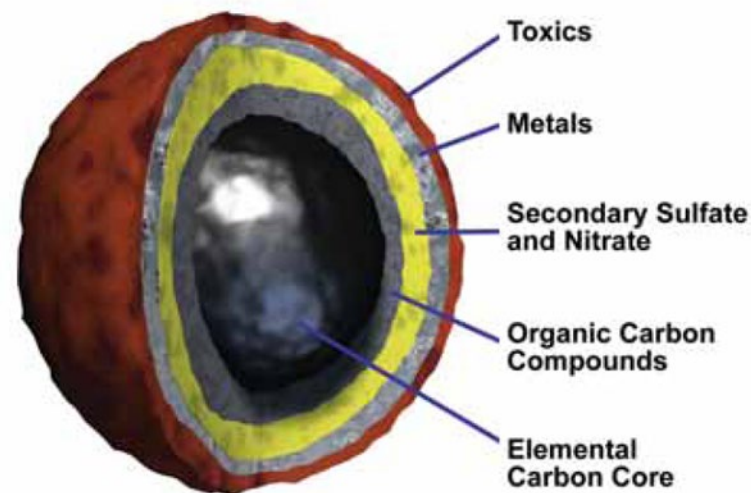
# Traffic Related Air Pollution

- Complex mixture
  - Particulate matter (PM<sub>2.5</sub>, PM<sub>10</sub>, Ultrafines)
  - Vapors (PAH, VOC)
  - Gases (NO<sub>x</sub>, CO, CO<sub>2</sub>, SO<sub>x</sub>)
- Dynamic chemistry
  - Sunlight
  - Heat
  - Humidity

# Ultrafine particles: diesel exhaust particles

- Traffic-Related Air Pollution (TRAP)
  - “Elemental Carbon Attributed to Traffic”
  - Ultrafine particles <100nm diam
  - Translocate to **brain**, liver, spleen, and kidneys
- Pathophysiology
  - Oxidative stress at cellular level

Diesel particles are carbon at their core with toxics and carcinogenic substances attached to their surfaces.



All EHP content is accessible to individuals with disabilities. A fully accessible (Section 508-compliant) HTML version of this article is available at <http://dx.doi.org/10.1289/ehp.1205555>.

Research | Children's Health

# Traffic-Related Air Pollution Exposure in the First Year of Life and Behavioral Scores at 7 Years of Age

*Nicholas C. Newman,<sup>1</sup> Patrick Ryan,<sup>2,3</sup> Grace LeMasters,<sup>3</sup> Linda Levin,<sup>3</sup> David Bernstein,<sup>4</sup> Gurjit K. Khurana Hershey,<sup>5</sup> James E. Lockey,<sup>3</sup> Manuel Villareal,<sup>4</sup> Tiina Reponen,<sup>3</sup> Sergey Grinshpun,<sup>3</sup> Heidi Sucharew,<sup>2</sup> and Kim N. Dietrich<sup>3</sup>*

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# Why ADHD?

- Common illness, expected to be found in our population
- Symptoms related to “dysfunction” in pre-frontal/frontal cortex
- Ultrafine particles have been found in pre-frontal cortex in human cadaver studies

Calderón-Garcidueñas, et al., 2008; Biederman & Faraone, 2005

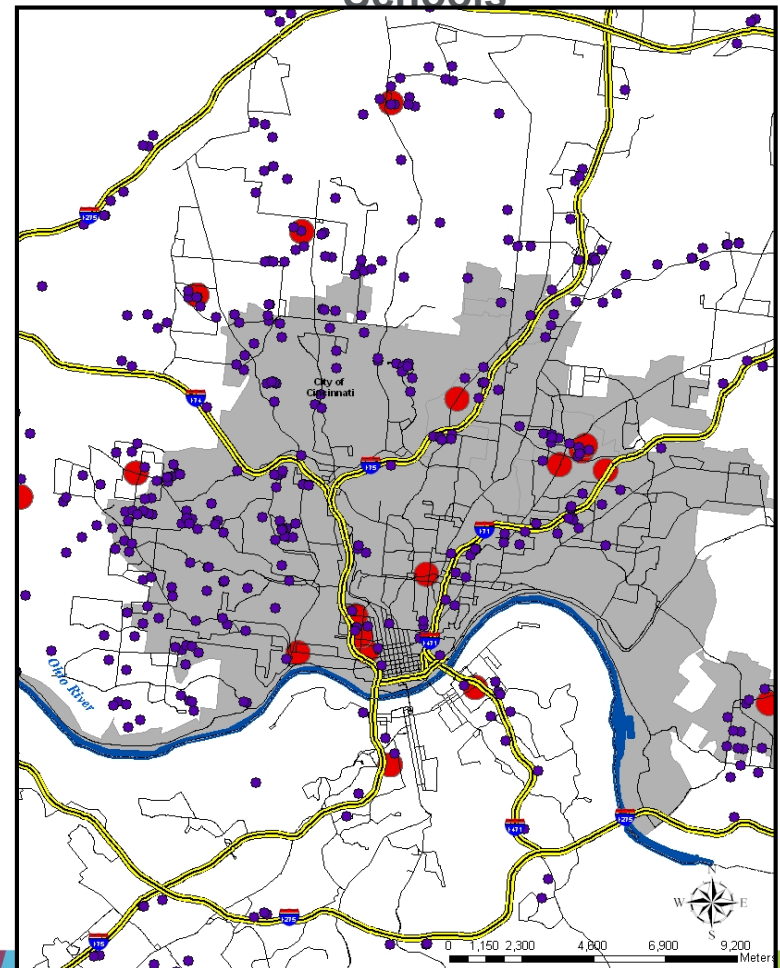
# Cincinnati Childhood Allergy and Air Pollution Study

Sampling Sites

Elevation, Land-use

Homes,  
Daycares,  
Schools

- Prospective birth cohort identified 2001-2003
- Geocoded birth addresses, those <400m or >1500m from major highway were eligible
- All children had parent with positive SPT
- 762 children at enrollment
- 597 at age 7 years with BASC-2



# Behavioral Measurement



- Behavioral Assessment System for Children-Parent Rating Scale, 2<sup>nd</sup> Edition (BASC-2)
- Validated measure used in clinical psychology
- T score calculated for composites & subscales
  - Mean 50, Standard Deviation 10
  - 60+ at risk
- Internal validity measures removed questionable data (n=21)

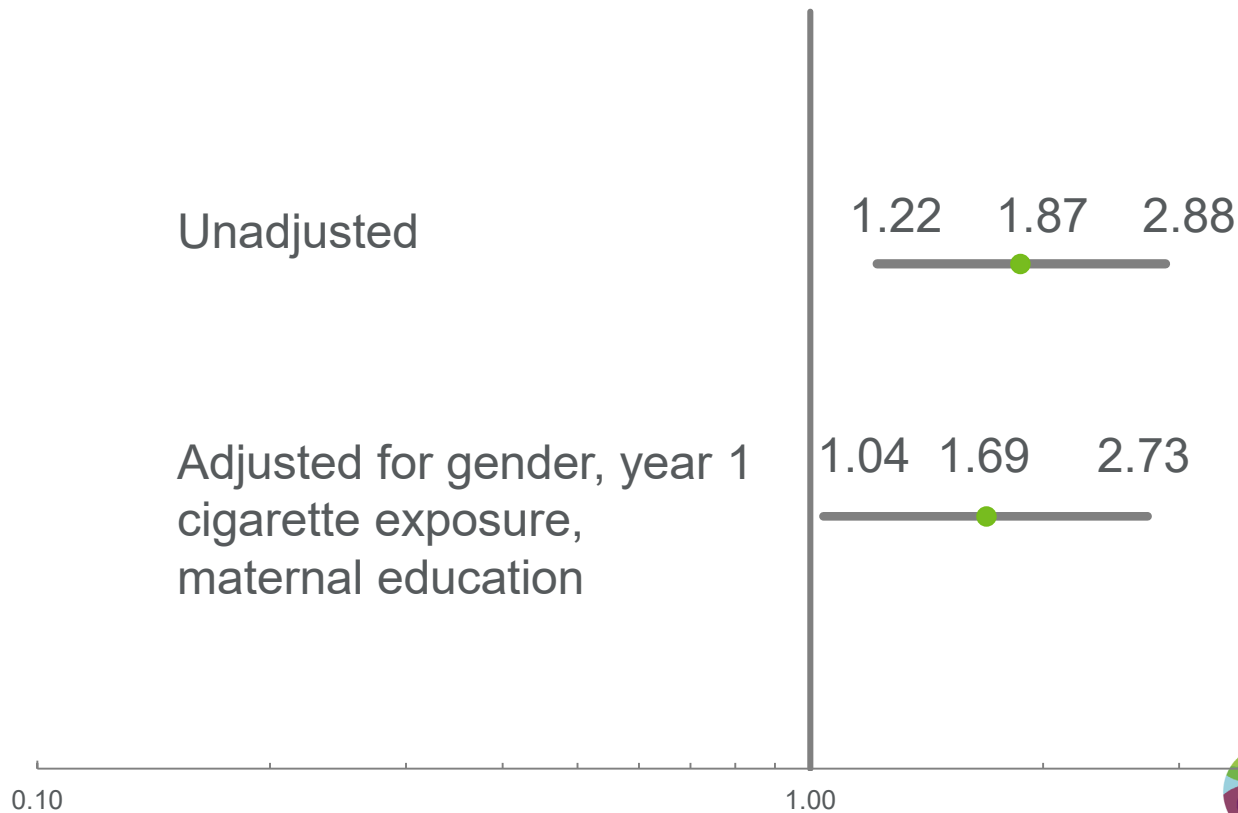
# Descriptive Statistics

n=576

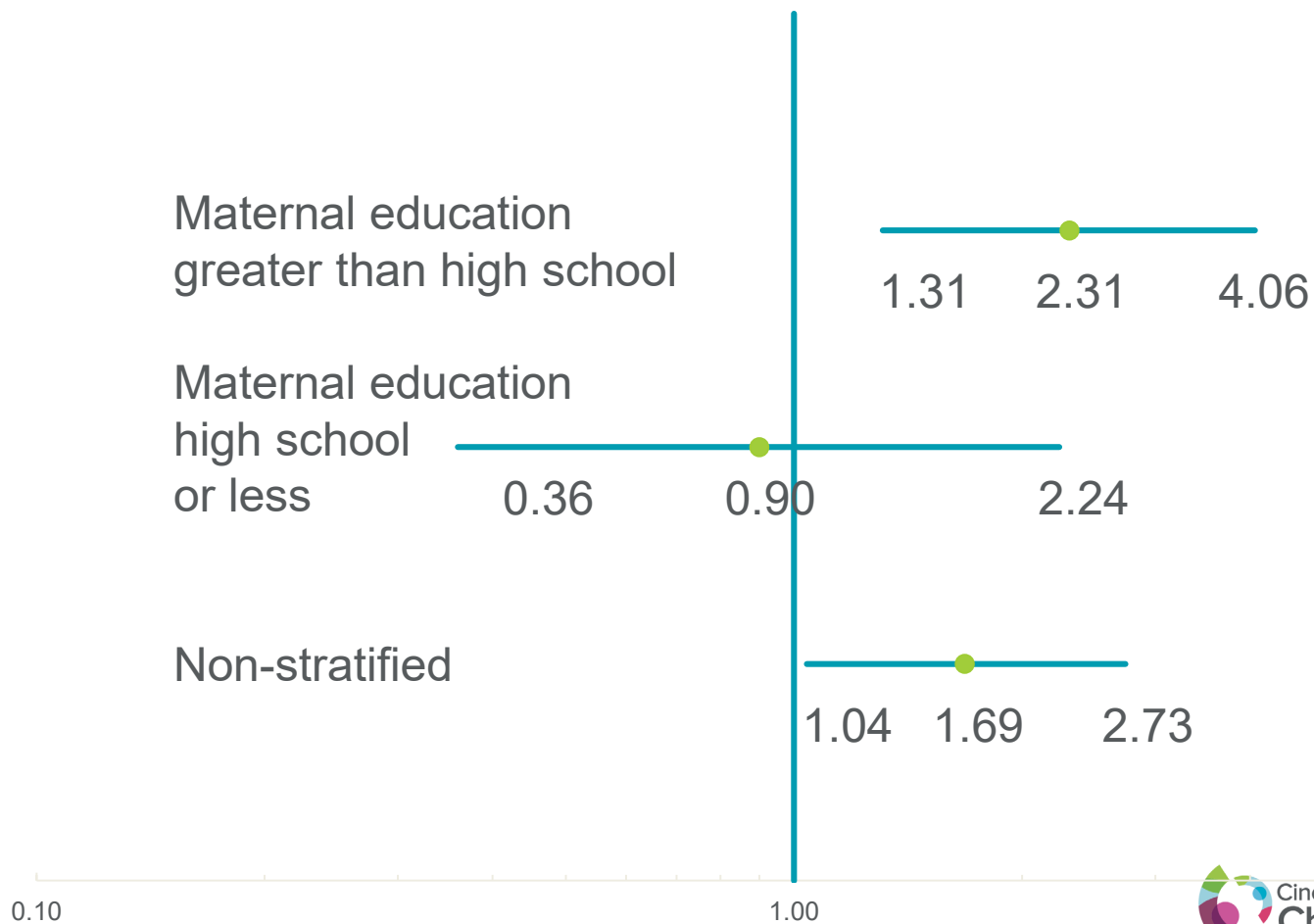
Characteristic	%	Mean (SD)
African American	20	
Male	55	
Mother's education (HS/GED or less)	21	
Family income <\$30k/year	34	
TRAP (ECAT) Exposure, Year 1		0.4 (0.1) $\mu\text{g}/\text{m}^3$
Cigarette Exposure, Year 1	22	
Home built prior to 1950	27	
BASC-2 Hyperactivity Score >59 (at risk range)	18	

# Hyperactivity adjusted odds ratios Logistic Regression

TRAP dichotomized at highest tertile  $0.4\mu\text{g}/\text{m}^3$



# Stratified Model: Hyperactivity, adjusted odds ratios



# Maternal Education



- Why does maternal education matter?
  - Is this a surrogate marker of maternal ADHD?
    - Lower educated mothers more likely to have ADHD?
  - Are more highly educated parents more likely to report symptoms in their children?
- Maternal education strongly correlated with income, breast feeding duration



# Discussion: Biological Plausibility

- TRAP exposure associated with:
  - Neuroinflammation
  - Mucosal inflammation of respiratory tract
- Neurological and immunological systems immature during first year and may be particularly vulnerable to TRAP exposure
- Dopaminergic pathways may be more sensitive to oxidative stress of TRAP exposure



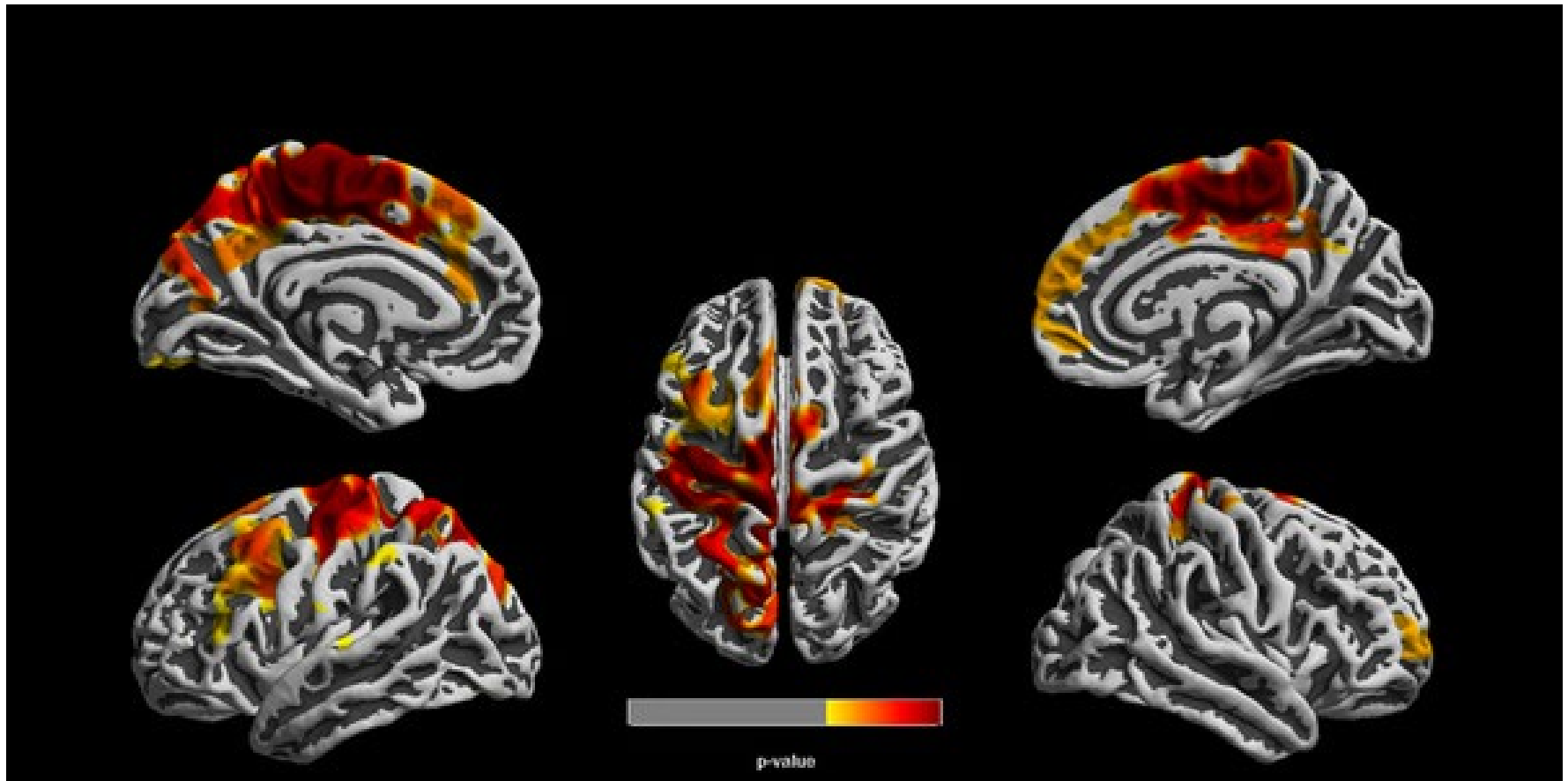


# Future directions



- CCAAPS Brain – ongoing
  - Neuroimaging
  - Extensive neurobehavioral assessment
  - Additional biomarkers
  - Information regarding parents
- Exposure to TRAP after the first year of life
- Gene x Environment interaction

Fig 1. Statistically significant clusters using threshold free cluster enhancement.



Beckwith T, Cecil K, Altaye M, Severs R, Wolfe C, et al. (2020) Reduced gray matter volume and cortical thickness associated with traffic-related air pollution in a longitudinally studied pediatric cohort. PLOS ONE 15(1): e0228092.

<https://doi.org/10.1371/journal.pone.0228092>

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0228092>



# Pediatric Environmental Health Specialty Units (PEHSU)

- April 1997, Executive Order “Protection of Children from Environmental Health Risks and Safety Risks”
- First programs in Boston & Seattle (1999)
- Experts on environmental conditions effecting children
- Funding for the PEHSU program is provided by ATSDR, with support from EPA



# Translating into practice

- Environmental health is not part of standard medical school curriculum
- Environmental health is not required as part of pediatric training
- PEHSU Network provides consultation, education and outreach

# Cincinnati Children's Environmental Health & Lead Clinic

- Lead poisoning
  - Outpatient
  - Inpatient
- Other metals
- Mold
- Indoor Air Quality
- Pesticides

Approximately  
200 new  
cases/year overall

# Summary

- Lead exposure in childhood is a risk factor for poor adult functioning
- Traffic-related air pollution is becoming recognized as a neurodevelopmental toxicant
- Translating research into action is a slow, painstaking process



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  - T32-ES010957
  - P30-ES006096
  - R01-ES11170
- CCAAPS families

# Post-test quiz



- True or False
  - Childhood lead exposure is a risk factor for adult incarceration
    - True
  - Traffic-related air pollution exposure is a risk factor for childhood behavioral problems
    - True

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