

# Human Health and EDCs

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Reproductive diseases/disorders		Increase	Period	Location	Ref.
↑	Testicular cancer	1-6%	1953-1999	Europe	[35]
		60%	1973-2003	USA	[36]
	Certain childhood cancers	20-24%	1976-2005	USA	[37]
	Autism	57%	2002-2006	USA	[38]
	ADHD	3% per year	1997-2006	USA	[39]
	Birth Defects				
	<i>Cryptorchidism</i>	200%	1970-1993	USA	[40]
	<i>Gastroschisis</i>	300%	1978-2005	California	[41]
	<i>Congenital hypothyroidism</i>	138%	1987-2003	New York	[42]
Reproductive function		Increase	Time	Location	Ref.
↓	Reported difficult conceiving and maintaining pregnancy				
	<i>All ages</i>	60% more women	1982-2002	USA	*Brett
	<i>&lt;25 years old</i>	200% more women	1982-2002	USA	*Brett
	Prematurity	2.9% shorter gestation	1992-2002	USA	[44]
	Preeclampsia	19-36%	1968-2002	Norway	[45]
	Gestational diabetes	122%	1989-2004	USA	[46]
	Premature puberty				
	<i>Age at onset of breast development</i>	1-2 years younger	1940-1994	USA, Denmark	[47,48]
	<i>Age at onset of menstruation</i>	2.5-4 months younger	1940-1994	USA	[47]
Sperm Count	~1% decline per year	1931-1994	Western countries	[49,50]	
Sperm Testosterone	1% decline per year	1987-2004	Boston , USA	[51]	





Environmental  
Chemical and  
Physical Agents



Nutrition



Life Experience



Social and Built  
Environment



# Overview

- **Methodological issues in Environmental Epidemiology**
- **EDCs and “more well known” effects**
- **EDCs and “more emerging” effects**
- **Interpreting epidemiological and other evidence**



Exposures may be more reflective of real world

Exposures often higher, only one chemical, often adults

Controlled exposure

Exposures can be difficult to estimate



May be confounding (e.g. diet, smoking)

Genetic variability

Outcomes can be difficult to ascertain

More directly relevant

**Years to obtain and people affected**

Often homogenous

Can better measure outcomes

Need to extrapolate

Studies quicker



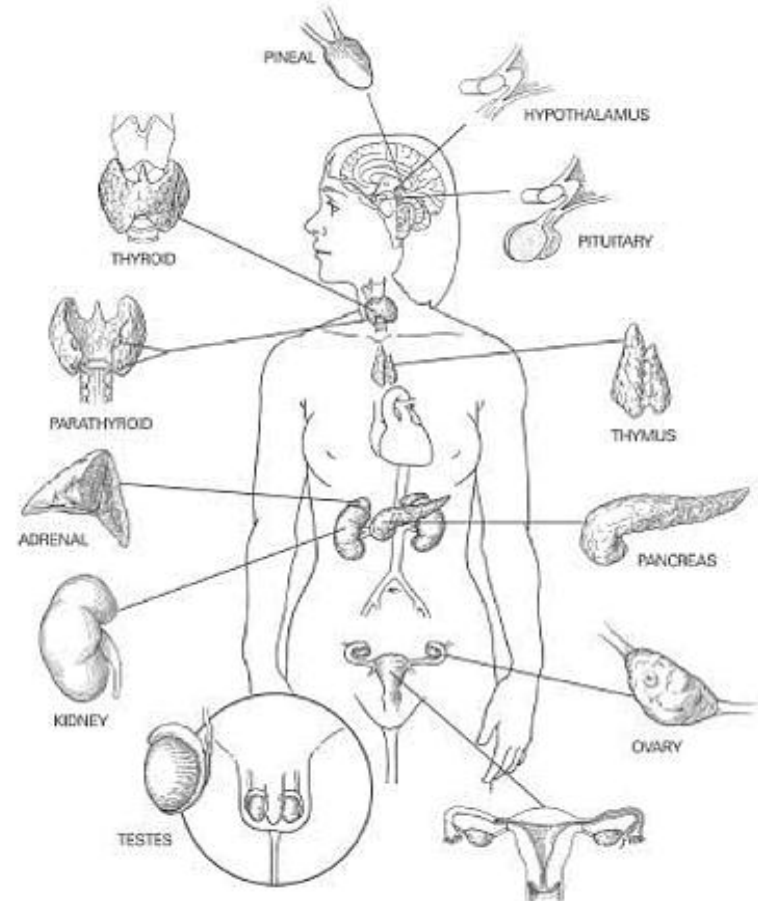
# Challenges to environmental epidemiology

- **Relative Risks often modest**
  - Particulate matter air pollution – RR 1.06 (6% increase in risk)
  - But everyone is exposed
- **Lack of data and studies**
  - No data does not mean no effect – it just means no data



# Some health effects have “more well known” empirical basis

- **Women’s reproductive health effects**
  - Example: estrogen and female reproductive effects
- **Men’s reproductive health effects**
  - Example: testosterone and male reproductive effects
- **Hormonally mediated cancers**
  - Example: breast cancer
- **Neurological effects**
  - Example: thyroid and neurological effects





# Women's Reproductive Health- Prenatal Exposure to DES



Yes...

**desPLEX**  
to prevent ABORTION, MISCARRIAGE  
PREMATURE LABOR

recommended for use  
in ALL pregnancies...

96 per cent live delivery with desPLEX  
in one series of 1200 patients\*—  
— bigger and stronger babies, too.<sup>1</sup>

No gastric or other side effects with desPLEX  
— in either high or low dosage<sup>2,4,5</sup>

(Each desPLEX tablet starts with 25 mg. of diethylstilbestrol, U.S.P., which is then ultramicrozoned to smooth and accelerate absorption and activity. A portion of this ultramicrozoned diethylstilbestrol is even included in the tablet coating to assure prompt help in emergencies. desPLEX tablets also contain vitamin C and certain members of the vitamin B complex to aid detoxification in pregnancy and the effectuation of estrogen.)

For further data and a generous  
trial supply of desPLEX, write to:  
Medical Director

- DES widely prescribed late 1940s - 1970s for treatment of threatened miscarriage.
- Considered safe and effective
- Estimated 2-8 million births affected
- Adverse effects in **children**;
  - Vaginal cancer in female offspring (<.1%) and breast cancer
  - Reproductive tract dysfunction in male & female offspring (>90%).
- Adverse effects in **grandchildren**;
  - Menstrual irregularities, ovarian cancer
  - Hypospadias (deformed penis)



# EDCs and women's reproductive health – fibroids and endometriosis

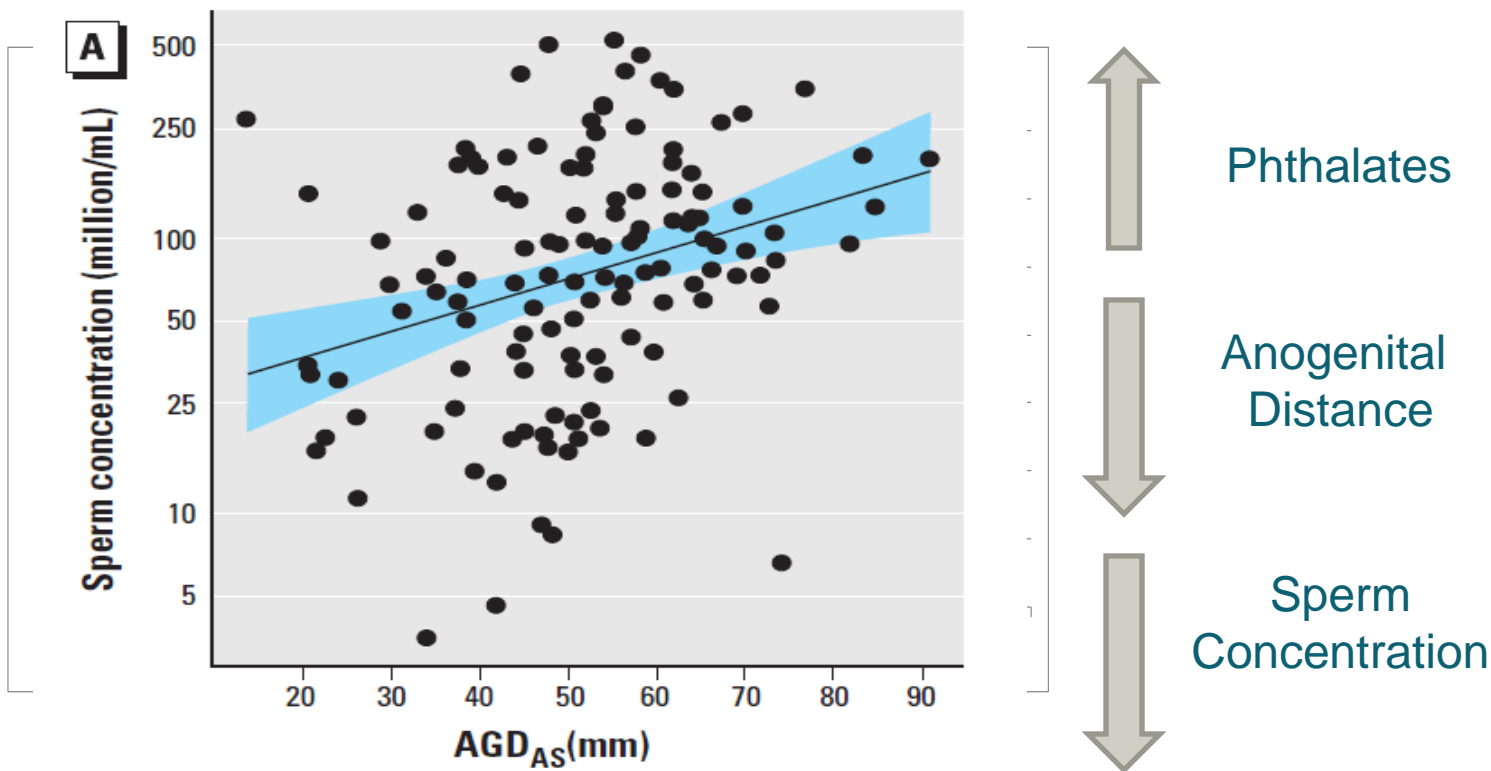
- ***Phthalates* – can disrupt estrogen levels**
  - Several studies suggest an association
    - However, differences in the phthalate associated (e.g. DBP vs. DEHP)
    - Studies are often small, cross-sectional, and rely on surrogates of effects
- **Persistent organochlorine pollutants (*POPS*)–**
  - Studies find association with some POPs
    - But the type varies (dioxins, PCBs, HCH)
    - Studies vary in approach and findings

**RESEARCH FOCUS ON ADULTS**



# Male reproductive effects – example testosterone and phthalates

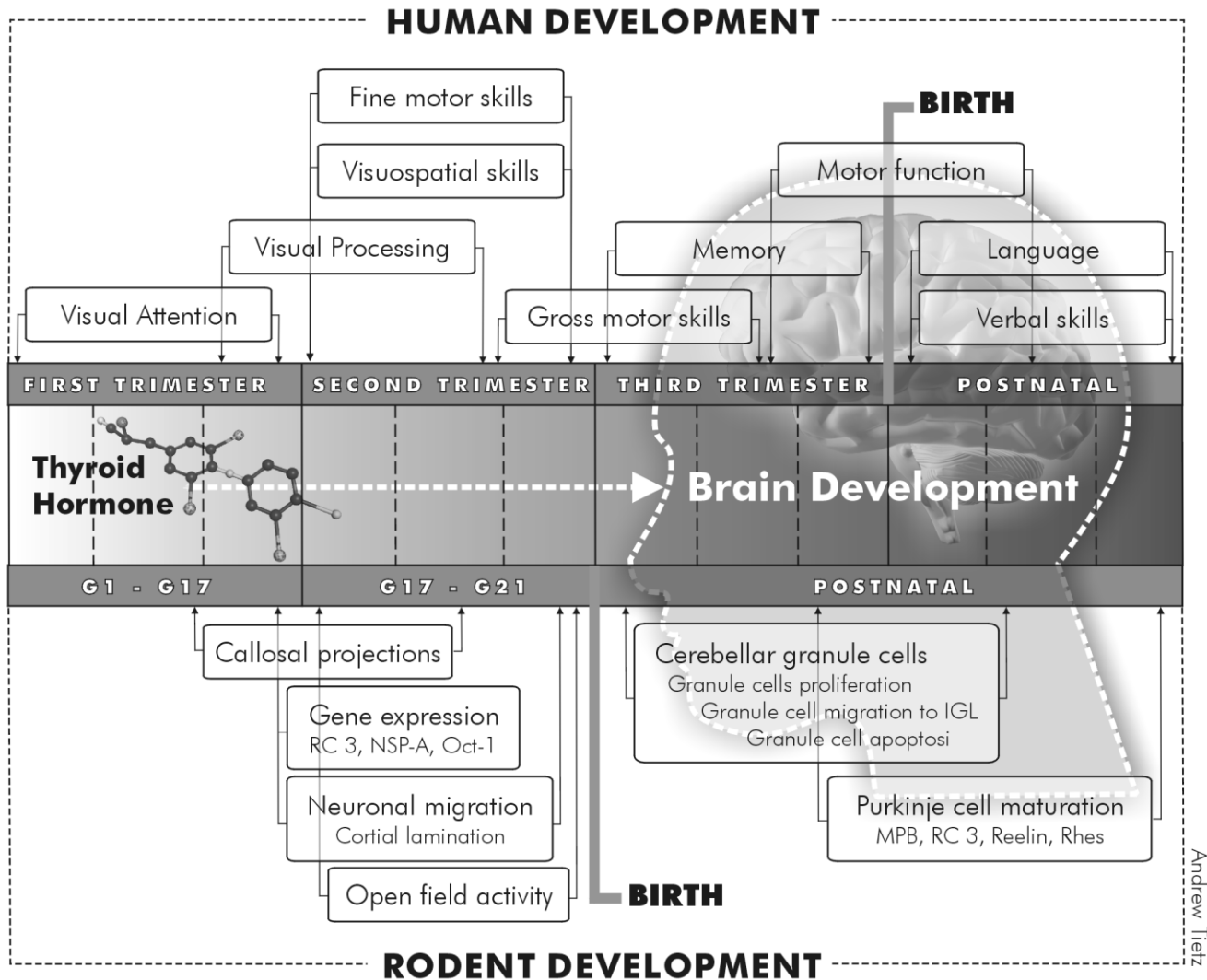
Phthalates associated with effects on male reproductive tract  
Anogenital Distance



**Figure 3.** Partial regression plot (mean  $\pm$  SE) of sperm and (B) AGD<sub>AP</sub>.



# Neurodevelopment – Thyroid Hormones



# PBDE exposures and thyroid hormone disruption during pregnancy

- PBDEs associated with changes in TH during pregnancy in small number of studies
  - Associated with changes in TH
  - Direction varies

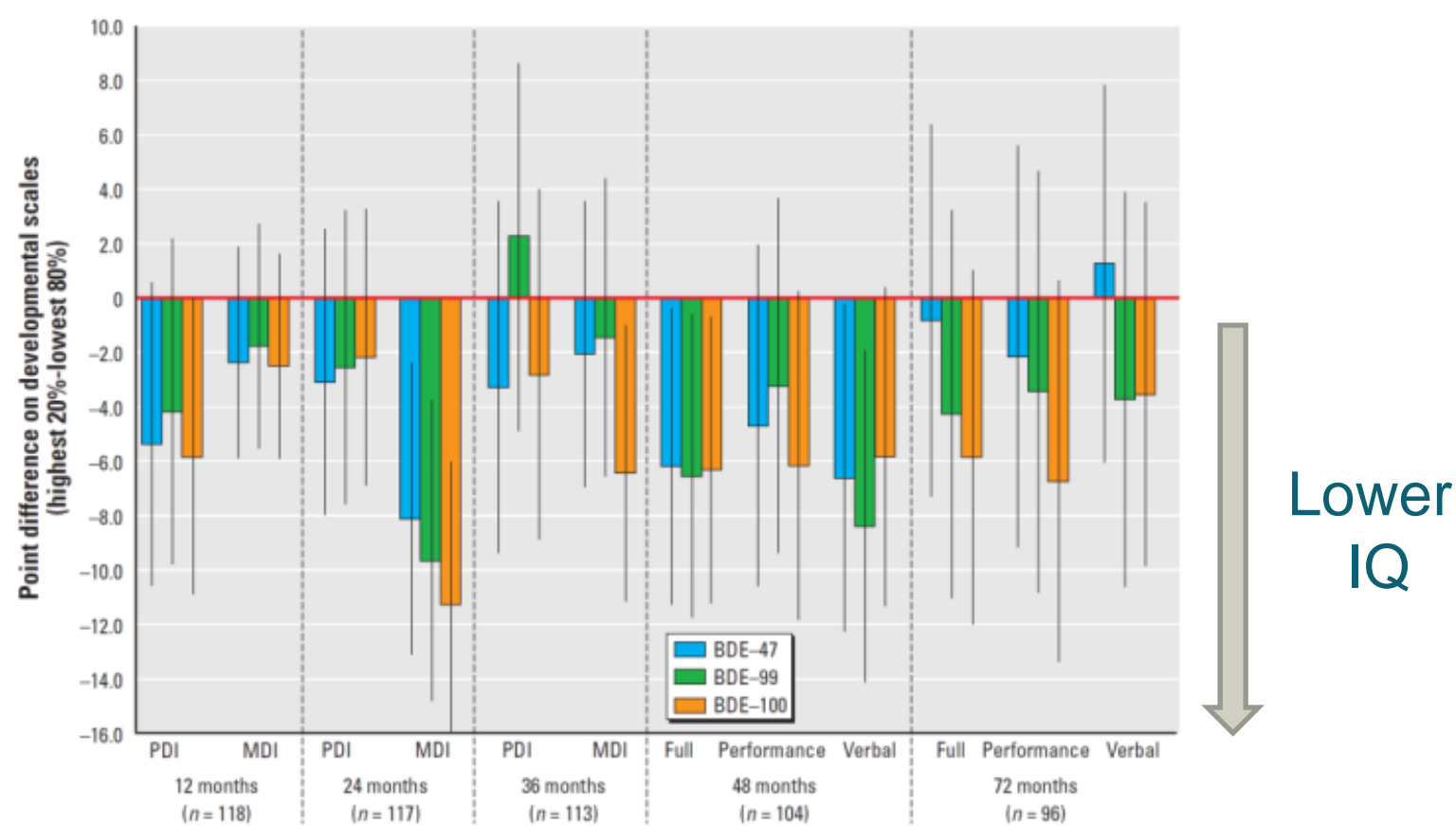


Chevrier et al. 2010; Herbstman et al. 2011, Zota 2011



# PBDE associated with effects on the developing human brain

Children with higher prenatal exposures to PBDEs 47, 99, or 100 scored lower on tests of mental and physical development (including IQ tests).



**Figure 1.** Difference in mean developmental score (and 95% confidence interval around the mean) comparing individuals in the highest quintile (20%) of exposure with those in the lower 80% of BDEs 47, 99, differences were adjusted for age at testing, race/ethnicity, IQ of mother, sex of child, ges-

# Some health effects have “newer” empirical evidence

- **Adverse birth outcomes – preterm delivery, low birthweight**
  - Example thyroid hormones
- **Metabolic disorders**
  - Obesity & Diabetes



# Pregnancy complications associated with thyroid disease

	Hypothyroidism ↓	Hyperthyroidism ↑
Miscarriage	X	
Pregnancy-induced hypertension	X	
Pre-eclampsia		X
Placental abruption	X	
Preterm delivery/labor	X	X

Brent GA and Hershman JM. 2004. Thyroid disease and pregnancy. Encyclopedia of Endocrine Diseases





# Prenatal PBDE exposure and low birth weight

Each 10-fold increase in concentrations of BDE-47, -99, and -100 was associated with an approximately 115-g decrease in birth weight

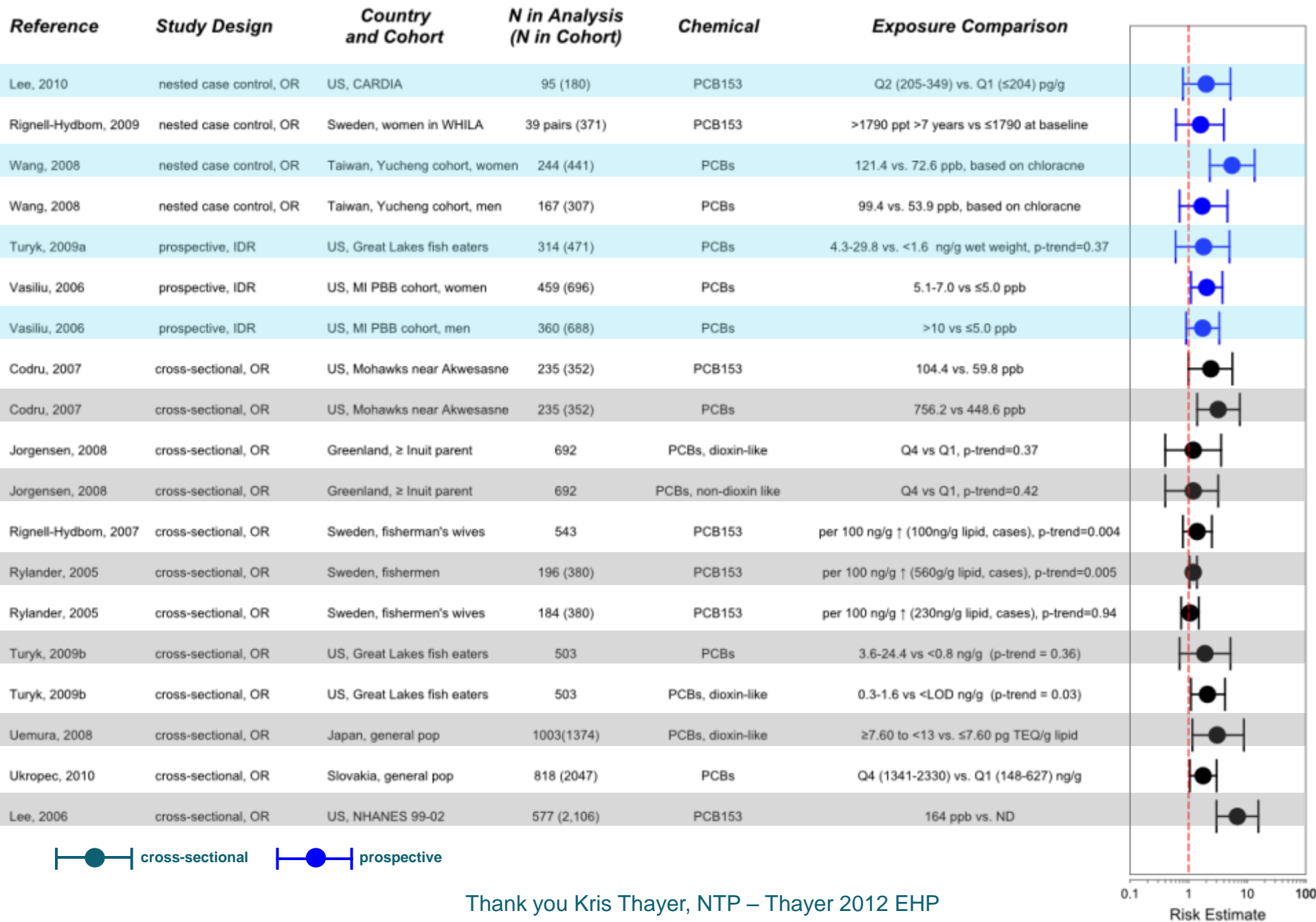


*Low birth weight effects may be mediated by thyroid-mediated pathway*

Harley et al., Association of Prenatal Exposure to Polybrominated Diphenyl Ethers and Infant Birth Weight. American Journal of Epidemiology. 2011



# PCBs and Diabetes



Thank you Kris Thayer, NTP – Thayer 2012 EHP



# One Chemical – Different outcomes



- On the basis of epidemiologic and other data available to the C8 (PFOA) Science Panel, we conclude that there is
- **PROBABLE link between exposure to PFOA and**
  - testicular cancer and kidney cancer but **not** any of the other cancers that were considered
  - pregnancy-induced hypertension
- **NOT a probable link between exposure to PFOA and**
  - Type II (adult-onset) diabetes, miscarriage or stillbirth, preterm birth or low birth weight



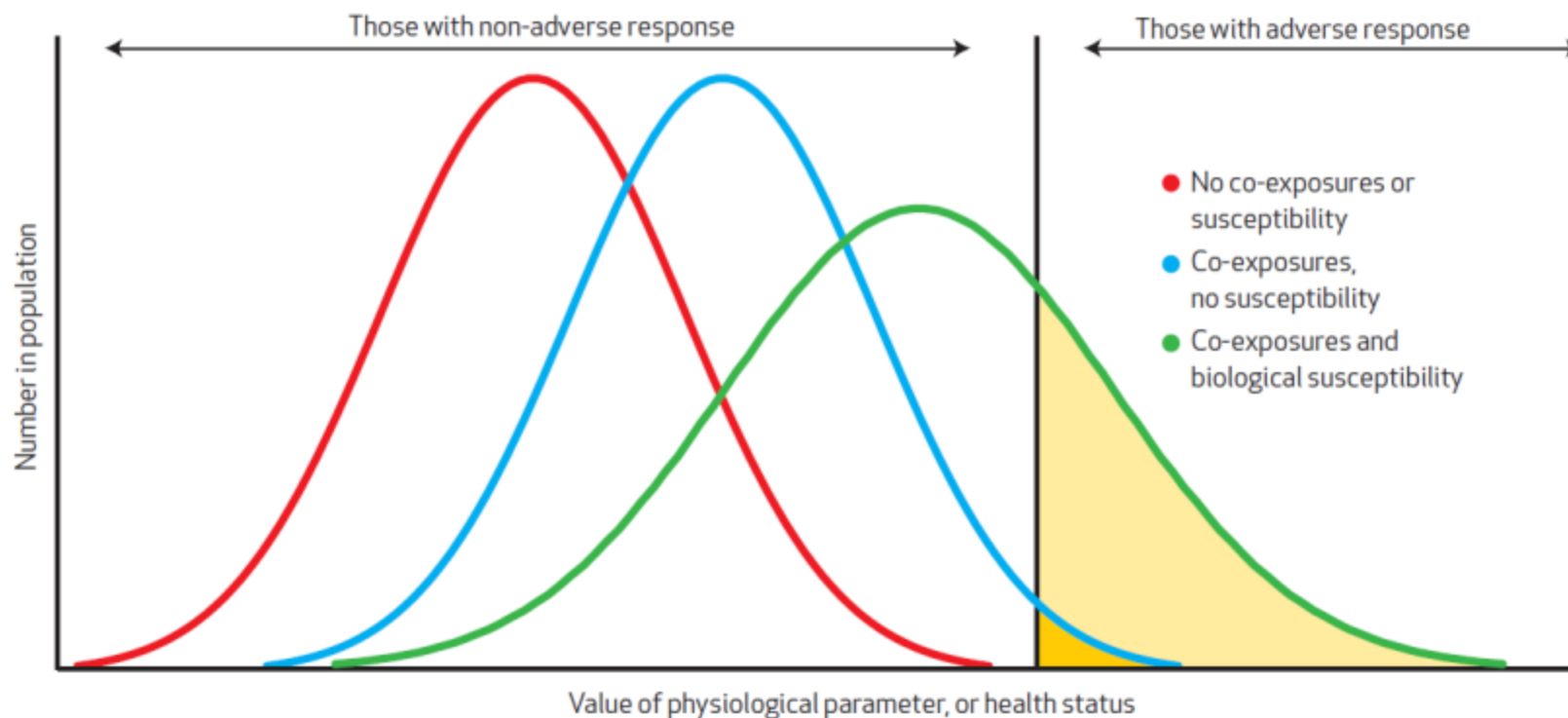
# FACTORS THAT INFLUENCE RISK



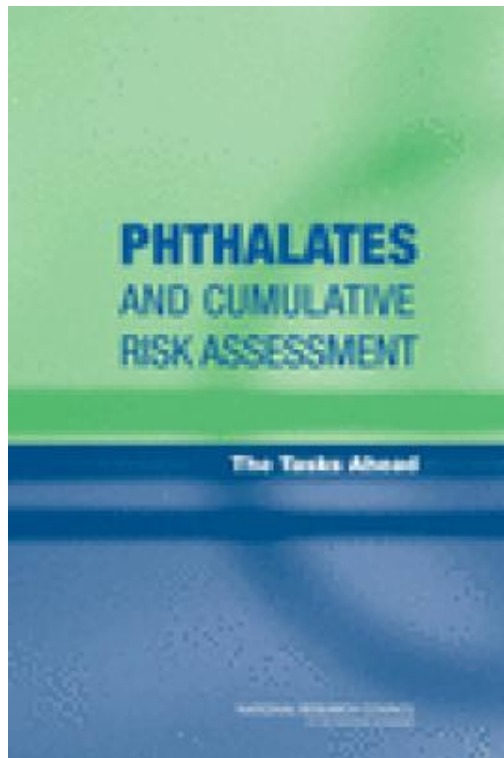
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## The Effect Of Biological Susceptibility And Co-exposure To Other Chemicals On The Relationship Between Individual Chemical Exposure And Adverse Health Outcomes



# US National Academy of Sciences recommends upgrading approach based on new science







Lead a known neurotoxicant and added to gasoline in the 1920s



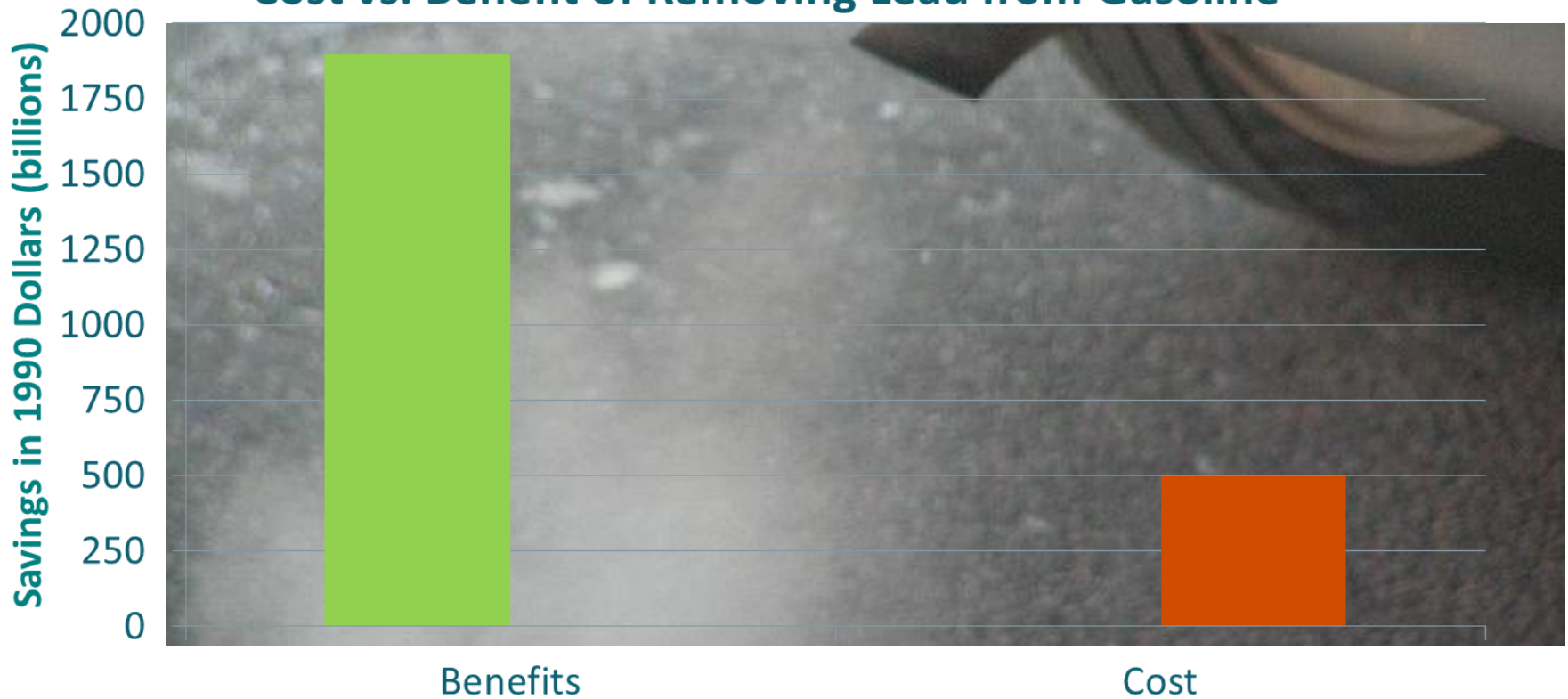
Lead removed from gasoline 50 years later (**1970s**)



Wikipedia and mercury car info webpages



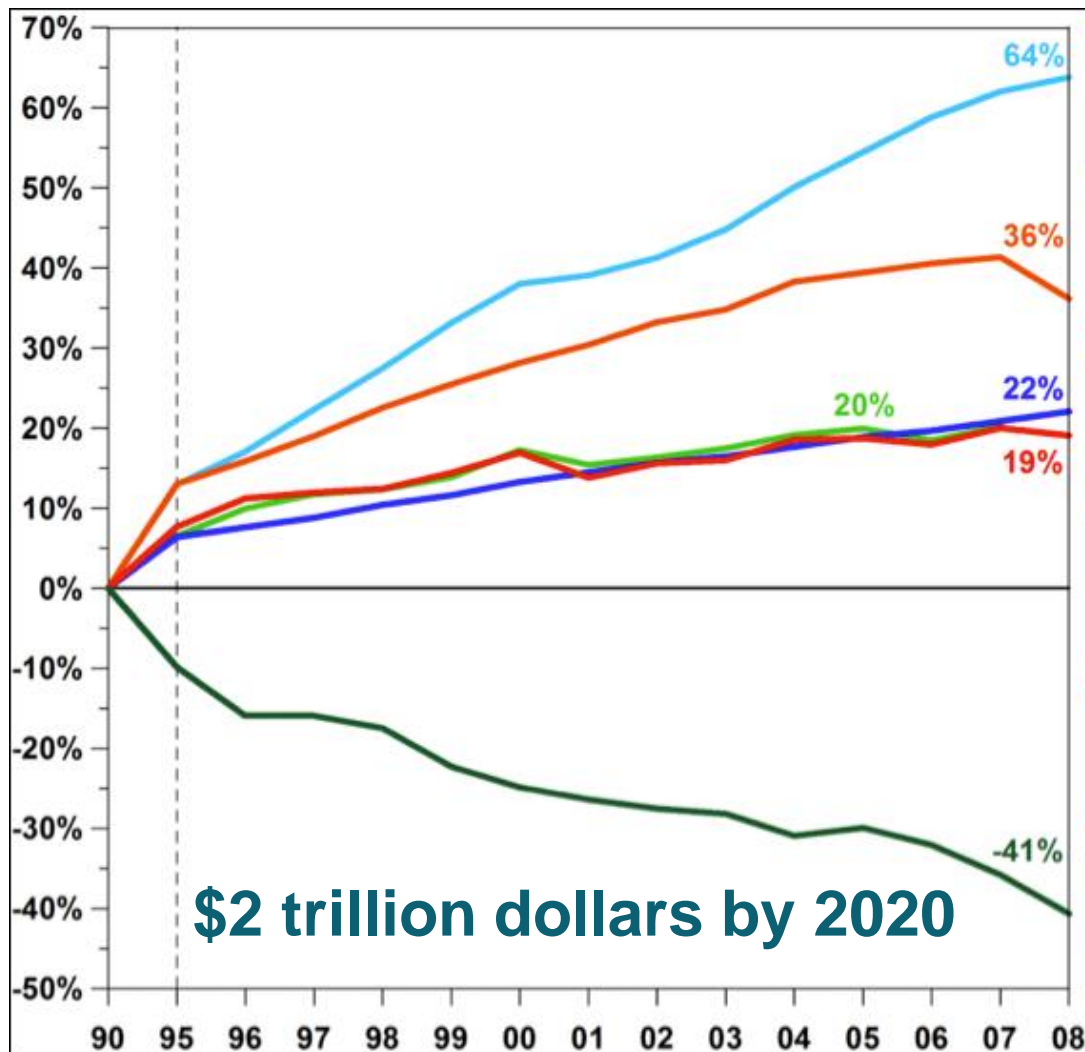
## Cost vs. Benefit of Removing Lead from Gasoline



Aol. Original

Facebook IPO Valuation Sets Record:  
Is It Really Worth \$104 Billion?





Gross Domestic Product



Vehicle Miles Traveled



Population



CO<sub>2</sub> Emissions

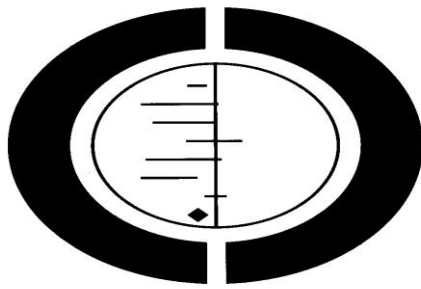


Energy Consumption



Aggregate Emissions  
(Six Common Pollutants)





**THE COCHRANE  
COLLABORATION**

Preparing, maintaining and disseminating  
systematic reviews of the effects of health care



Grades of  
Recommendation  
Assessment, Development  
and Evaluation



Navigation Guide

Weight of evidence  $\neq$  Causality



# Summary

- EDCs can be risk factors for many chronic health conditions – both more “traditional” and “newer” effects
- Epidemiology studies provides supporting evidence
  - Uncertainties can be enhanced for certain exposures and outcomes
  - Needs to be evaluated in combination with nonhuman streams of evidence

