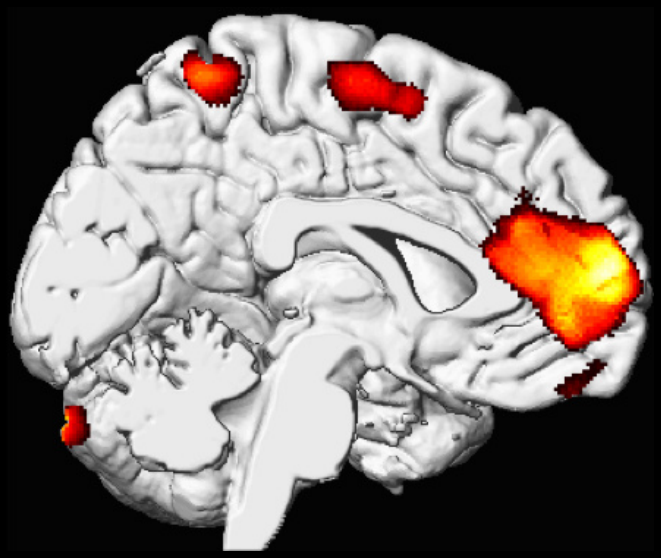
The Impact of Toxins on the Developing Brain

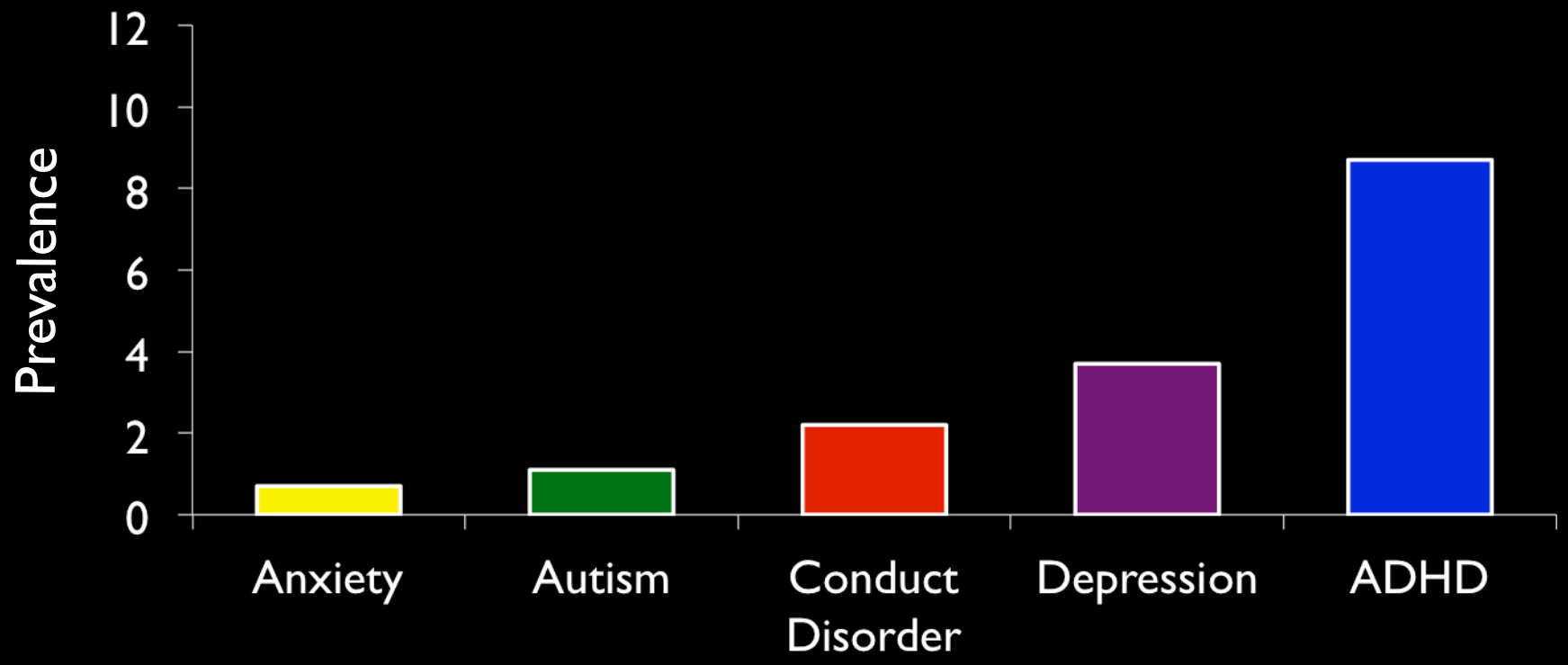


The HOME Study

Cincinnati Children's Environmental Health Center

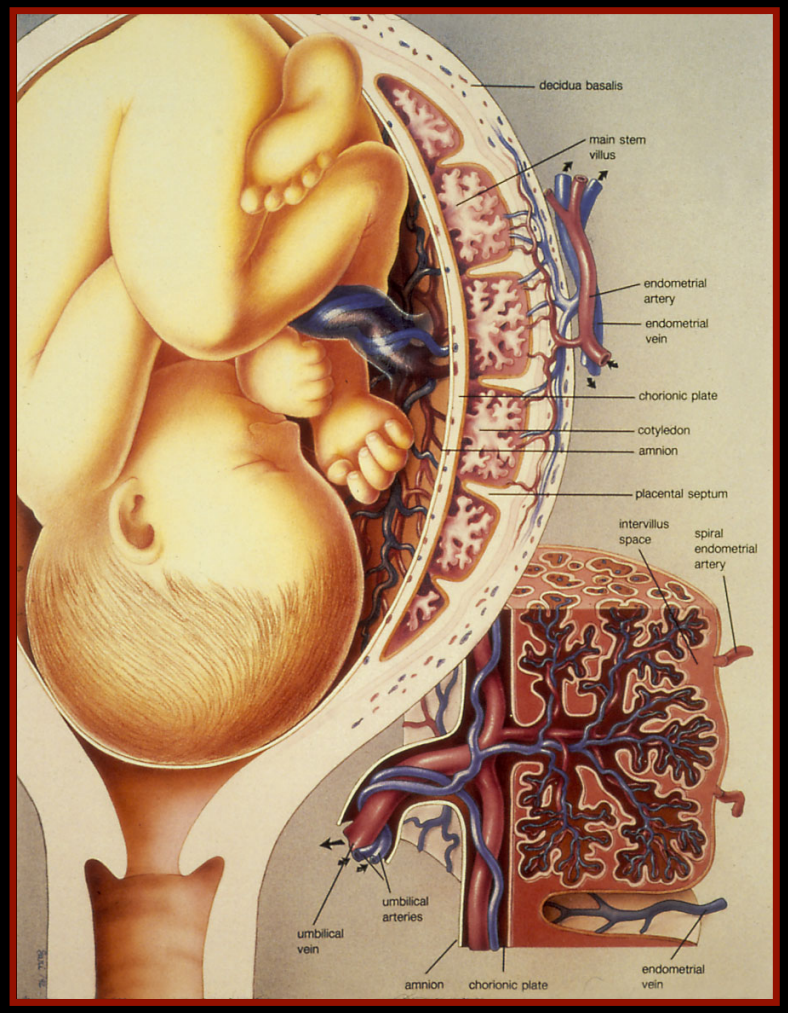
Bruce Lanphear, MD, MPH
Child & Family Research Institute, BC Children's Hospital
Faculty of Health Sciences, Simon Fraser University

Brain-based Disorders in Children



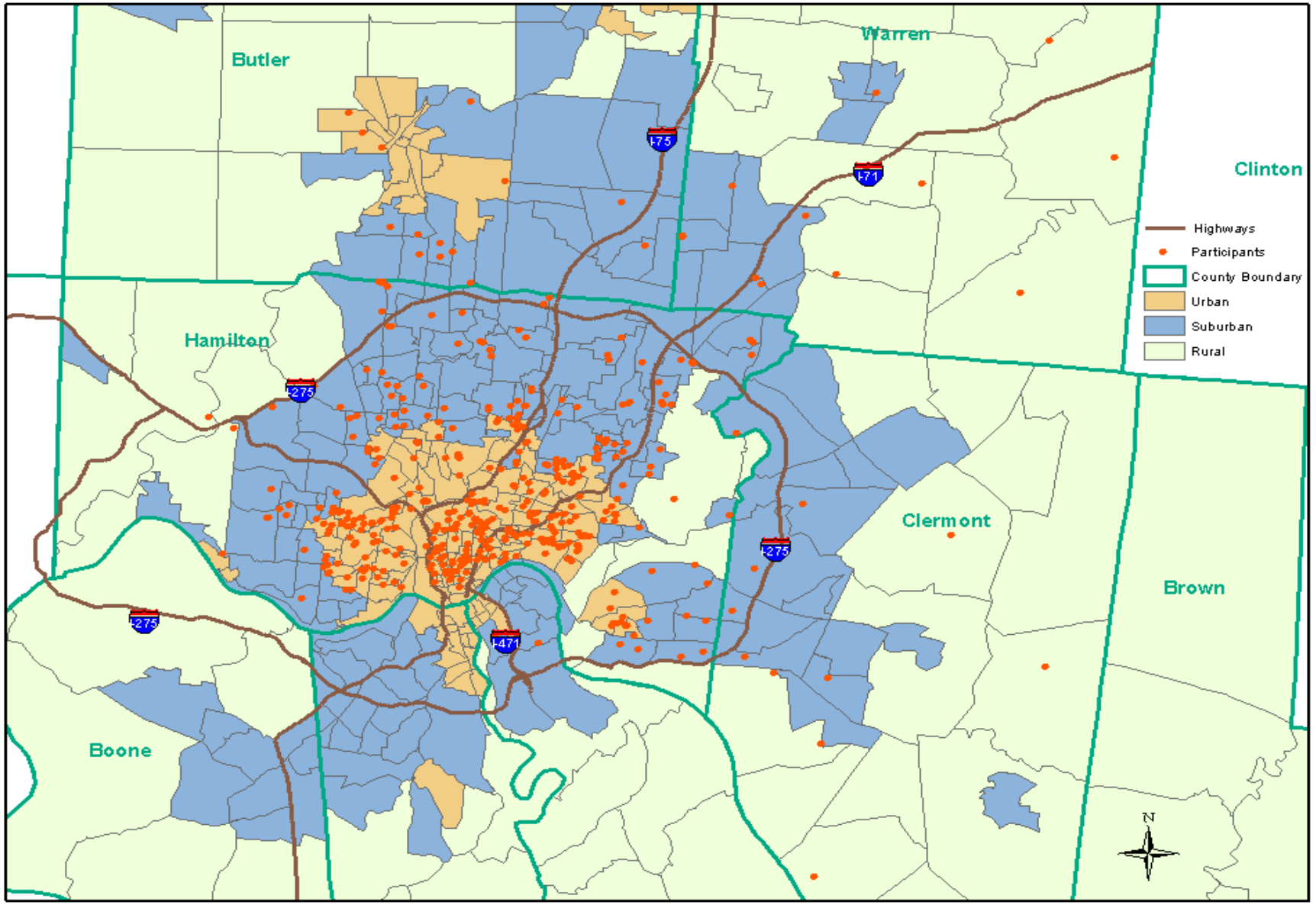
Merikangas KR, He JP, Brody D, et al. Prevalence and treatment of mental disorders among US children in the 2001-2004 NHANES. Pediatrics 2010;125:75-81. Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders, United States, 2008. MMWR Surveill Summ 2012; 61:1-19. Boyle CA, Boulet S, Schieve LA, et al. Trends in the prevalence of developmental disabilities in US children, 1997-2008. Pediatrics 2011;127:1034-1042.

Factors that Impact Brain Development



- Sex
- Nutrition
- Preterm Birth
- Social Stressors
- Built Environment
- Maternal Depression
- Genetic Susceptibility
- Preschool Attendance
- Environmental Toxins

HOME Study Participants



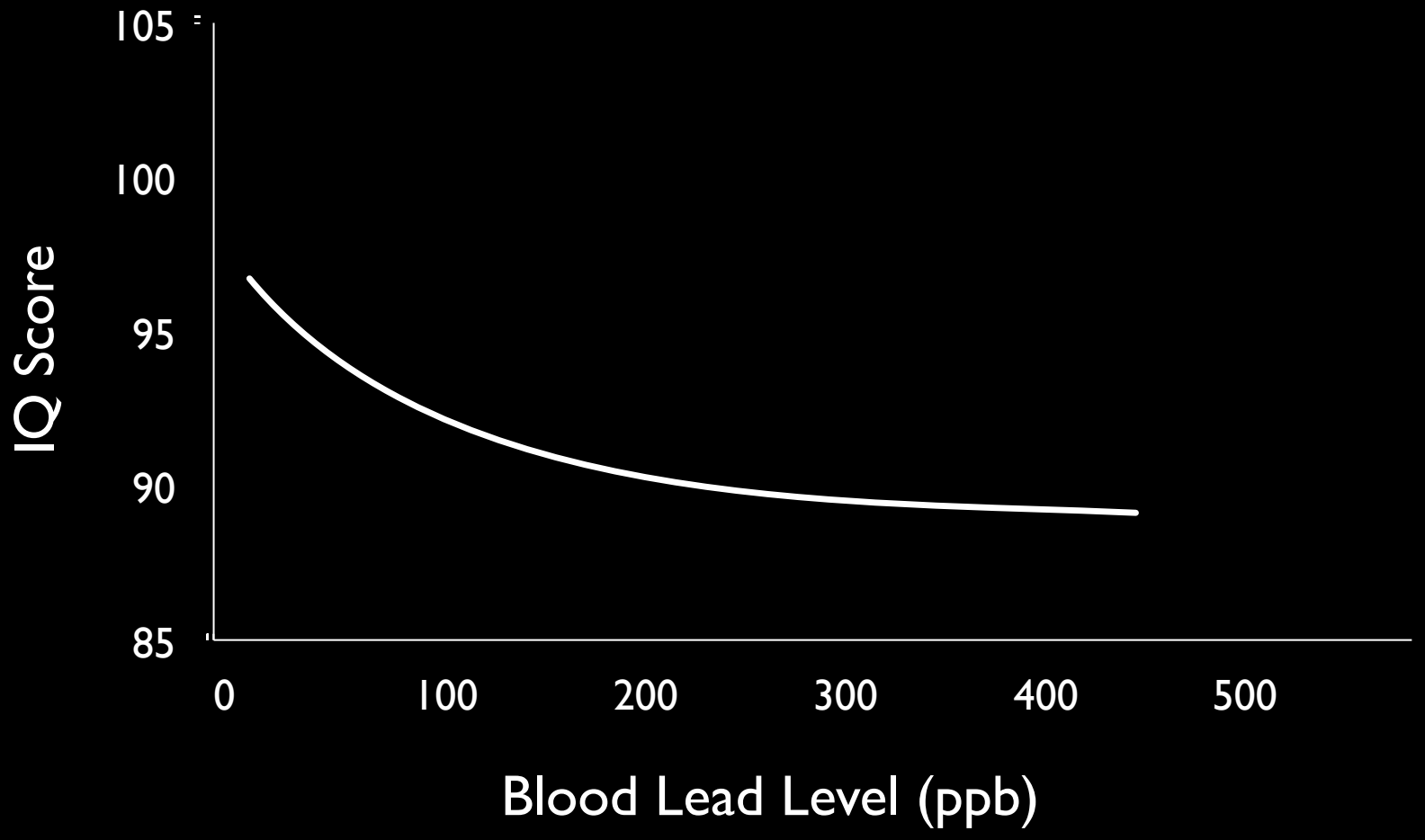
Chemicals Measured

Lab	Matrix	Analyte	16 wk	BHV	26 wk	Birth Maternal	Birth Child	4 wk	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5	P3 (7.5-9)
CDC	B	Lead	458	--	398	374	317	--	316	253	228	167	179	203
CDC	B	Mercury	419	--	337	374	317	--	316	253	228	167	179	203
CDC	B	Cadmium	--	--	--	--	--	--	--	--	228	167	179	203
CDC	B	Folate	349	--	--	43	--	--	--	--	--	--	-	--
CDC	S	Cotinine	445	--	395	350	294	--	283	218	213	157	-	--
CDC	M	Cotinine	--	--	--	--	372	--	--	--	--	--	-	--
CDC	H	Cotinine	--	--	--	--	--	--	--	--	--	--	-	--
Barr	M	BPA	--	--	--	--	374	--	--	--	--	--	-	--
CDC	U	BPA	462	--	406		--	--	293	246	246	180	211	234
CDC	U	Phthalates	462	--	406	360	--	--	293	245	246	180	211	234
CDC	U	Flame retardants	--	--	--	--	--	--	--	--	--	--	-	234
Barr	M	Phthalates	--	--	---	---	374	--	--	--	--	--	-	--
CDC	S	NPP	101	--	101	99	92	--	--	--	--	--	-	--
CDC	S	PCB	388	--	--	--	--	--	--	--	--	--	-	--
CDC	S	PFOA(PFCs)	368	--	35	90	266	--	--	--	208	--	-	200
CDC	S	PBDE	388	--	43	80	266	--	118	95	181	--	169	200
CDC	BRM	PBDE	--	--	--	--	--	73	--	--	--	--	-	--
Duke	VAC	PBDE	--	--	--	--	--	--	120	97	97	--	-	--
CDC	M	PCB	--	--	--	--	90	--	--	--	--	--	-	--
Barr	M	Sex steroids	--	--	--	--	374	--	--	--	--	--	-	--
Barr	M	Cortisol	--	--	--	--	374	--	--	--	--	--	-	--
CDC	S	OrganoChlor	388	--	99	148	140	--	--	--	--	--	-	--
CDC	M	OrganoChlor	--	--	--	--	90	--	--	--	--	--	-	--
CDC	U	OrganoPhosph	451	--	395	352	--	--	356	321	299	180	211	
CDC	U	Pyrethroid	442	--	388	342	--	--	293	262	268	179	208	
Barr	U	Herbicides	50	--	50	49	--	--	--	--	--	--	-	--
Richardson	U	Pyrethroid	--	--	--	--	--	--	--	--	22	--	211	--
GeneCore	DNA	Genotype	1	--	353	18	318	--	25	13	10	--	-	--
SFU	DNA	Genotype	--	--	--	--	319	--	25	13	10	--	-	--
Richardson	RNA	Genotype	--	--	--	--	---	--	--	--	--	--	89	--
Arora	T	Multiple	--	--	--	--	---	--	--	--	--	--	-	70
UW	S	Thyroid	226	--	--	--	294	--	--	--	--	--	-	--
UW	S	Sex steroids	--	--	--	--	294	--	--	--	--	--	-	--
Dartmouth	U	Arsenic	20*	--	324*	--	--	--	--	--	--	--	-	--
Dartmouth	U	Cadmium	20	--	324	--	--	--	--	--	--	--	-	--
Dartmouth	U	Iodine	20	--	324	--	--	--	--	--	--	--	-	--
Duke	U	PBDE	--	--	--	10	--	--	--	--	10	--	-	--
EPA	W	PFC	--	263	--	--	--	--	--	--	--	--	-	--
ARUP	S	Vaccine antibodies	--	--	--	--	--	--	--	209	--	--	-	--

B	Whole blood
BRM	Breastmilk
	Hair
S	Serum
SA	Saliva
T	Teeth
VAC	Vacuum dust
W	Water

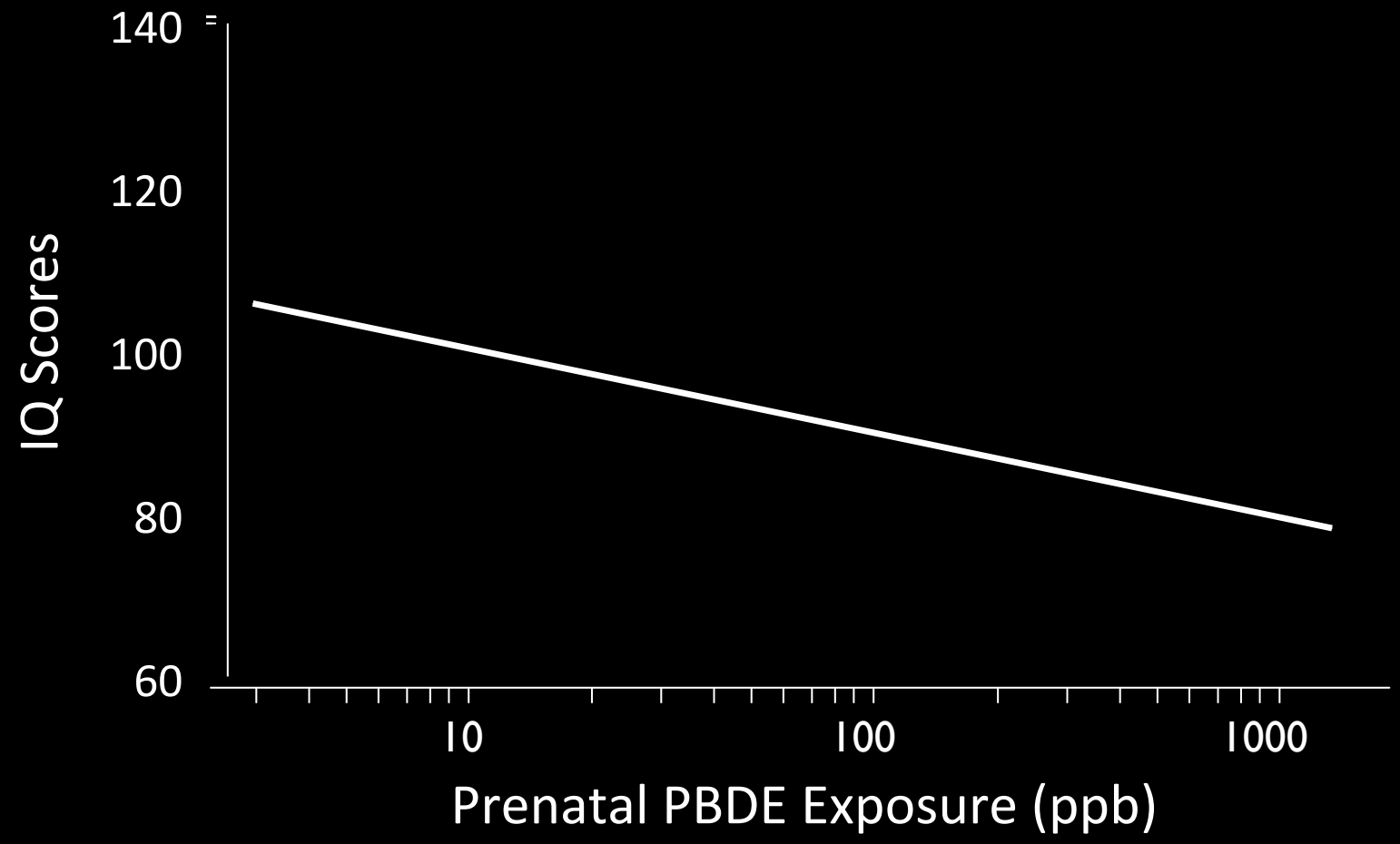
The Ongoing Search for a Threshold

Lead Toxicity and IQ Deficits



Lanphear BP, et al. EHP 2005;113:894-899.

Prenatal Flame Retardant (PBDE) Exposure and IQ Scores in 5-year old Children



Chen A, et al. EHP 2014;122:856-862

Reading Scores and SHS Exposure in US Children, NHANES III, 1998-1994

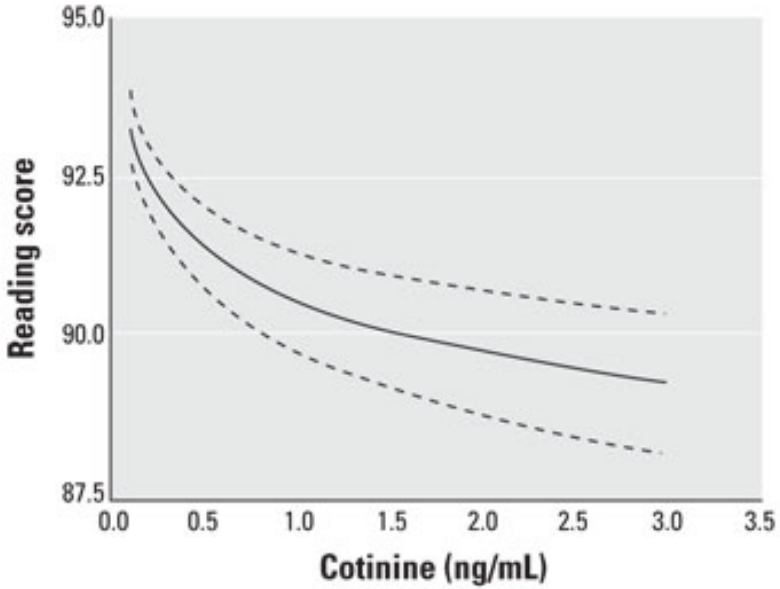


Figure 1. Log-linear regression line for reading scores by serum cotinine levels. Dashed lines indicate 95% confidence interval.

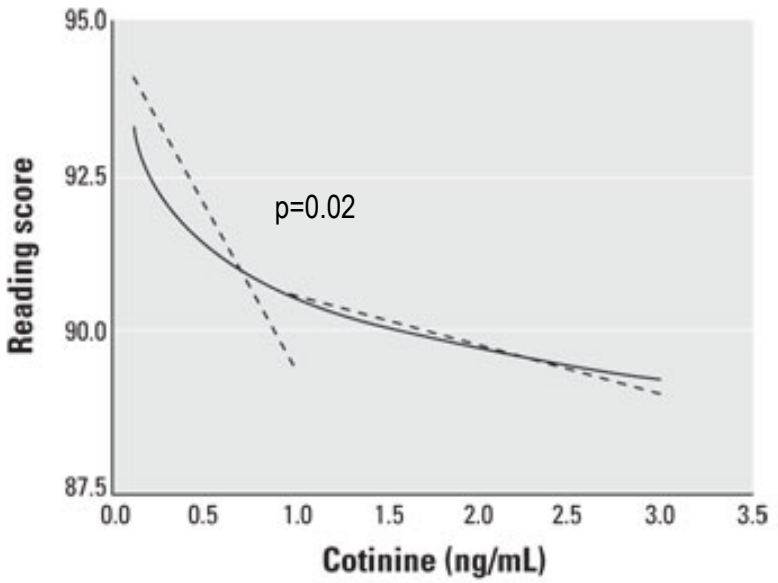
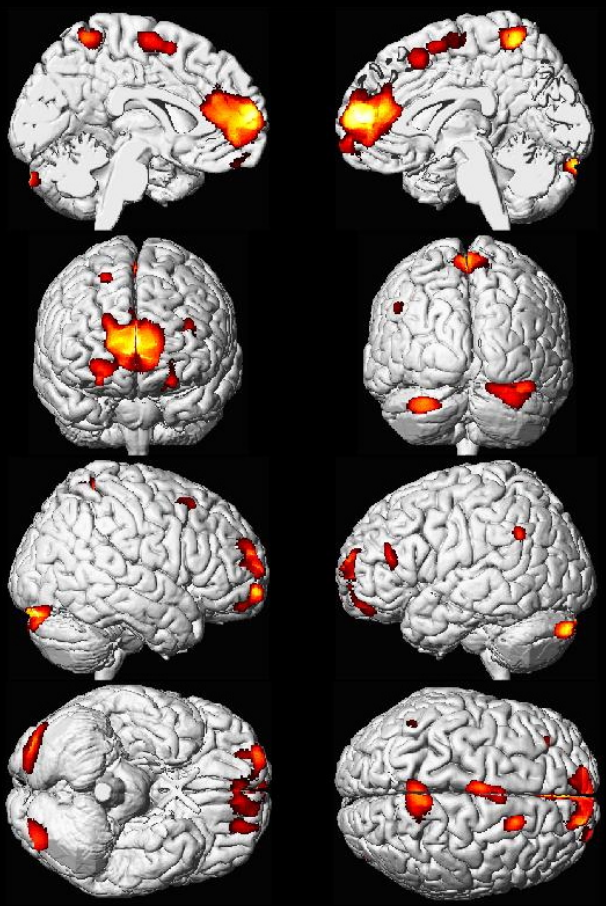


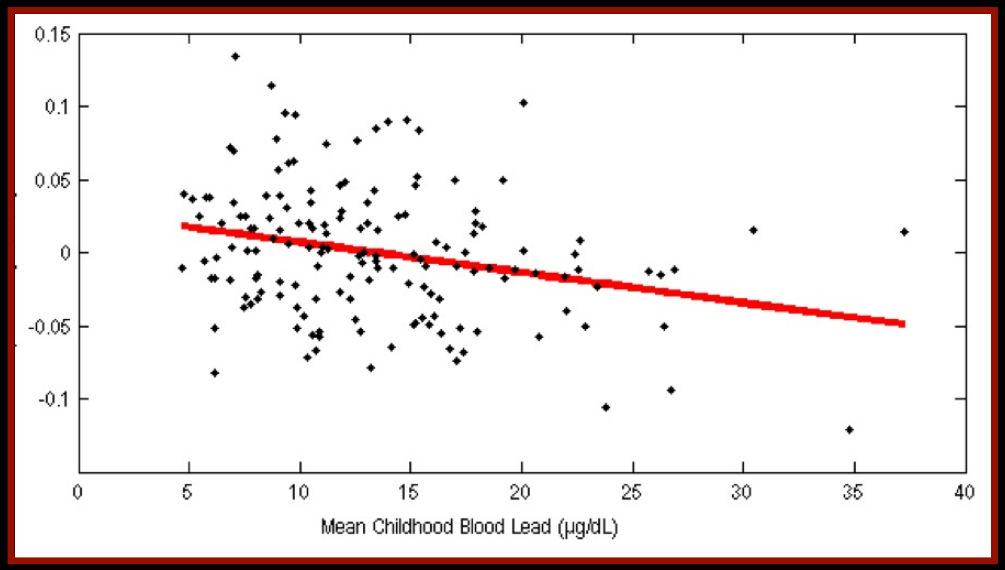
Figure 2. Log-linear model for cotinine (solid line) versus linear models for cotinine among children with cotinine above and below 1 ng/mL (dashed lines; ~ 80th percentile).

Yolton K, et al. Environ Health Perspect 2005;113:98-103.

No Acceptable Level?

Gray Matter Loss by Childhood Lead Exposure

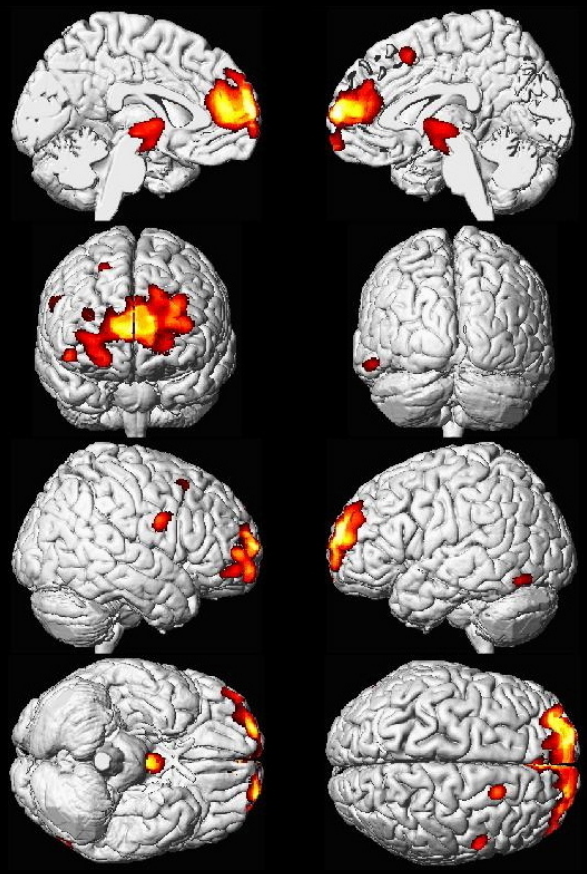




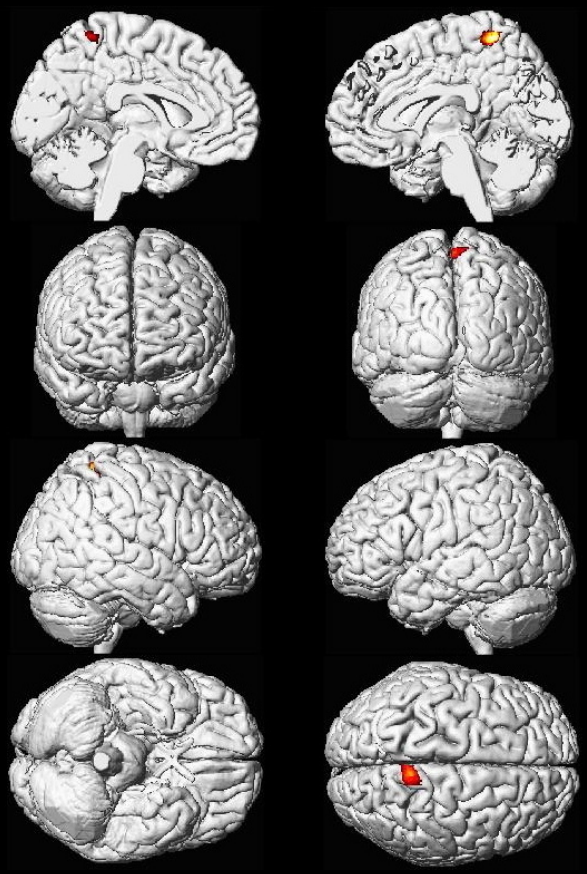
Adjusted for child's age, birth weight. Gestational age, IQ, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, et al. PLoS Medicine 2008).

Reduction in Gray Matter by Childhood Blood Lead Levels and Subject's Sex

Men (n=83)

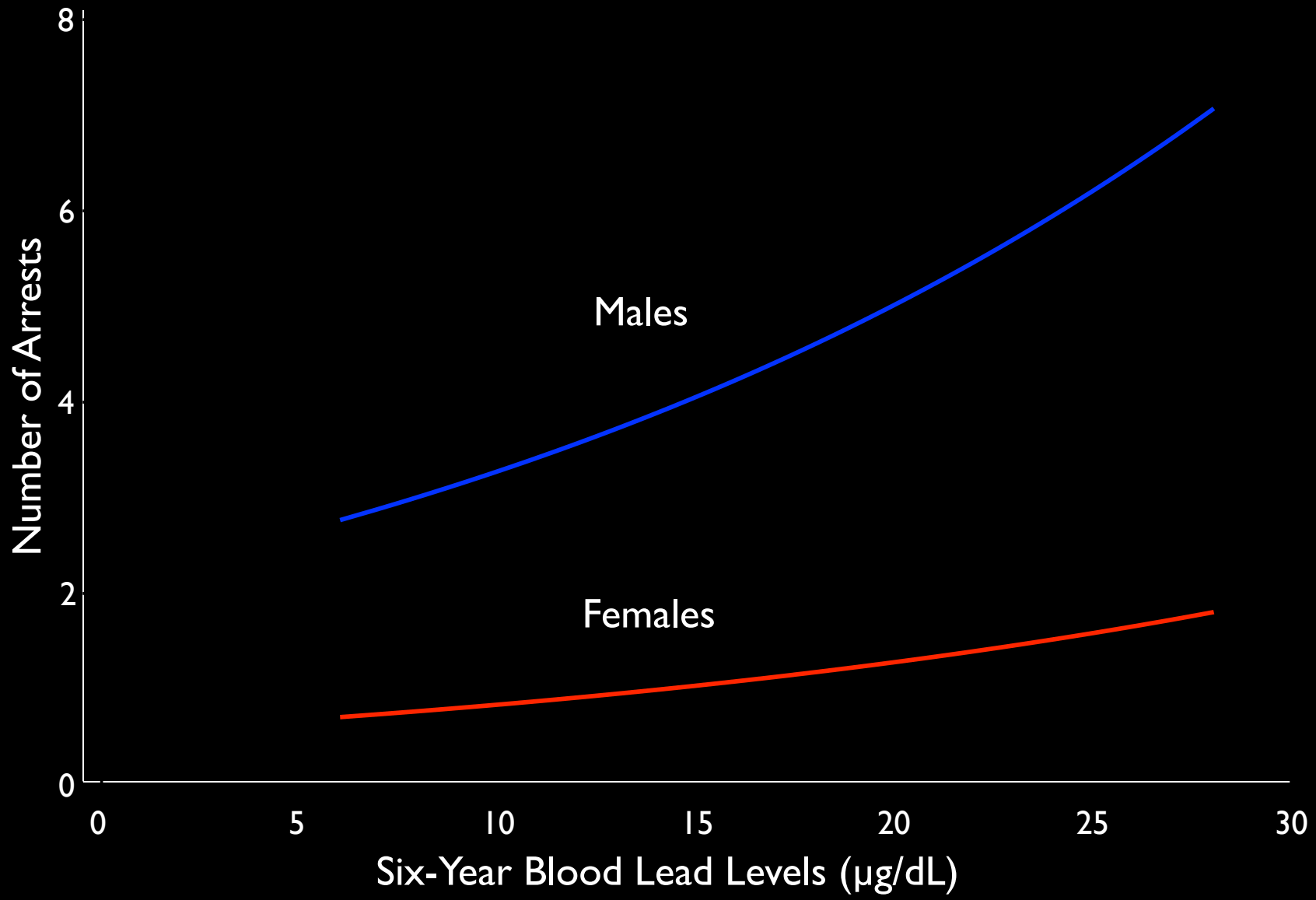


Women (n=74)



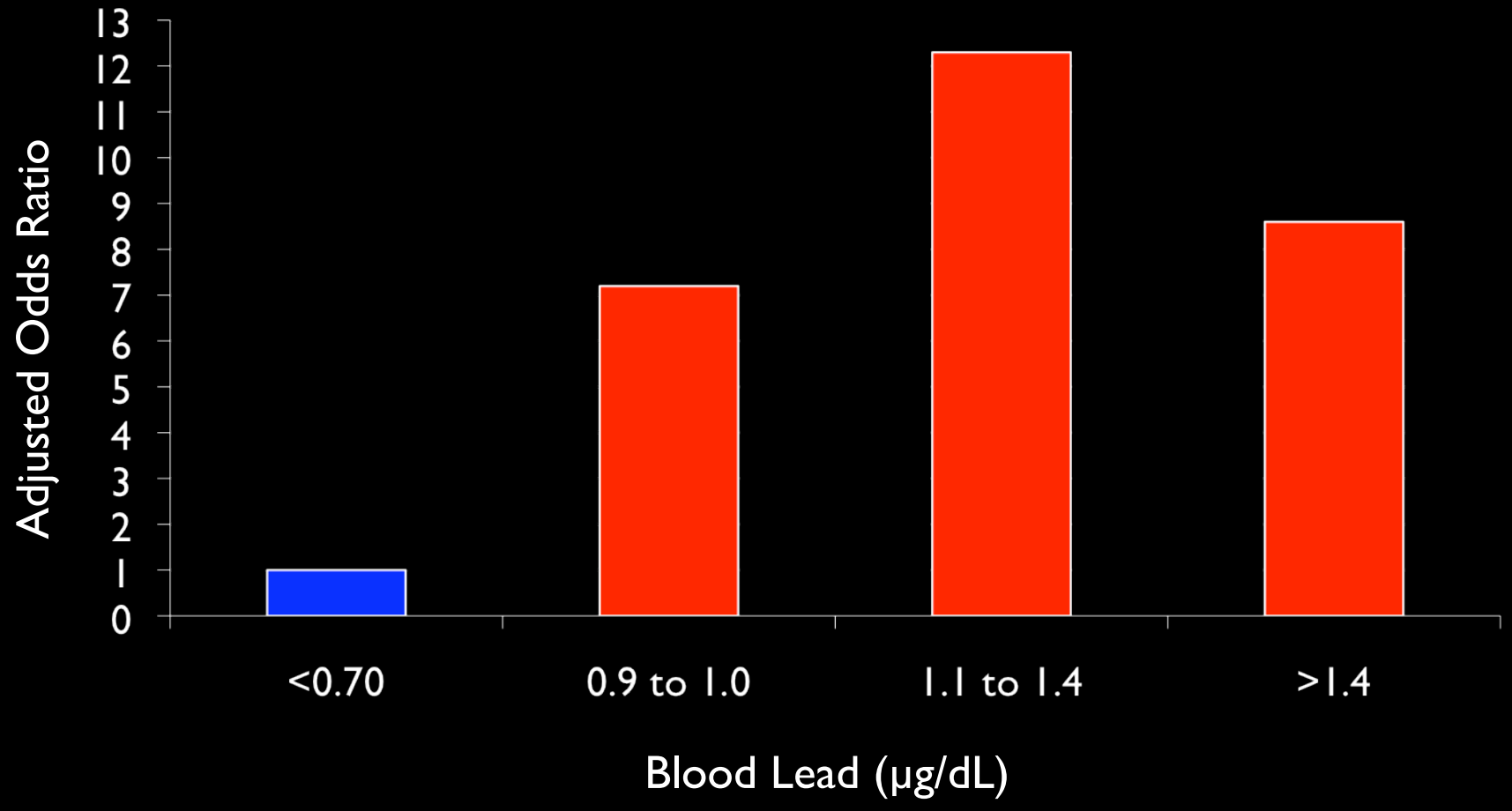
Adjusted for child's age, birth weight. Gestational age, IQ, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, et al. PLoS Medicine 2008).

Number of Arrests by Childhood Lead Exposure



Wright J, PLoS Med 2008;5:e101.

Conduct Disorder and Blood Lead Levels in US Children, 8 to 15 years, NHANES 2001-2004



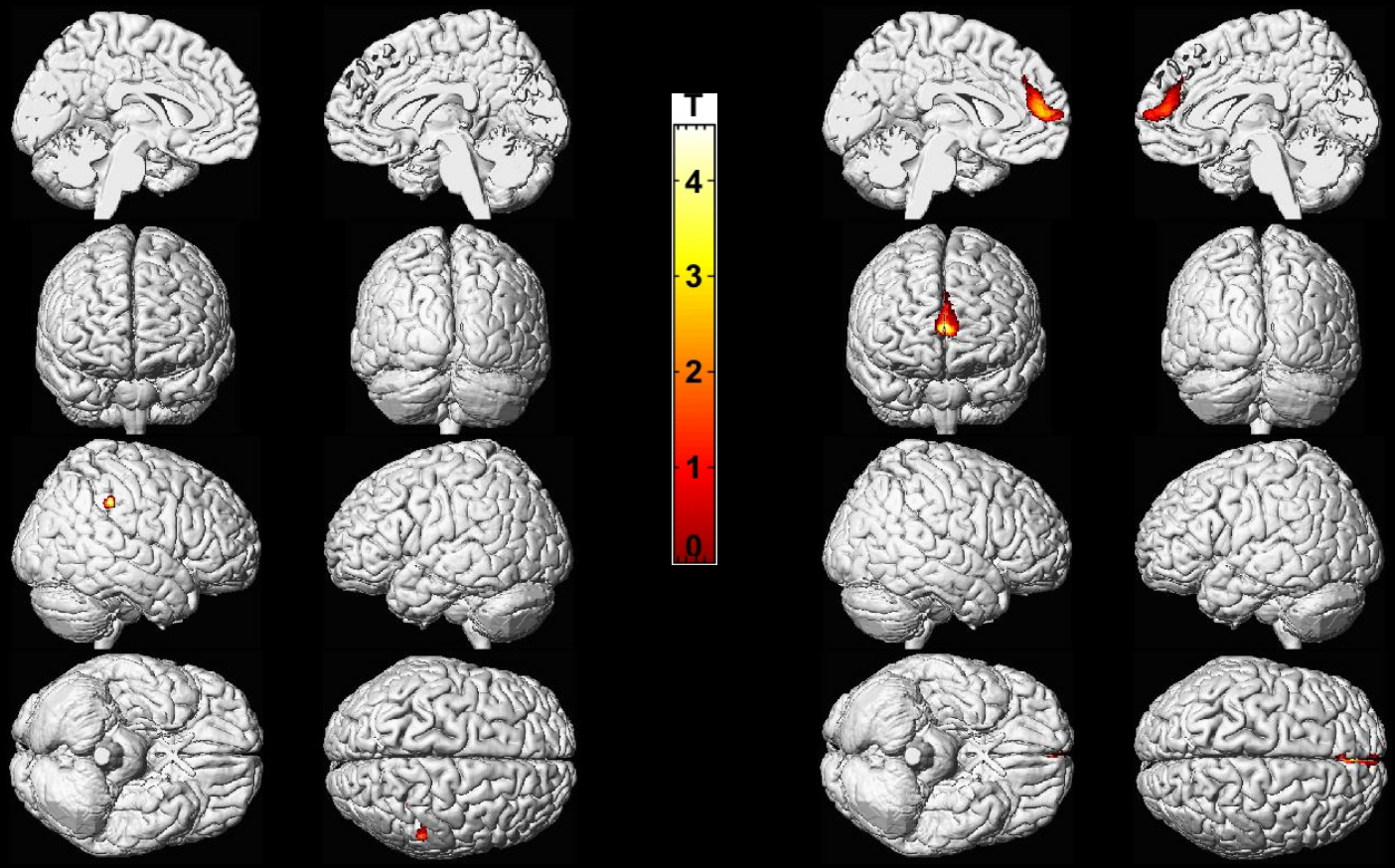
Braun J, et al. Environ Health Perspect 2008;116:956-62.

Windows of Vulnerability

Developmental Trajectory of Lead Exposure by Gray Matter Deficits

Year 1

Year 2

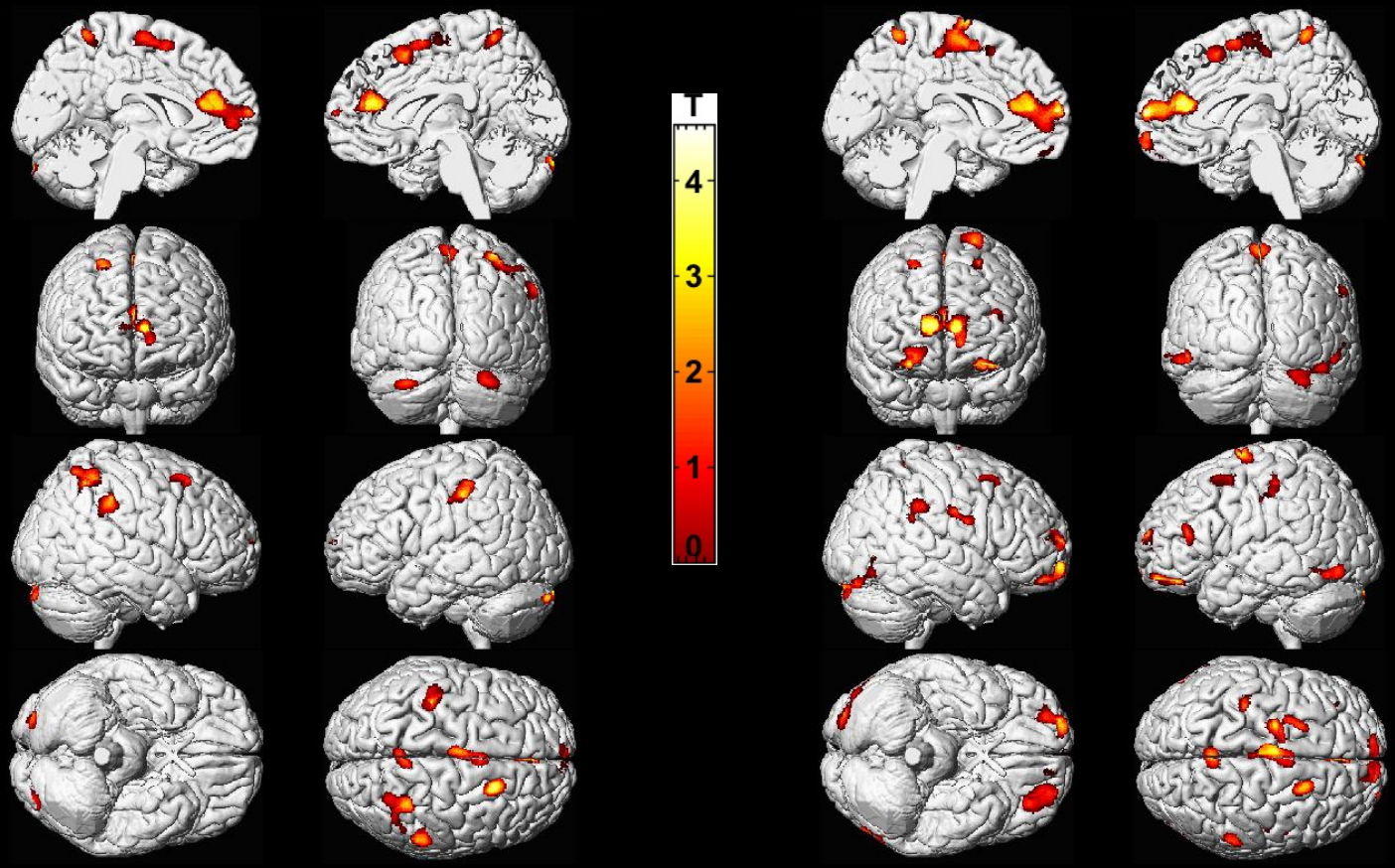


Brubaker CJ, Dietrich KN, Lanphear BP, Cecil KM. The influence of age of lead exposure on adult gray matter volume. Neurotoxicology 2010;31:259-266.

Developmental Trajectory of Lead Exposure by Gray Matter Deficits

Year 3

Year 4

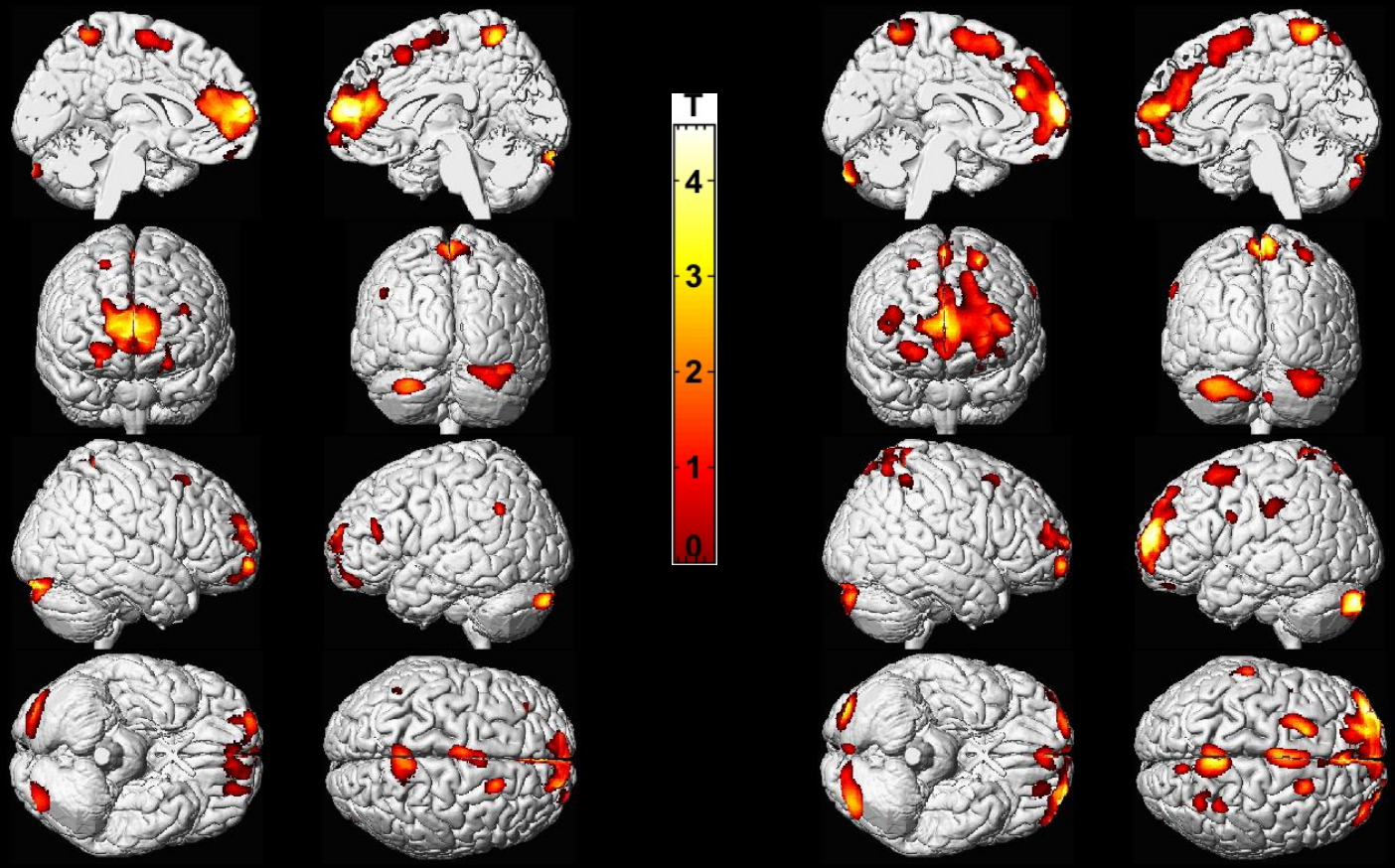


Brubaker CJ, Dietrich KN, Lanphear BP, Cecil KM. The influence of age of lead exposure on adult gray matter volume. Neurotoxicology 2010;31:259-266.

Developmental Trajectory of Lead Exposure by Gray Matter Deficits

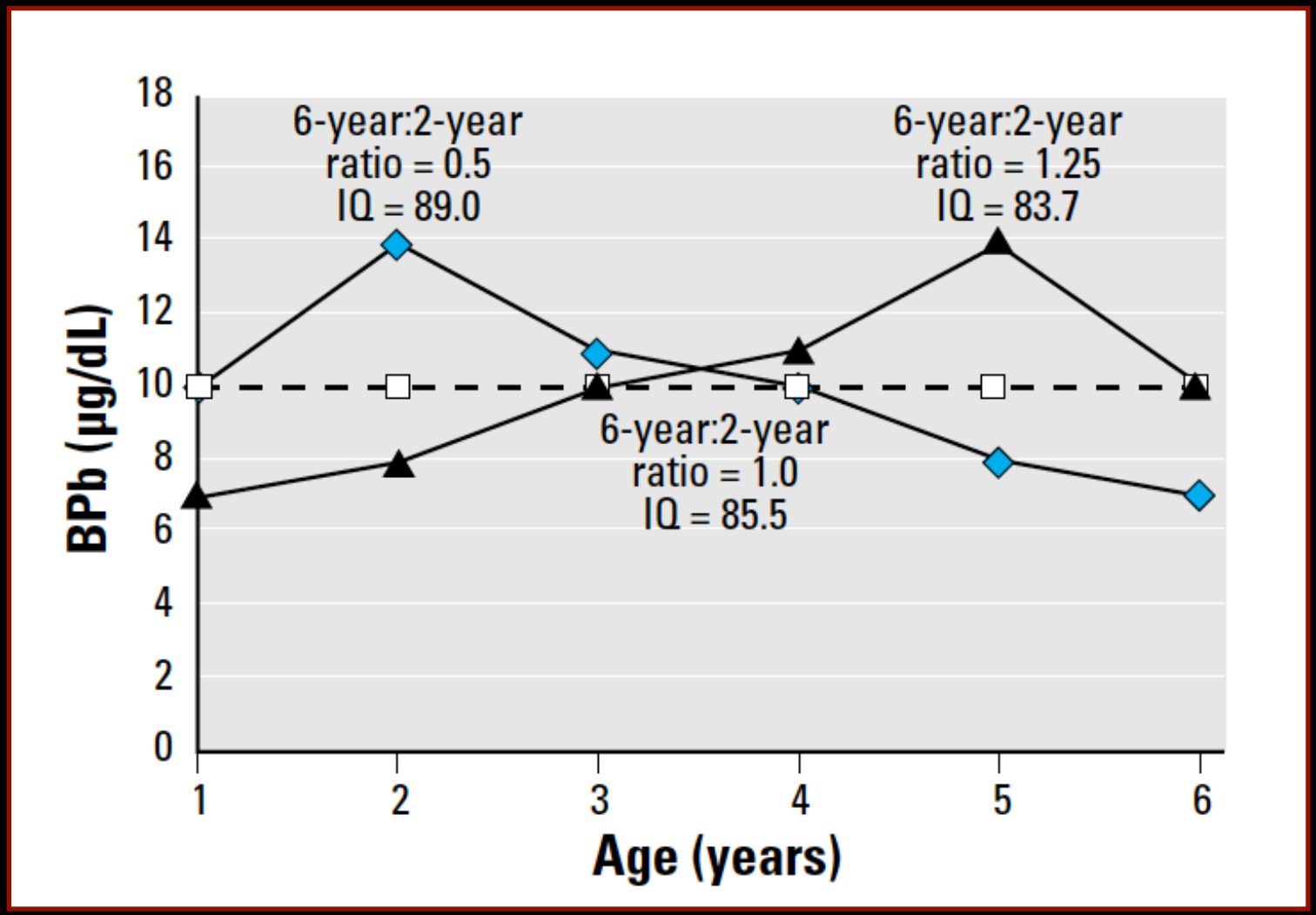
Year 5

Year 6



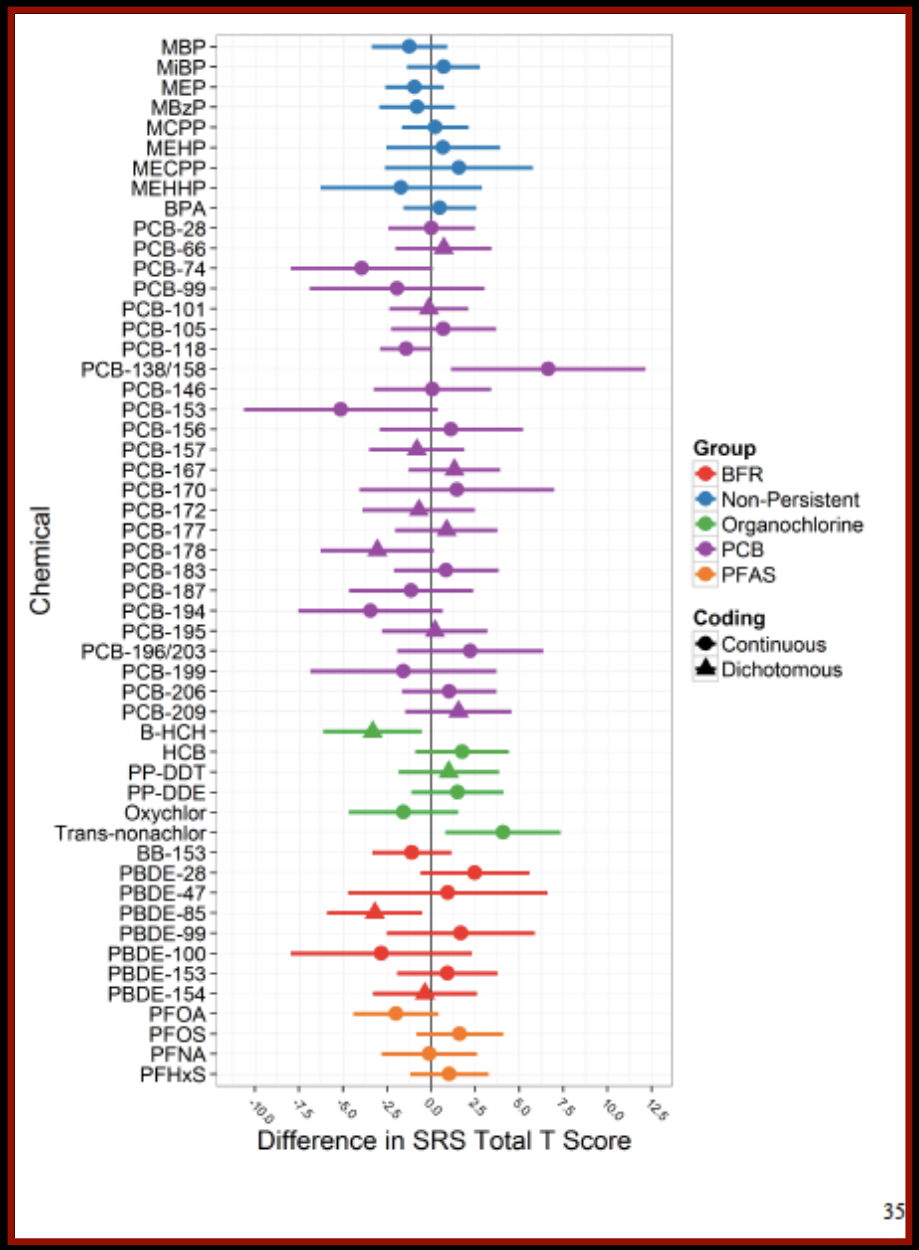
Brubaker CJ, Dietrich KN, Lanphear BP, Cecil KM. The influence of age of lead exposure on adult gray matter volume. Neurotoxicology 2010;31:259-266.

Age of Vulnerability of Lead Toxicity



Hornung R, et al. EHP 2009;117: 1309-1312.

Prenatal Exposures to EDCs and Autistic Behaviors in Children



Braun J, et al. EHP 2014 (online).

10x OPs

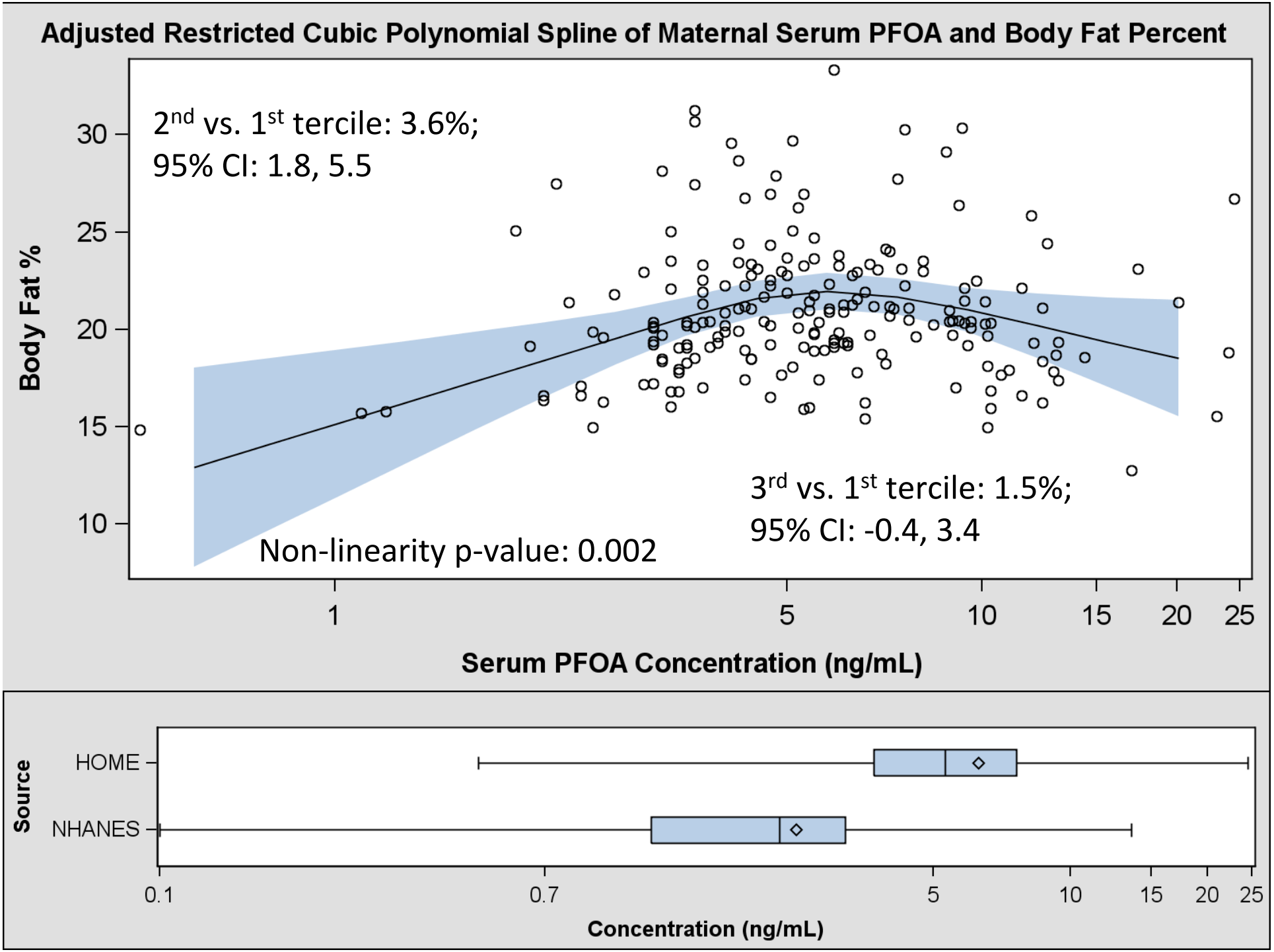
-151 grams

-0.5 week

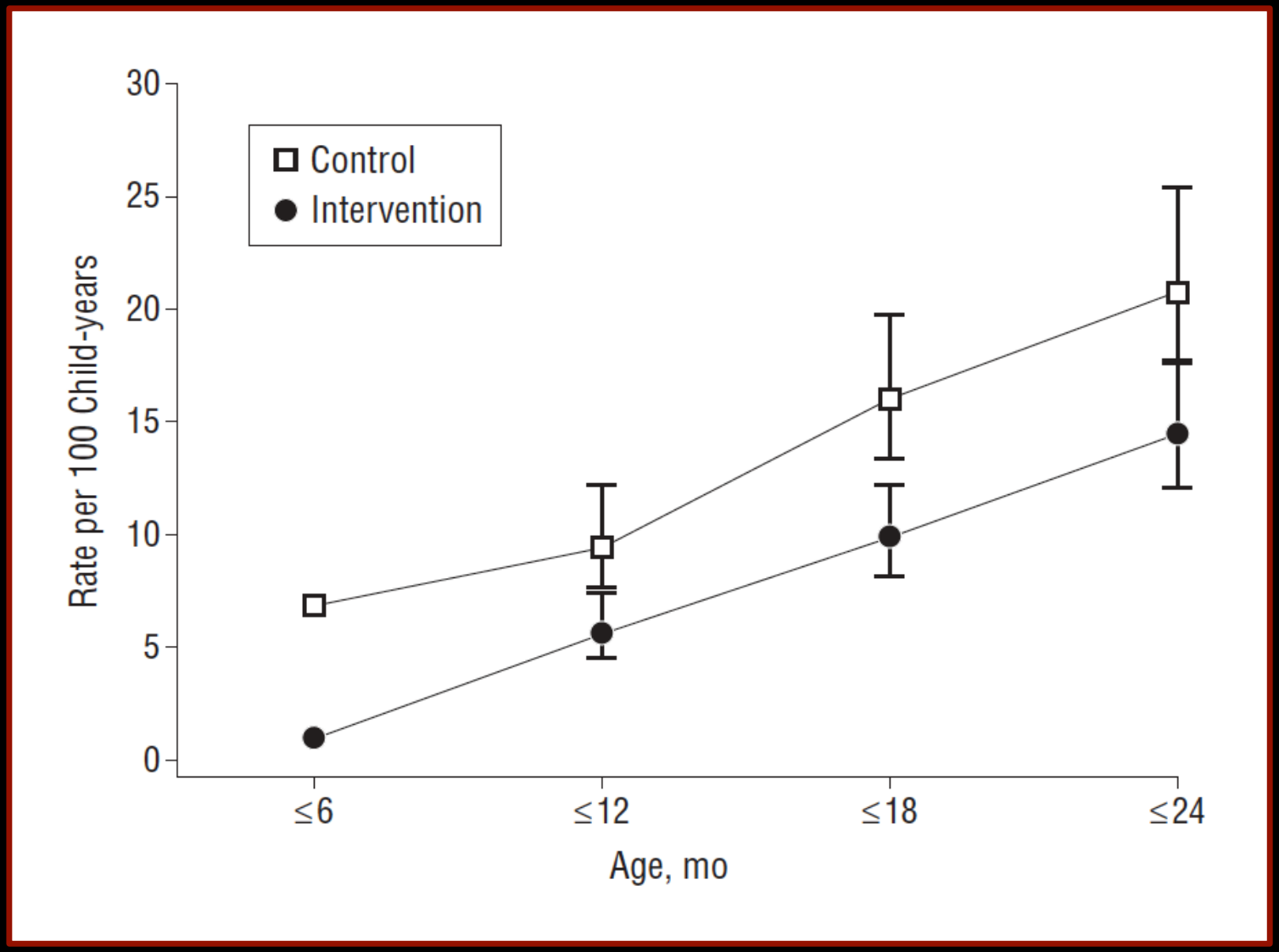
Rauch SA, et al. EHP 2012;120:1055-1060.

Source of High PFOA Exposure

- DuPont fluoropolymer plant located on Ohio River 250 miles upstream of Cincinnati, OH
- Cincinnati draws drinking water from Ohio River
- Investigating tap water as a potential source of exposure in HOME Study women

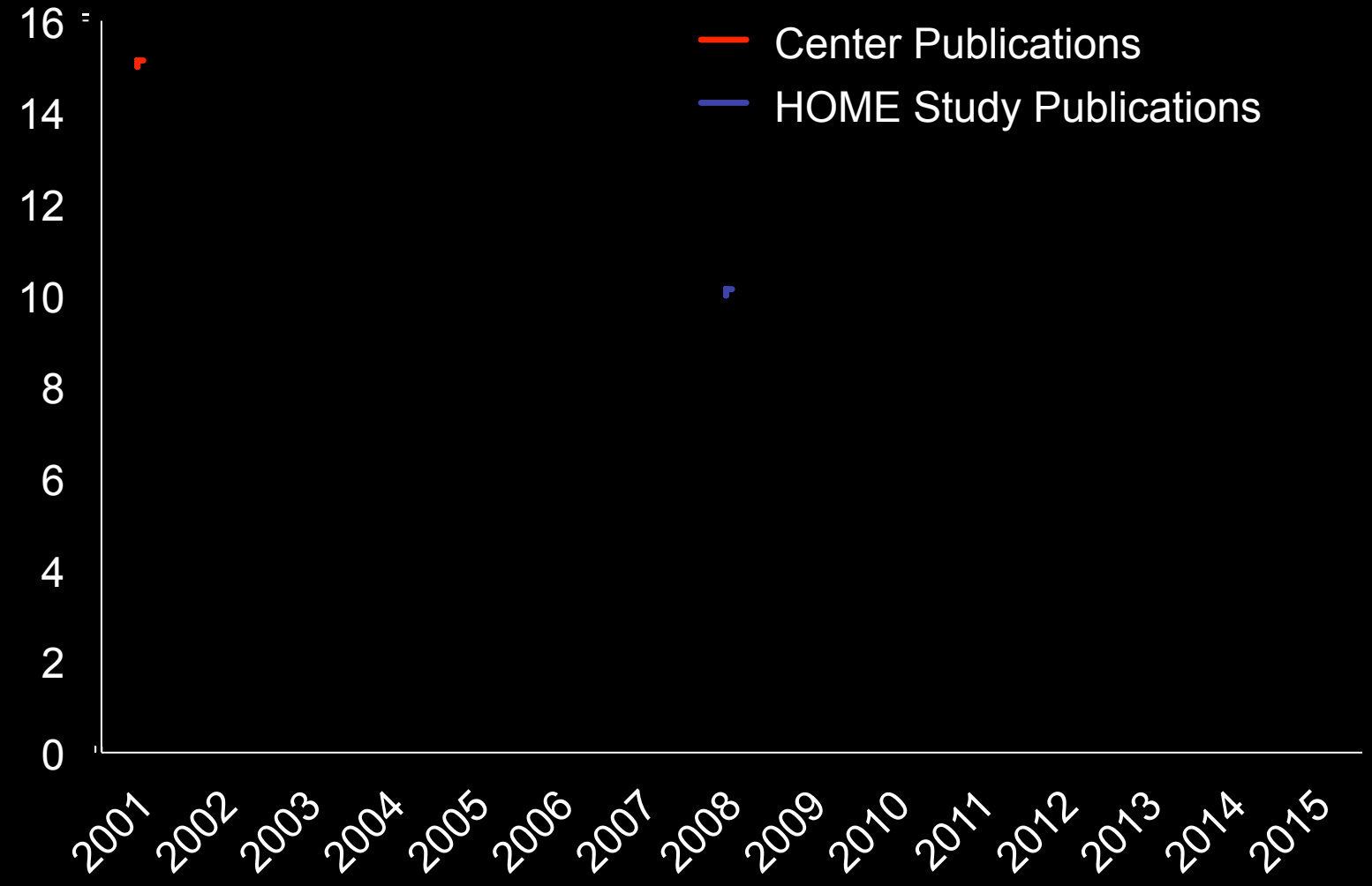

Adjusted Restricted Cubic Polynomial Spline of Maternal Serum PFOA and Body Fat Percent
2nd vs. 1st tercile: 3.6%;
95% CI: 1.8, 5.5
3rd vs. 1st tercile: 1.5%;
95% CI: -0.4, 3.4
Non-linearity p-value: 0.002
Body Fat %
30
25
20
15
10
1
5
10
15
20
25
Serum PFOA Concentration (ng/mL)
Source
HOME
NHANES
0.1
0.7
5
10
15
20
25
Concentration (ng/mL)

A RCT to Reduce Residential Injuries



Phelan KJ, et al. APAM 2011;165:339-345.

Number of Publications



New Directions

- Phenols and neurobehavior in childhood
- Measurements of toxicants in deciduous teeth
- Measurement of non-brominated flame retardants and neurobehavior in childhood
- Toxicants and internalizing symptoms in preadolescents
- Endocrine disrupting chemicals and obesity in preadolescents

The HOME Study Team

Investigators

Cincinnati

Mekibib Altaye
Aimin Chen
Kim Dietrich
Tanya Froehlich
Rick Hornung
Jane Khoury
Kieren Phelan
Paul Succop
Heidi Sucharew
Kim Yolton

External

Joseph Braun
Amy Kalkbrenner
Bruce Lanphear
Adam Spanier
Heather Stapleton
Manish Arora
Glenys Webster
Nimesh Patel

HOME Study Staff

Stacey Liddy
Sam Morgan
Yingying Xu
Ann Popelar
Leah Tyzinski
Mim Larkin
Sarah Stewart
Sharon Penko
Suzette Baez
Hadley Sauers
Will Bell
Jason Meyer
Diana Henderson
Jessica Cruey
Hafiz Mohamed
Keith Payne
Donna Strauss
Robert Tamer

HOME Study Families

Collaborations