Asking the Right Questions: Are Women of Childbearing-Age at Risk of Exposure to Multiple Pollutants?

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- **Declarations**

– The content is solely the responsibility of the author and does not necessarily represent the official views of NIH/NIEHS. These funding sources had no role in the study's design or analysis.

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Superfund Research Program of Brown University

resolving the complex health, engineering, and community challenges of contaminated environments
http://www.brown.edu/Research/SRP

Are We Really Asking the Right Questions?

- *Why are we waiting nine months to find out about maternal and fetal exposures to environmental chemicals?*
- *Are women of childbearing age at risk of exposure to multiple pollutants?*
- *To what extent are they exposed?*
- *Which subgroups are exposure more than others?*

Topics

- Concurrent Exposure to Multiple Environmental Chemicals
- Pervasive, Persistent, Co-Occur
- Neurotoxicants
- Mechanistic Studies of Binary Chemical Combinations
- Body Burden
- Human Studies
- Vulnerability

- Research Study
- Implications for Policy

Concurrent Exposure to Multiple Environmental Chemicals

Anthropogenic Chemicals (100,000)

- 6,716 chemicals EPA ChAMP Requirements
- 2,889 each >1,000,000 pounds per year
- 3,249 each > 25,000 pounds per year

Natural Chemicals

- Elements (90)
- Inorganic Compounds
- Organic Compounds

Pervasive, Persistent, Co-Occur

- Pervasive
  - Remote Locations
  - Sentinel Species
- Persistent
  - Climate Factors
  - Climate Change
- Co-Occur
  - Common Spatial and Temporal Distributions

Concurrent Exposure to Multiple Environmental Chemicals

Hazardous Waste in U.S. (2011)
4,090,000 pounds Disposed/Released
8% annual increase

Pervasive, Persistent Toxics
36% annual increase

Lead	35% increase
Mercury	10% increase
Dioxins	35% increase
PCBs	36% increase

Toxic Release Inventory
21,000 facilities
676 chemicals

Superfund Sites (2004)
- 67,000,000 live within 4.0 miles
- 38,000,000 live within 2.5 miles

Neurotoxicants

- Lead (Pb), mercury (Hg), and polychlorinated biphenyls (PCBs) are known neurotoxicants in animal models and human populations.
- Health effects from co-exposure and biologically-effective dose are relatively unknown.
- There is a need to assess chemicals' cumulative risk for neurotoxicity, even though they may not share the same mode of action.

Meacham et al. (2005).; Radio et al. (2010); National Research Council (2008)

Mechanistic Studies of Binary Chemical Combination (MeHg-PCBs)

Reference	Antagonistic	Non-Additive	Additive	Synergistic
Bemis & Seegal (1999)				X
Sitarek & Gralewicz (2009)	X			
Coccini et al. (2006)		X		
Costa et al. (2007)			X	
Roegge et al. (2004)			X	

Reference	Antagonistic	Non-Additive	Additive	Synergistic
Goldoni et al. (2008)	MeHg then PCB153		PCB153 then MeHg	

(Radio et al. 2010; Meacham et al. 2005)

Body Burden

- The body burden from past exposures as well as those maternal exposures that occur during gestation can transfer to the fetus via the placenta and to infant and child during lactation.
- Childbearing-aged women in general and not just those who are currently pregnant are of special public health concern.
- Little is known about the prevalence of co-exposures to these chemicals among childbearing-aged women.

Human Studies

Reference	Outcome	PCBs	Hg	Pb
Qin et al. (2010)	uterine leiomyomas	$p<0.05$	$p<0.01$	$p<0.01$
Denham et al. (2005)	attainment of menses	$p<0.05$	$p=0.08$	$p<0.05$

Reference	Subjects	Percent Detectable PCBs, Hg, Pb	Percent Detectable VOCs
Woodruff et al. (2011)	pregnant	89% - 100%	38% - 94%
	non-pregnant	96% - 100%	47% - 95%

(National Research Council 2006; Woodruff et al. 2011)

Vulnerability

- Exposure
- Resistance
- Resilience/Recovery

(Turner et al., 2003; Aday, 2001; Kasperson, 2001; Kasperson, Kasperson, Turner, Dow, & Meyer, 1995; Sexton, 1997)

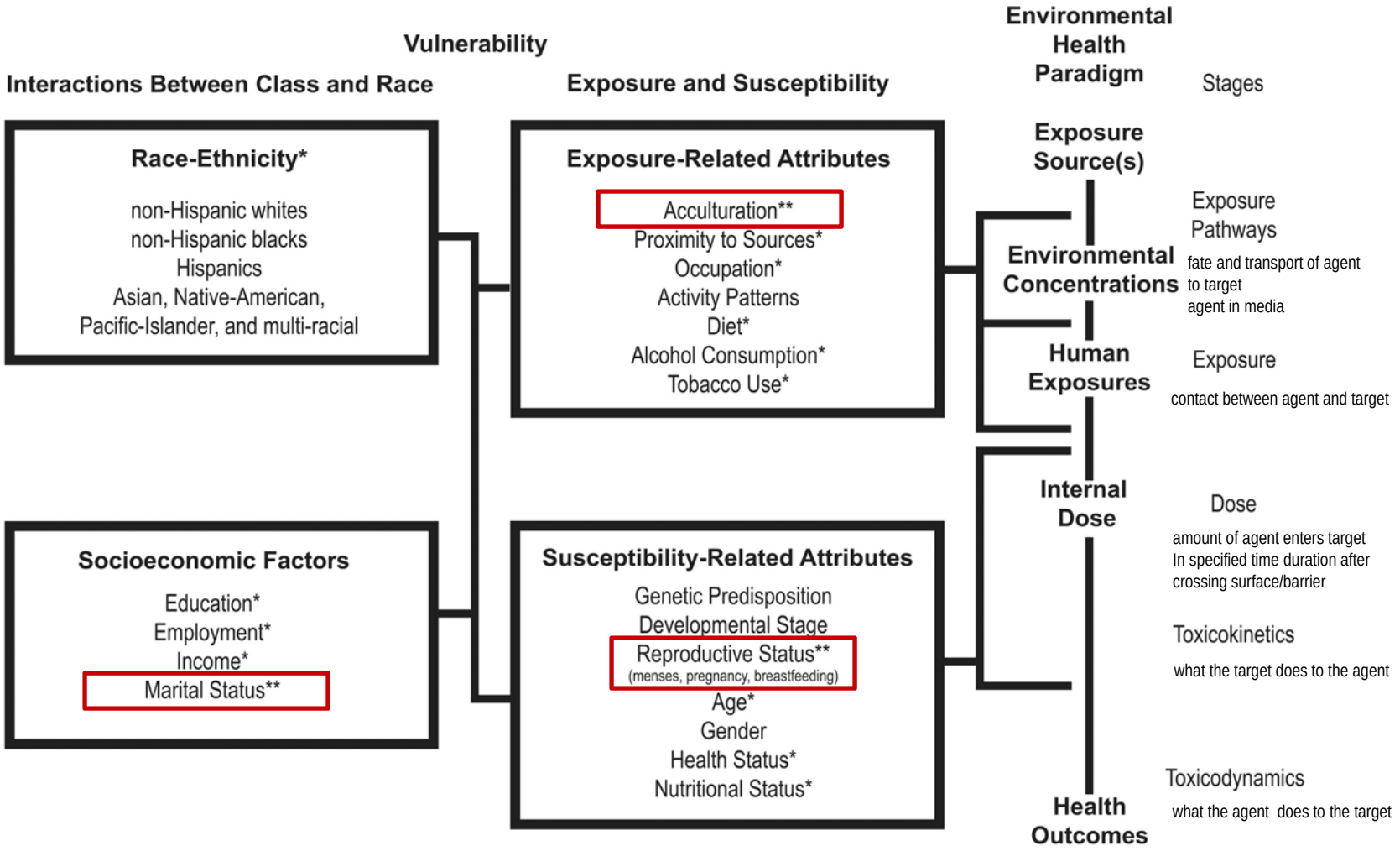


Figure 1. Modified Environmental Health Paradigm.

Adapted from Sexton et al., 1993

Aim and Research Questions

The aim of this research was to characterize the body burden and covariates for exposure to three neurotoxicants among childbearing-aged women living in the U.S. 1999 through 2004.

1. What was the percentage of childbearing-aged women who had body burdens at or above the median for lead, mercury, and PCBs?

2. What was the extent of their mixed exposures?

3. What, if any, subsets of these women were disproportionately burdened by two or more of these environmental chemicals based on susceptibility-related attributes, exposure-related attributes, socioeconomic factors, and race-ethnicity?

Methodology

CDC (2008)

Research Design. Descriptive and Exploratory Study

Data Source. Centers for Disease Control and Prevention National Center for Health Statistics National Health and Nutrition Examination Survey (NHANES)
http://www.cdc.gov/nchs/nhanes.htm

Components. Demographics, Interviews, Physical Examination, Laboratory Tests including Biomonitoring and Environmental Monitoring

Methodology

CDC (2008)

Study Population. Childbearing-aged females aged 16-49 of all races and ethnicities who lived in the U.S. from 1999 to 2004.

Dependent Variable. Two or more xenobiotic levels at or above the median. Lead and total mercury were measured in blood. The sum of four PCB congeners (118, 138/158, 153, 180) were measured in serum.

Independent Variables. Measures of vulnerability: susceptibility- and exposure-related attributes, socioeconomic factors and race-ethnicity

Study Population

(NHANES unweighted and weighted 1999-2004)

Study Criteria	Laboratory Sample (unweighted)	Laboratory Sample (weighted)	All Chemicals and Reliable Dietary Recall (unweighted)	All Chemicals and Reliable Dietary Recall (weighted)
Age				
16-19 years old	1,321	22,209,998	1,085	18,510,469 (14%)
20-29 years old	994	49,713,270	884	45,347,515 (34%)
30-39 years old	818	42,250,320	702	36,357,837 (27%)
40-49 years old	575	39,459,259	502	34,286,213 (25%)
Race-Ethnicity				
non-Hispanic white	1,736	112,166,998	1,493	97,887,544 (73%)
non-Hispanic black	761	15,494,990	623	12,747,178 (10%)
Mexican-American	875	9,978,059	745	8,670,576 (6%)
other Hispanic	192	8,026,759	178	7,525,992 (6%)
other racial	144	7,966,041	134	7,670,743 (5%)
Total	3,708	153,632,847	3,173	134,502,033
lost from sample			535 (14.4%)	19,130,814 (12.4%)

Methodology

- Concatenated and Organized Dataset
- Operationalized Dependent and Independent Variables
- Constructed Software Instructions in 64-bit SAS© and SAS-callable SUDAAN©.

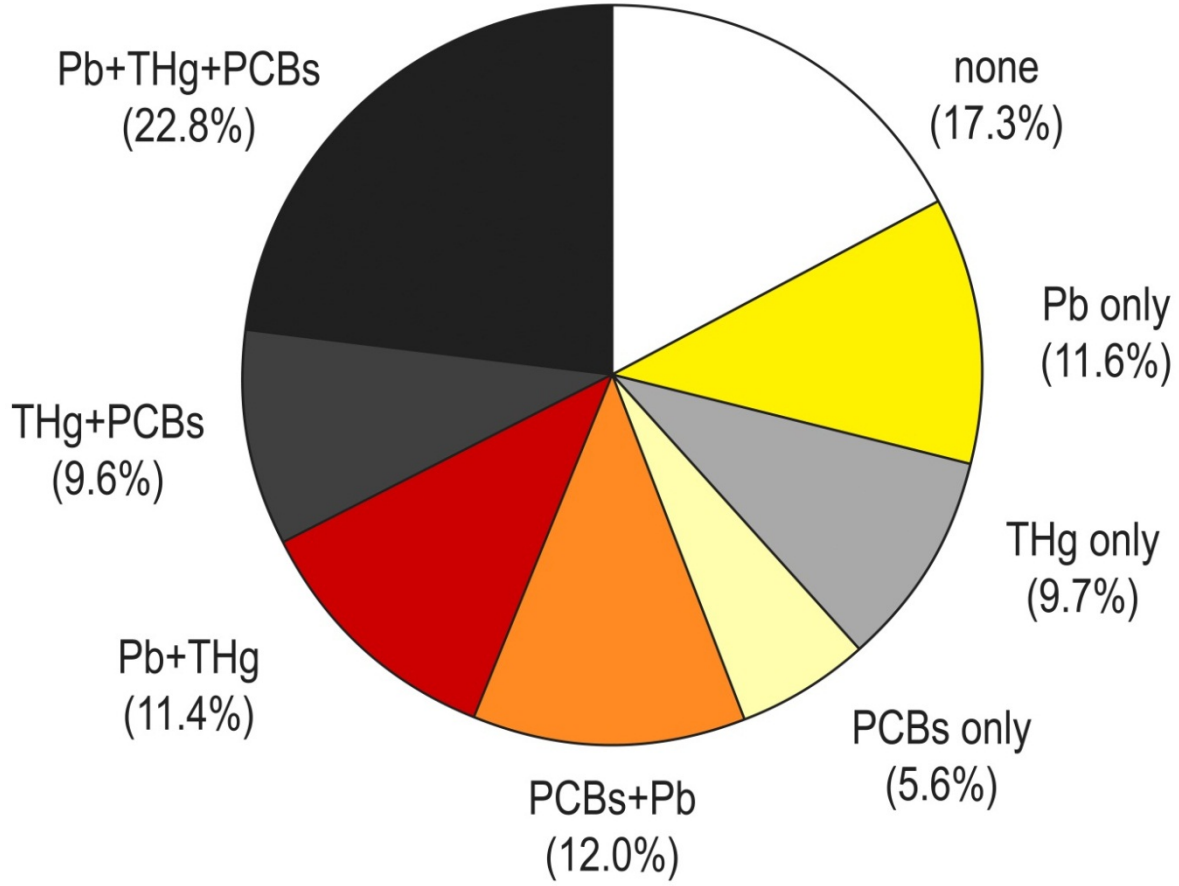
- Levels of Detection (LoD)
  - Each lipid-adjusted PCB congener varied as each sample from each individual had its own limit
  - For Pb and total Hg, values below LoD were imputed by NHANES

Xenobiotic Levels in Childbearing-Aged Women
(NHANES weighted data 1999-2004)

Xenobiotic	LoD	≥ LoD (%)	GM (SE)	50th Percentile	95th Percentile	CV (GSE/GM)
Lead [blood (µg/dl)]	0.3	98.50	0.93 (0.03)	**0.89**	**2.24**	0.03
Total Mercury [blood (µg/L)]	0.2	95.85	0.94 (0.06)	**0.99**	**5.55**	0.06
PCB 118 [serum (ng/g lipid)]	NA	67.50	5.95 (0.20)	5.14	20.22	0.03
PCB 138/158 [serum (ng/g lipid)]	NA	74.12	12.84 (0.52)	13.79	45.38	0.04
PCB 153 [serum (ng/g lipid)]	NA	78.29	17.09 (0.72)	18.18	60.72	0.04
PCB 180 [serum (ng/g lipid)]	NA	74.81	10.85 (0.40)	10.38	42.89	0.04
Σ PCBs [serum (ng/g lipid)]	NA	55.50	48.09 (1.82)	51.59	198.75	0.04

Percentage of Childbearing-Aged Women in U.S. burdened by specific xenobiotic combinations at or above the median

(NHANES weighted data 1999-2004)



Denham et al. (2005); Boucher et al. (2011); Stewart et al. (2006)

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Best-Fit Logistic Regression Model

(NHANES weighted data 1999-2004)

Variable Names
Age
Fish Consumption
Alcohol Consumption
Past Breastfed Child
Household Size
Education
Shellfish Consumption
Language Spoken at Home
Race-Ethnicity
Selenium Intake
Currently Breastfeeding
Employment

$p \leq 0.05$

Morello-Frosch & Schenassa (2006); Payne-Sturges & Gee (2006); Montoya (2007)

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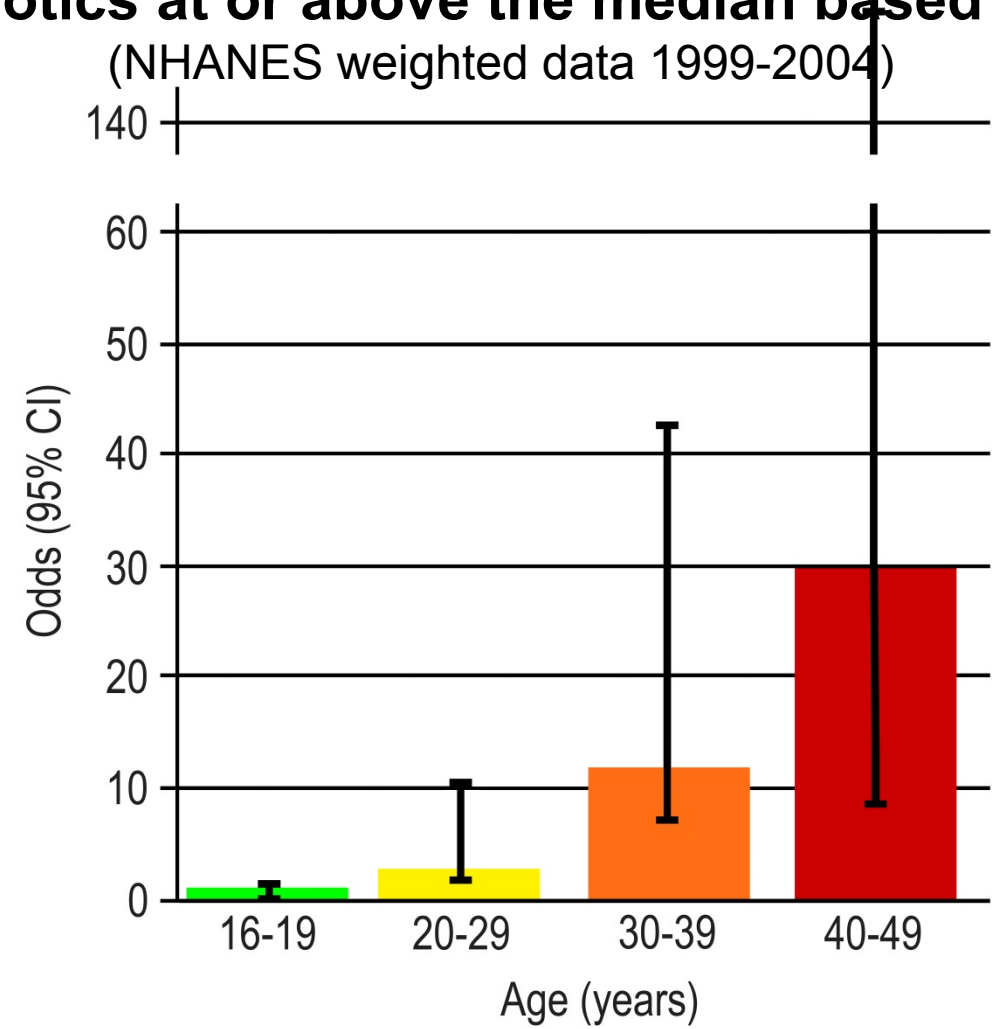
Odds of childbearing-aged women in U.S. with two or more xenobiotics at or above the median based on age

(NHANES weighted data 1999-2004)



Axelrad et al. (2009); Mushak (1998); Caldwell et al. (2009); Laden et al. (2001)

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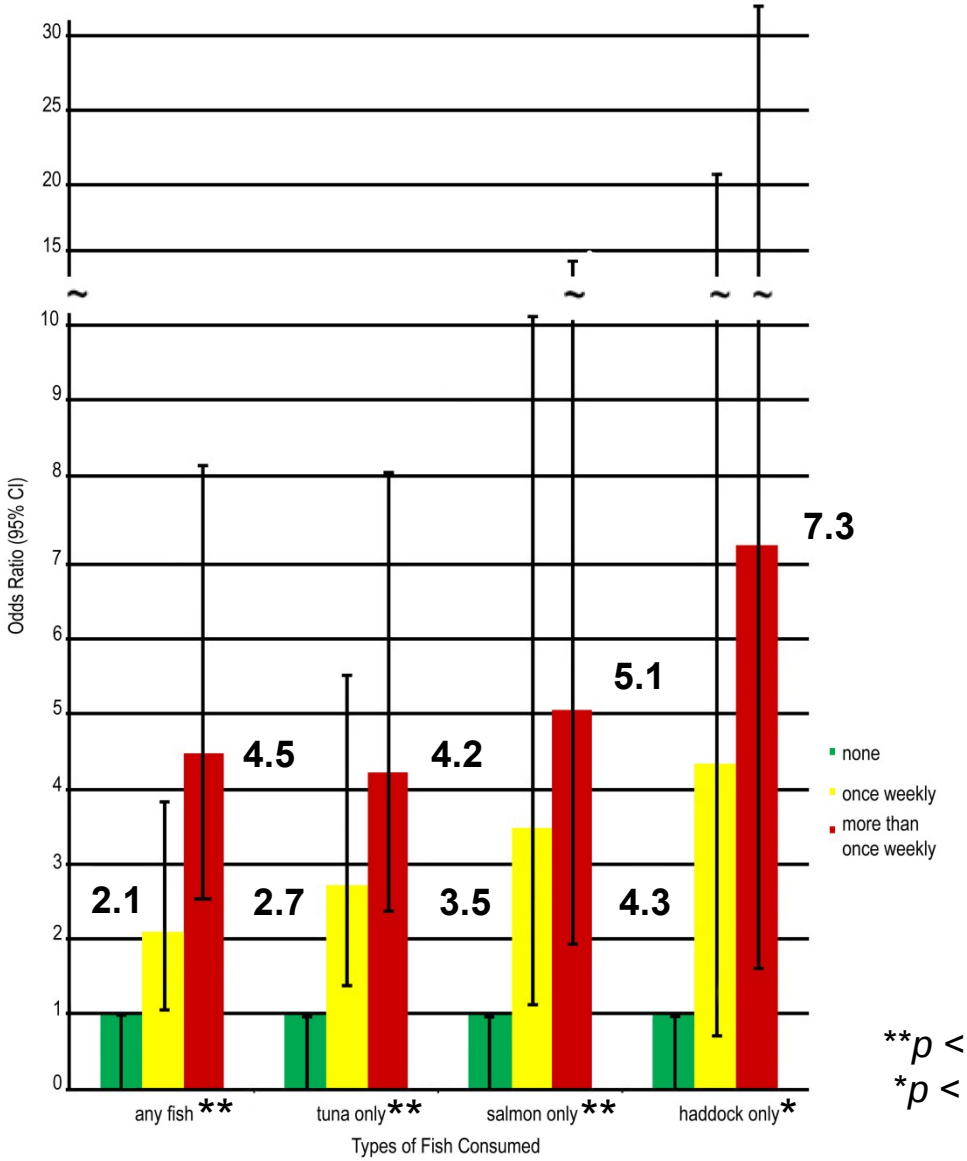
Odds of childbearing-aged women having two or more xenobiotic levels at or above median based on fish consumption



$^{**}p < 0.001$
$^{*}p < 0.02$

Grandjean et al. (1992); Gunderson (1995); Falco et al. (2006); Tran et al. (2004)

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Variable Names	df	-2LL Wald F	*P* value	Odds Ratio	95% CI
Alcohol Consumption	2	4.01	*0.03*		
never, seldom drinker[R]				1.00	ns
including 16-19 y/o data restricted					
drinker				0.63	0.33-1.19
heavy and/or binge drinker				**1.56**	0.81-3.01

Variable Names	df	-2LL Wald F	*P* value	Odds Ratio	95% CI
Past Breastfed Child	1	5.09	***0.03***		
never breastfed[R]				1.00	ns
breastfed more than one month				**0.56**	0.33-0.94

Currently Breastfeeding	1	1.20	*0.28*		
no[R]				1.00	ns
currently breastfeeding				1.97	0.56-6.89

ATSDR (2004); Gundacker et al. (2002); Arendt (2008); Needham et al. (2011); CDC NCEH (2010)

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Study Limitations

- cross-sectional study
  - associations, not causations
- goodness of fit (R^2=.25)
  - binary interactions (33% $p < 0.001$)
- limited understanding of exposure covariates
- body burden ≠ identify exposure sources
  - time and place
- generalized to U.S. population of childbearing-aged women only
- population-based study, not individualized risk
- only these three environmental chemicals

Conclusions

- Childbearing-Aged Women in U.S.
- Body Burden for Pb, Hg, PCBs
  - 23% all three xenobiotics at or above median
  - Equally likely to have two as one at or above median
- Covariates
  - increasing age
  - any fish consumption
  - heavy and/or binge drinking alcohol consumption
  - prior history of breastfeeding (lower)

Questions?

Implications for Policy

Is it safe?

Is it safe enough?

Should protecting the next generation by regulating environmental exposures of the current generation be addressed in public and environmental health policy?

Should pregnant and lactating women be protected exclusively?

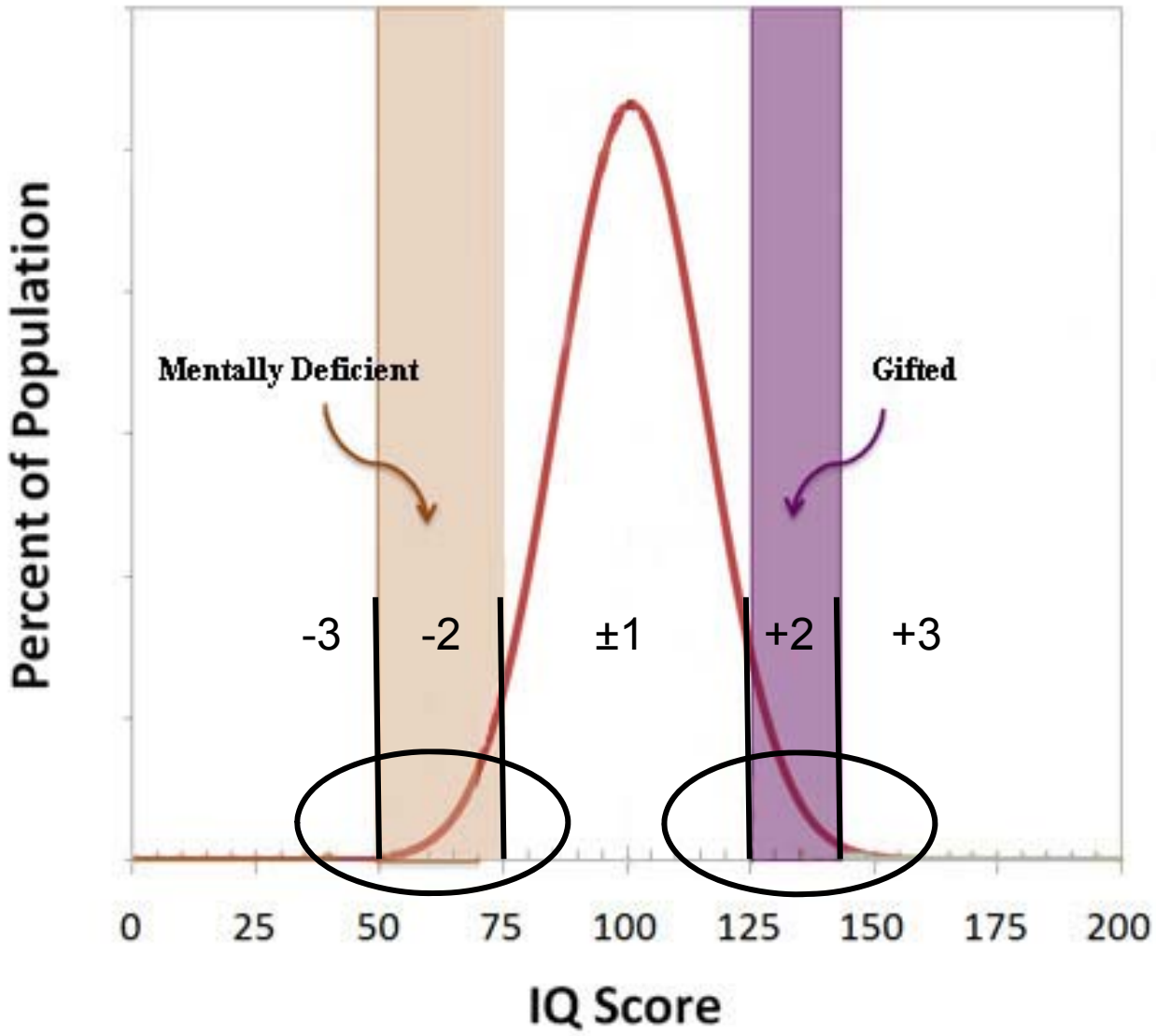
Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women

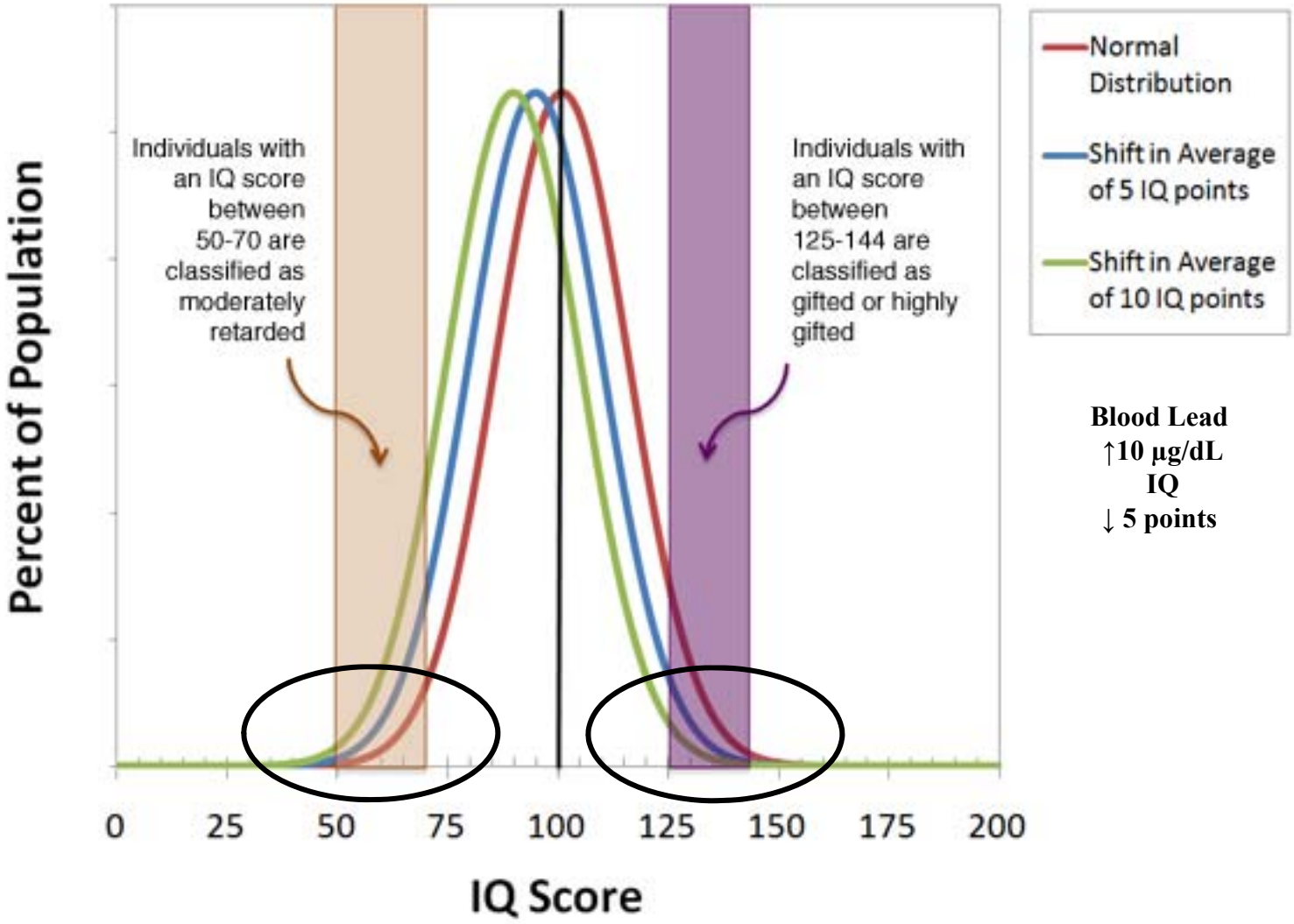
- Does NOT recommend routine prenatal testing
- If prenatal BLL ≥5 µg/dL, institute education and environmental, nutritional, and behavioral interventions
- Does recommend breastfeeding UNLESS breast milk lead level

  <40 µg/dL.
- If prenatal BLL ≥10 µg/dL, remove from occupational exposures

- Does NOT address return to work or compensability
- Fetal Protection Policy is neither acceptable nor legal

(NCEH, 2010)


Percent of Population
Mentally Deficient
Gifted
-3
-2
±1
+2
+3
0
25
50
75
100
125
150
175
200
IQ Score



Blood Lead
↑10 µg/dL
IQ
↓ 5 points

(Needleman 1989, p.643)

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Just think how smart we all could have been.

Thompson MR, Boekelheide K (2013). Multiple environmental chemical exposures to lead, mercury and polychlorinated biphenyls among childbearing-aged women (NHANES 1999–2004): body burden and risk factors. *Environmental Research,121*:23-30. doi:10.1016/j.envres.2012.10.005. PMC3578119.