A developmental perspective on early-life exposures to neurotoxicants

David C. Bellinger

Boston Children's Hospital

Harvard Medical School

Harvard T.H. Chan School of Public Health

Making the Link Between Environmental Exposures and Neurodevelopmental Disorders More Compelling to Stakeholders (public, regulators, politicians)

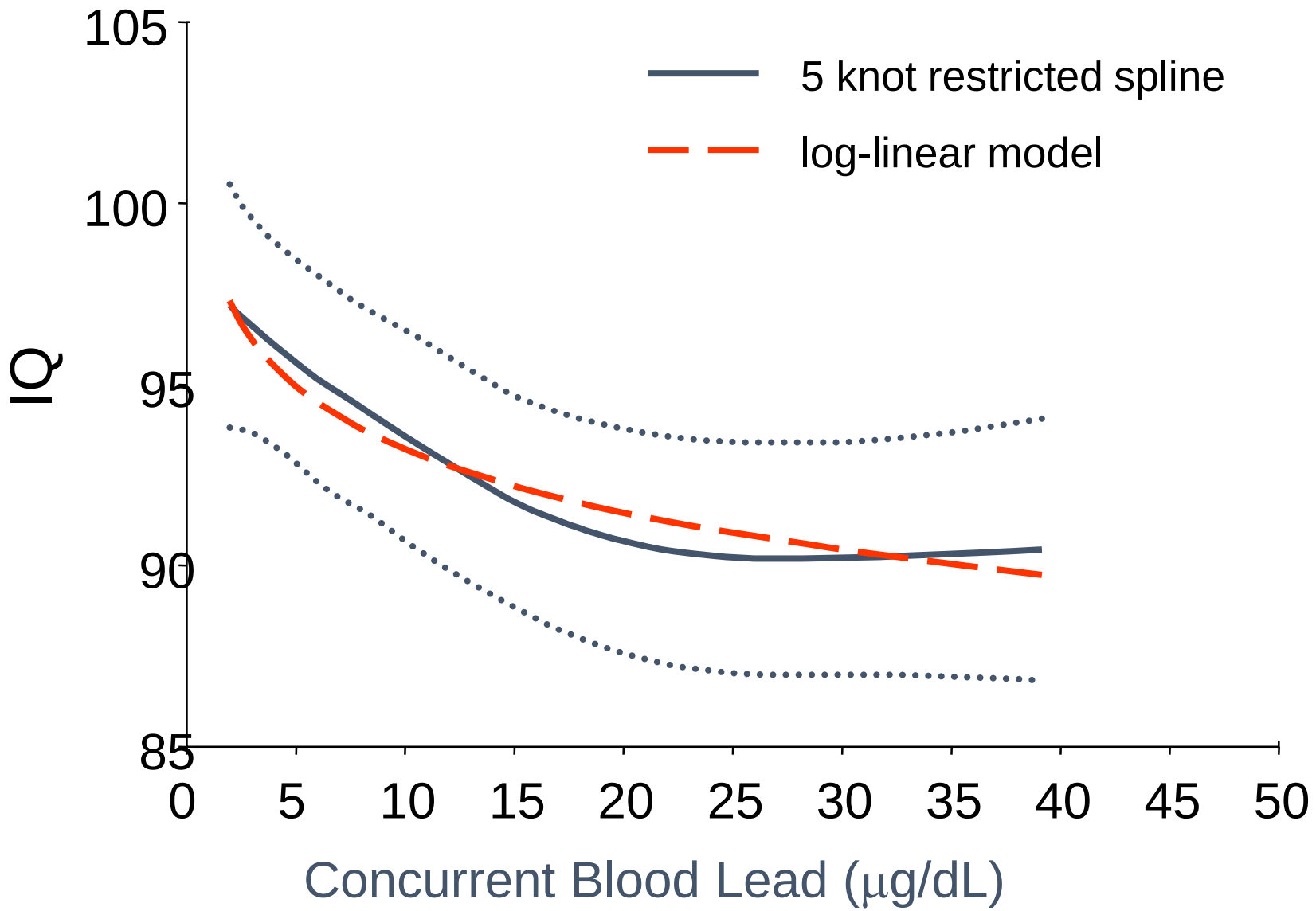
- Importance of developing a broader and more integrated story about how early-life exposure to a neurotoxicant can impact a child's developmental trajectory in multiple domains, the downstream effects: example of childhood lead exposure and criminal offending in young adulthood
- Early-life exposure to neurotoxicants affects how effectively an individual is able to respond to later neurological insults, i.e., an effect modifier that reduces resilience or cognitive reserve
- A focus on population rather than individual risk produces a more veridical assessment of the societal impact of neurotoxicant exposures (the "prevention paradox")

Association Between Childhood Lead Exposure and Criminal Behaviors in Adolescence and Young Adulthood

- Needleman HL et al. JAMA 1996;275(5):363-9.
- Nevin R. Environ Res 2000;83(1):1-22.
- Dietrich KN et al. Neurotoxicol Teratol 2001;23(6):511-8.
- Needleman HL et al. Neurotoxicol Teratol 2002;24(6):711-7.
- Nevin R. Environ Res 2007;104(3):315-36.
- Wright JP et al. PLoS Medicine 2008; 5(5), e101.
- Fergusson DM et al. J Epidemiol Community Health 2008;62(12):1045-50.
- Muennig P. Arch Pediatr Adolesc Med 2009;163(9):844-9.
- Mielke HW & Zahran. Environ Int 2012;43:48-55.
- Reyes JW. Economic Inquiry 2015;53(3):1580-605.
- Boutwell BB et al. Environ Res 2016;148:79-85.
- Taylor MP et al. Environ Health 2016;15:23.
- Boutwell BB et al. PLoS One 2017; 12(11), e0187953.
- Nkomo P et al. Environ Int 2017;109:136-145.
- Emer et al. Environ Res, 2020;180: article 108882
- Coulton et al. (2020)

Relationship of Concurrent Blood Lead Level and IQ:

Lanphear et al. *Environ Health Perspect* 2005;113:894-899



Blood Lead Level and ADHD: NHANES 1999-2002

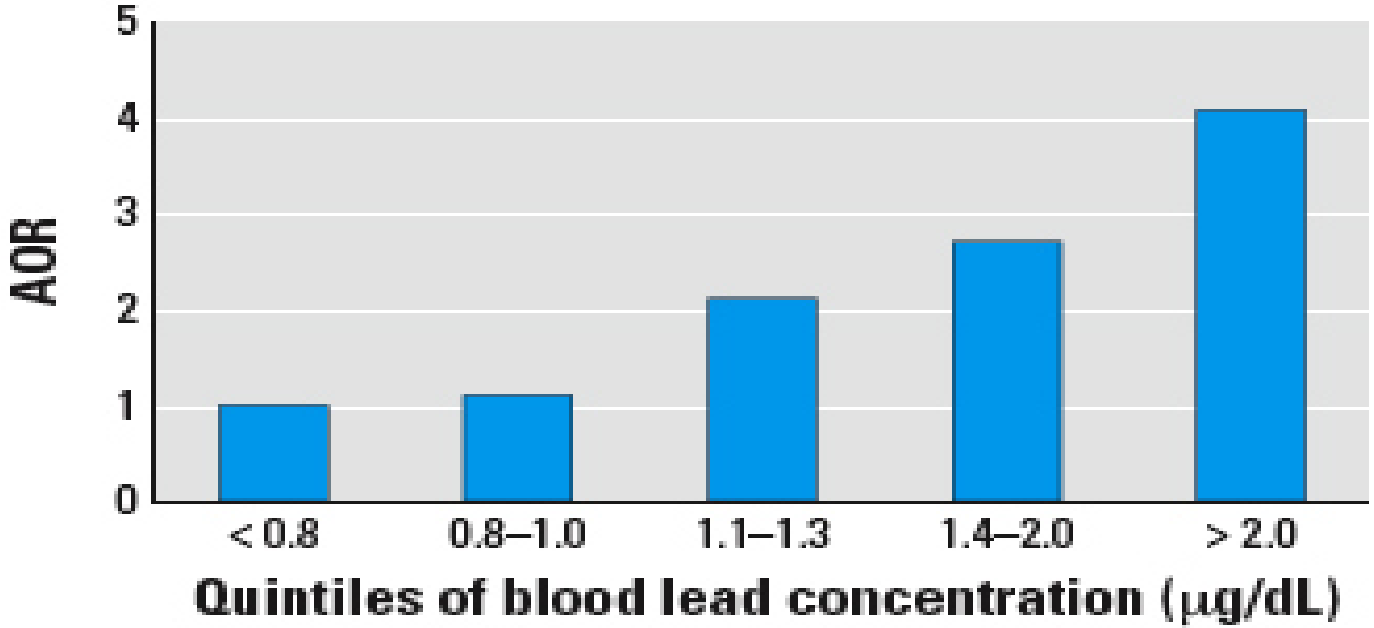


Figure 1. AOR for ADHD among U.S. children, NHANES 1999–2002, by blood lead concentration (µg/dL). The model was adjusted for child's age, sex, race/ethnicity, preschool attendance, serum ferritin, prenatal ETS exposure, smoker in the household, and insurance status.
p-value for trend = 0.012.

Braun et al. *Environ Health Perspect* 2006;114:1904-1909

Needleman et al., 1979
Nigg et al., 2008
Wang et al., 2008
Froehlich et al., 2009
Nigg et al., 2010
Goodlad et al., 2013
Kim et al., 2013
Park et al., 2016
Choi et al.2016
Darneshparvar et al., 2016
Nigg et al., 2016

Blood Lead Levels and Performance on End-of-Grade Reading Achievement Test, 2000-2004, NC 4th graders (N=8,600)

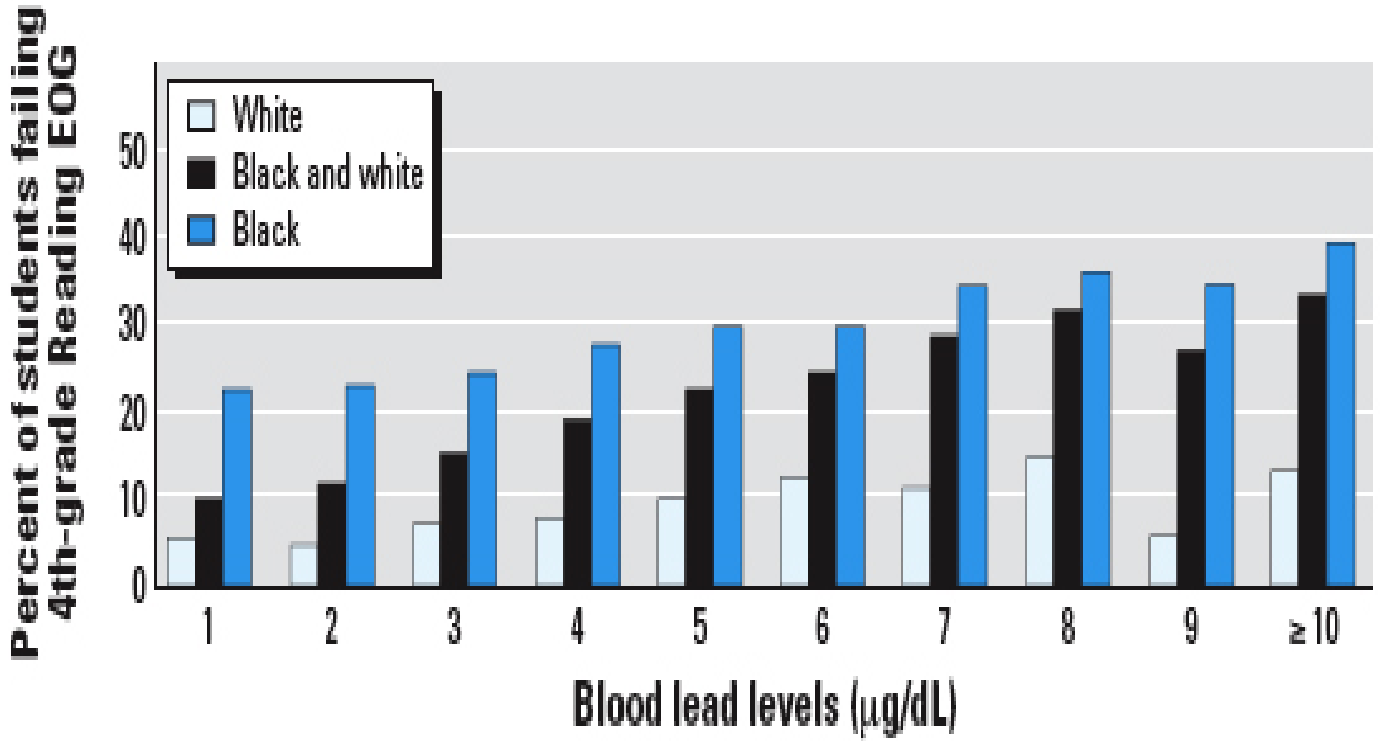
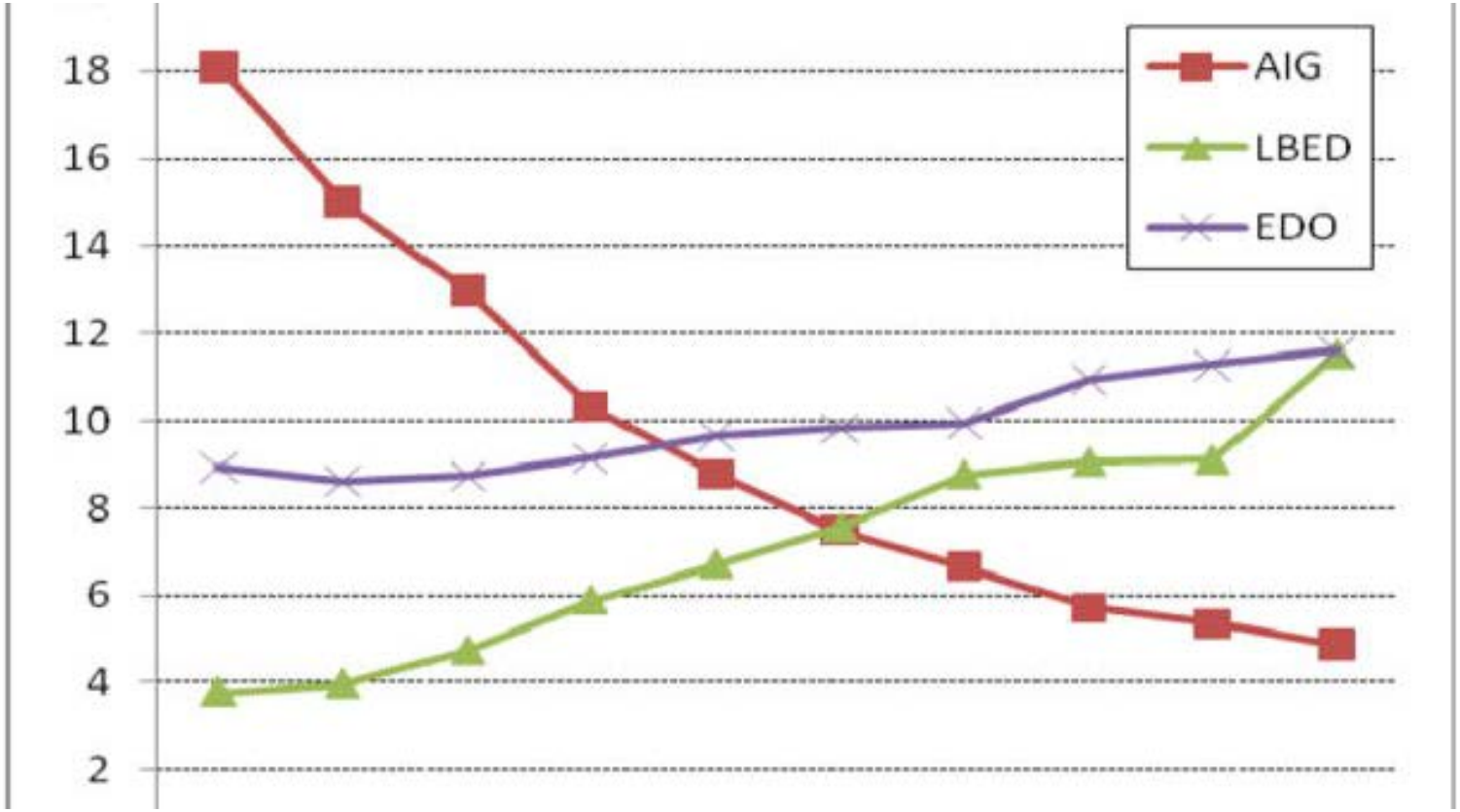


Figure 4. Percent of students failing 4th-grade Reading EOG.

Miranda et al., *Environ Health Perspect* 2007;115:1242-1247

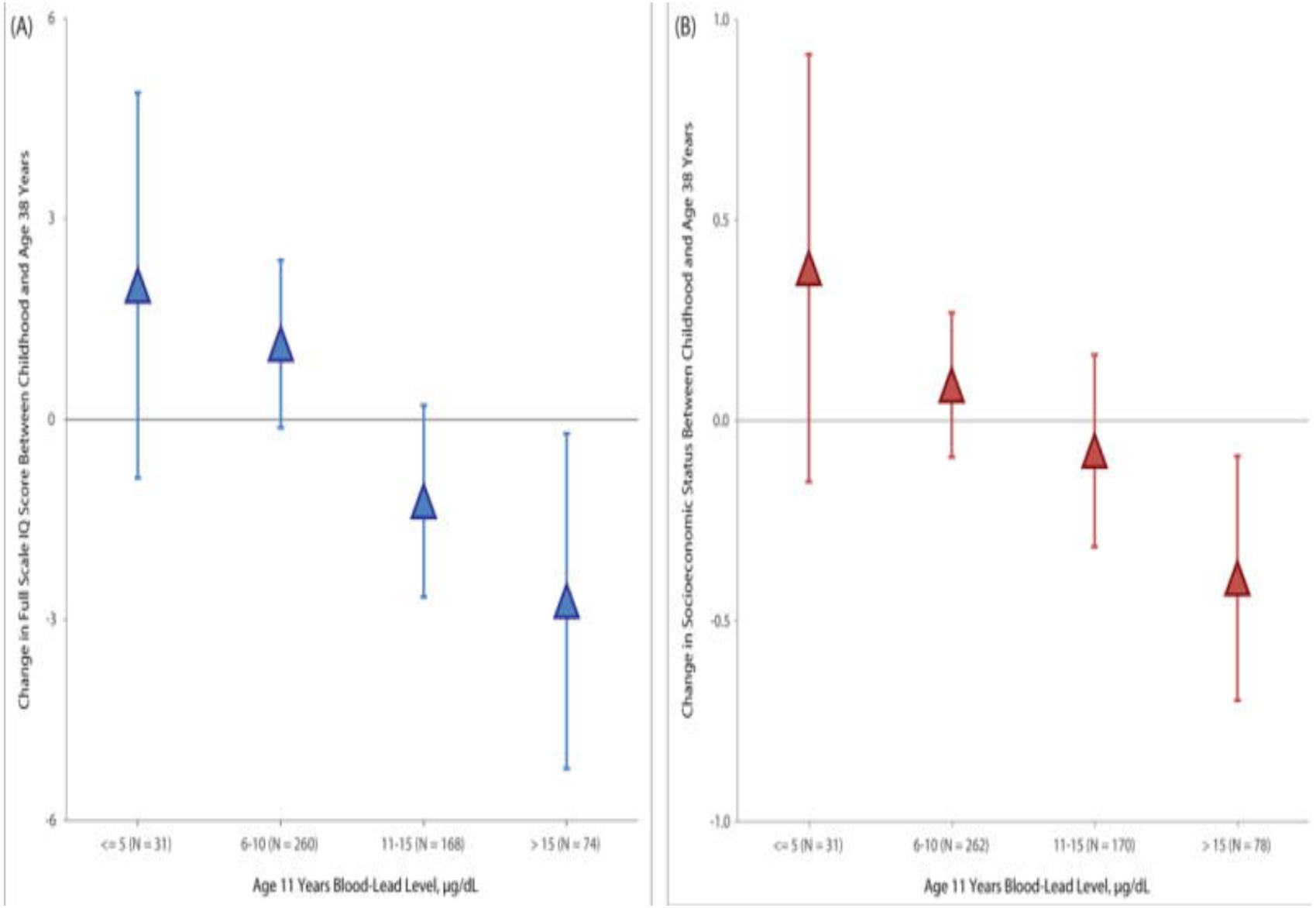
Blood Lead Level and "Exceptionality Designations" in 4th Graders (Miranda et al. Int J Child Health Hum Dev 2010:3:77-84)



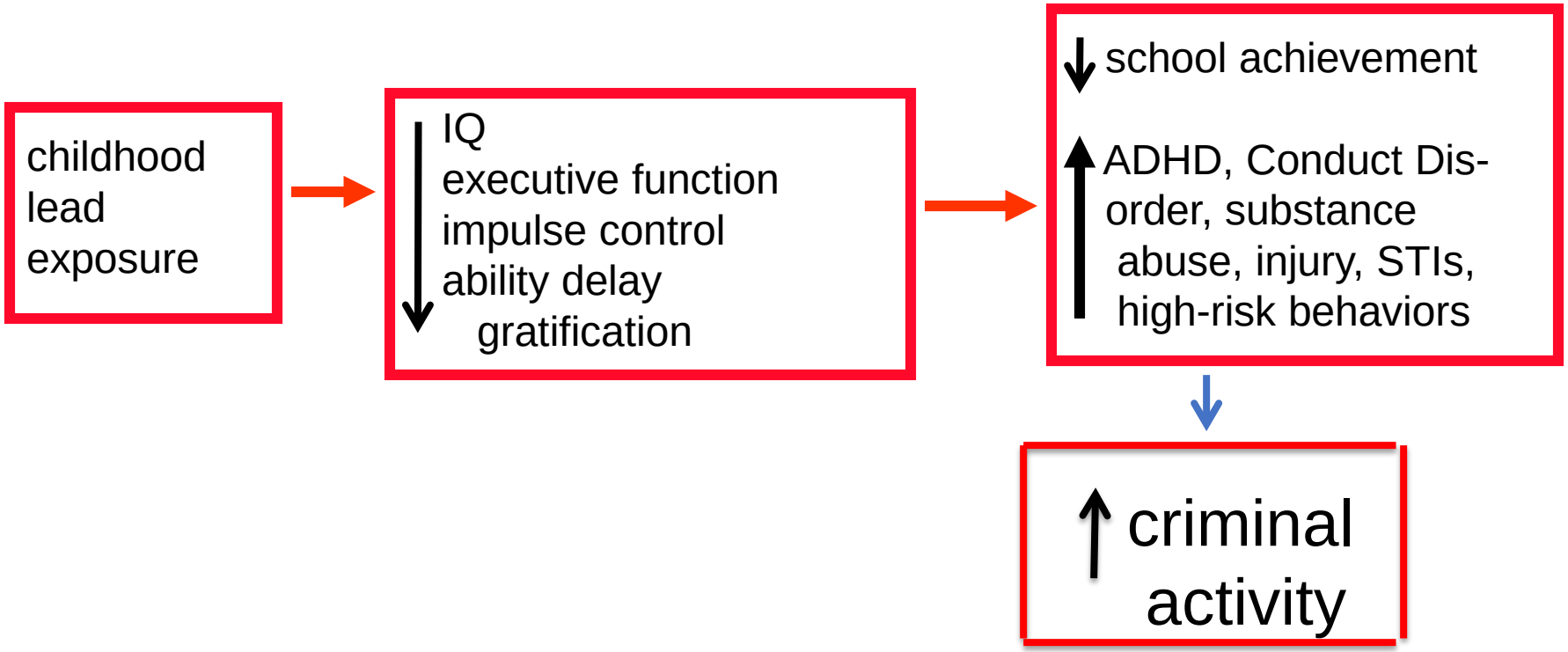
AIG: advanced and intellectually gifted
LBED: learning and behavioral exceptional
EDO: designated exceptional for other reasons (sensory, physical, ASD, severe IDD)

Change in IQ and SES: 11 to 38 Years by Blood Lead Concentration at 11 Years: Dunedin Study

(Reuben et al. JAMA 2017;317:1244-51)



Developmental Cascade Linking Childhood Lead Exposure to Adverse Outcomes in Adulthood: for some individuals, reduction in IQ might be the beginning, not the end of the story



Coulton et al. (2020) study of >10,000 children in Cleveland Metropolitan School District (https://www.ideastream.org/news/lead-exposure-sets-more-cleveland-children-on-a-poisoned-to-prison-path)

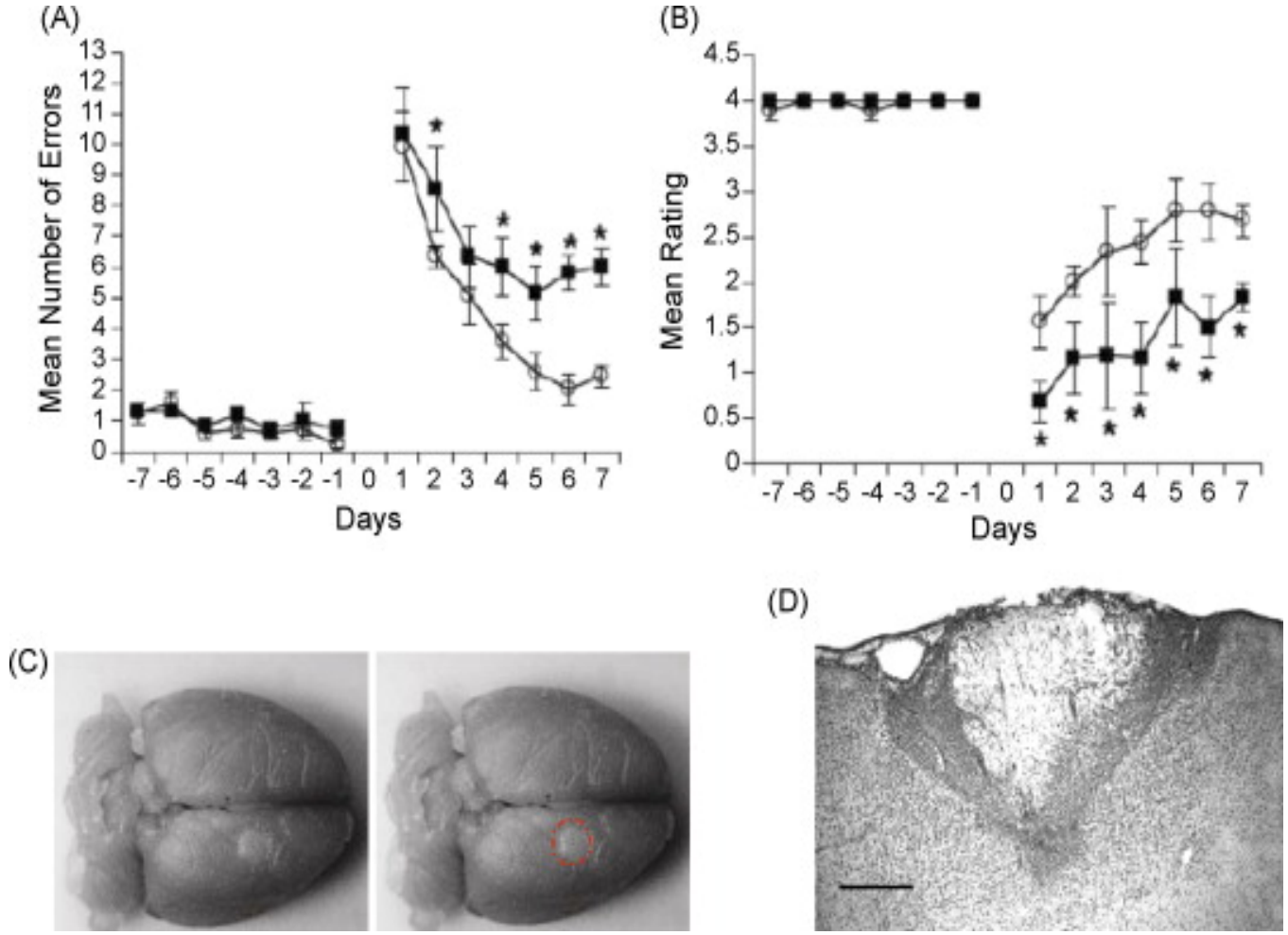
Children who, prior to age 3 years, had a blood lead concentration above 5 ug/dL (current CDC reference value) were:

- 27 percent less likely to be ready for kindergarten
- 30 percent more likely to enter the juvenile justice system
- 34 percent more likely to be incarcerated as young adults
- 40 percent more likely to experience some level of homelessness

Early-Life Neurotoxicant Exposure as an Effect Modifier: Early Lead Exposure Alters Adult Rat Response to a Photothrombotic Stroke in Hind Limb Parietal Sensorimotor Cortex

Square: lead-exposed
Circle: controls

A: beam walking;
B: proprioceptive limb placing

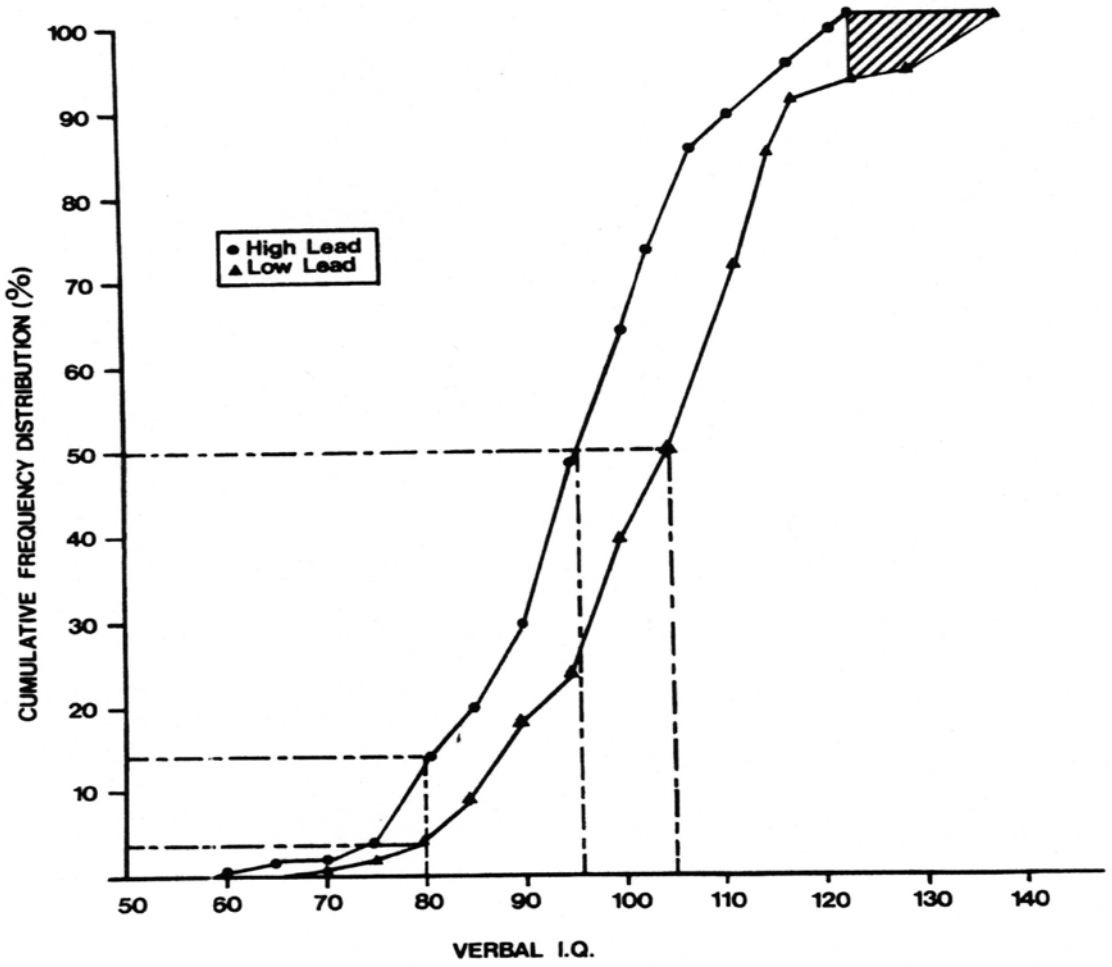


Schneider & Decamp. *Neurotoxicology* 2007;28:1153-57

Roots of Environmental Injustice

- Disadvantaged children tend to be:
  - more highly exposed to neurotoxicants
  - the same magnitude of exposure has greater adverse impact than on more advantaged children
  - early life exposures appear to make them less resilient in responding to later neurological insults and, perhaps, less able to benefit from environmental factors that support optimal development

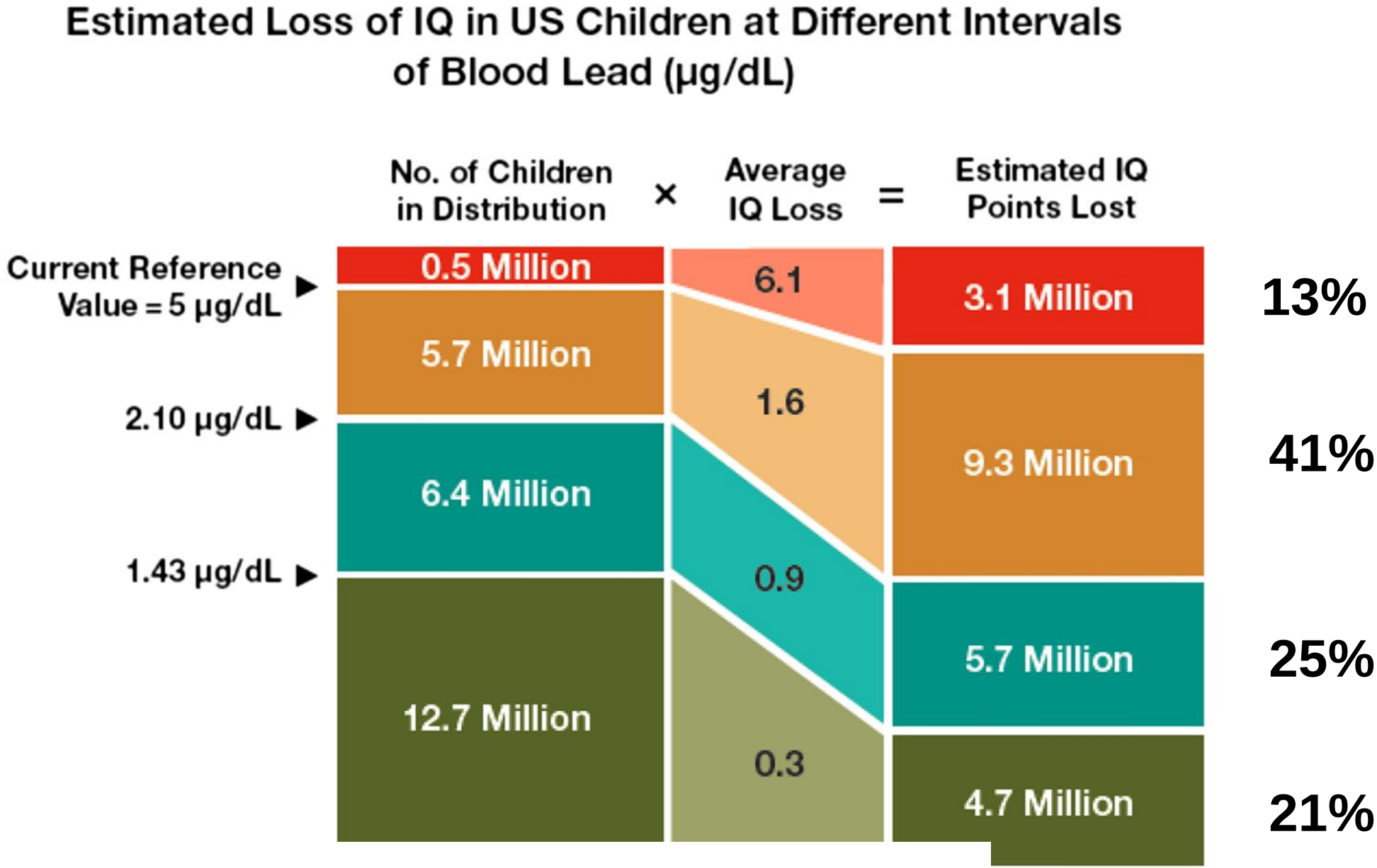
Focusing on Population Rather than Individual Risk in Quantifying Impact of Neurotoxicants



Needleman et al. *N Engl J Med* 1982;306;367

Total IQ Losses Associated with Medical Events/Conditions, US Children 0-5 Years (Bellinger, *Environ Health Perspect* 2012; 120:501-7)

Event/Condition	Total Number of IQ points Lost
Brain tumors	37,288
Duchenne muscular dystrophy	68,850
Congenital heart disease	105,805
Chemotherapy (ALL)	135,788
Type 1 diabetes	185,640
Methylmercury	**1,385,785**
Pediatric bipolar disorder	2,203,200
Traumatic brain injury	4,856,086
Nonorganic failure to thrive	5,355,000
Autism spectrum disorders	7,018,563
Iron deficiency	9,409,510
ADHD	16,799,400
Organophosphate pesticides	**18,978,019**
Lead	**22,947,853**
Preterm birth	34,031,025



Council on Environmental Health. Pediatrics 2016;138:e20161493