Trends and Future Direction of Research on Health Effects Related to Endocrine Disruptors

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Outline

- Progress in endocrine disruptor research
- Concern about susceptibility factors
- Importance of child cohorts
- Neurodevelopment, Breast cancer
- Genetic susceptibility
- Genome epidemiology
- Topics on endocrine disruptor research
- Summary

Progress in Endocrine Disruptor Research

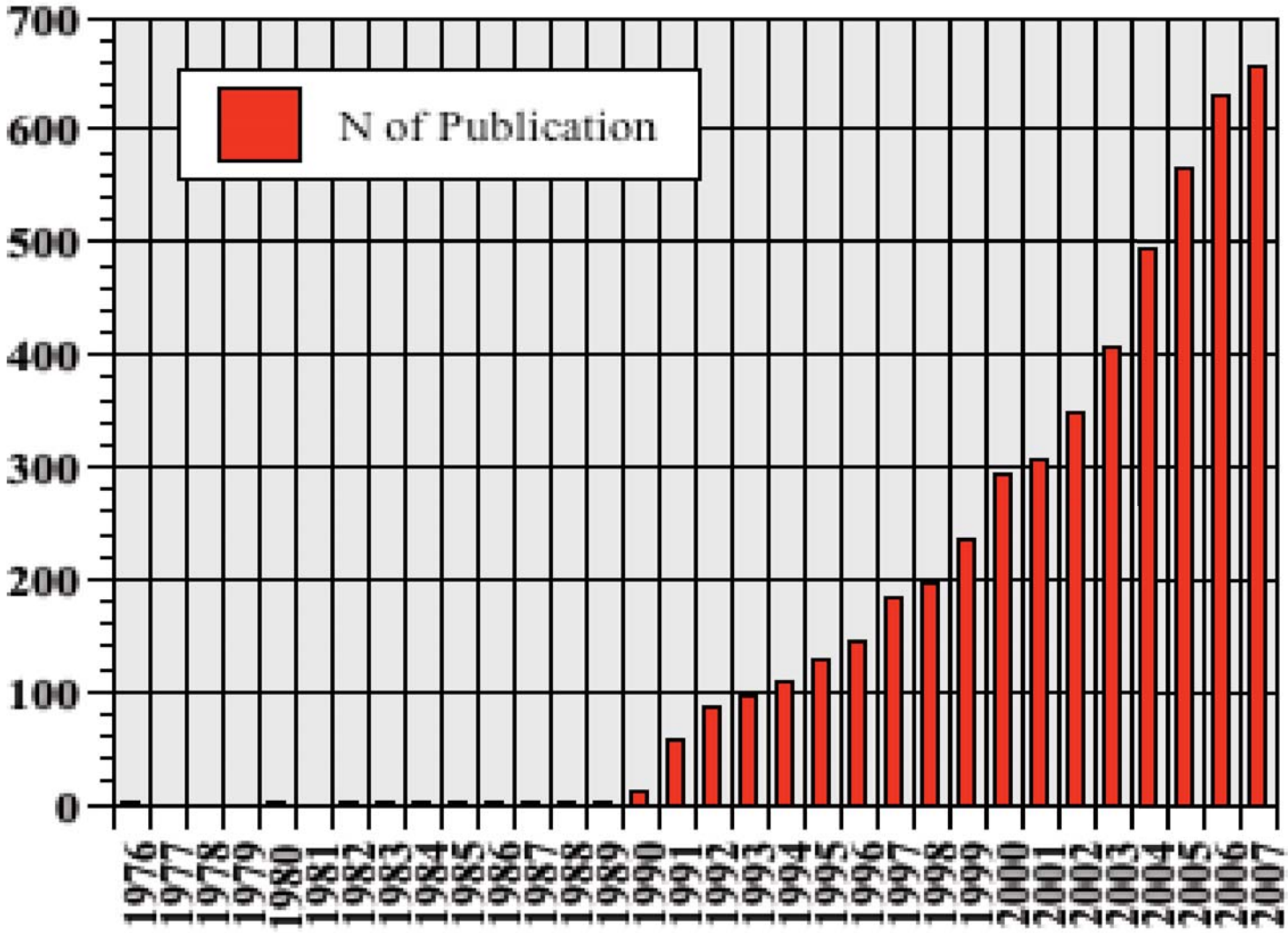
- Critical windows
- Effects at low doses
- Non-linear dose-response relationship
- Cross-talk among nuclear receptors
- Genetic polymorphism
- Epigenetic effects

Importance of exposure during perinatal period

Importance of Prospective Cohort Design for Early Life Studies

- Allows measurement of exposure that is not affected by outcome
- Facilitates assessment of exposure during critical windows

Trend of publications related to child cohort



Searched by “birth+cohort+child*” from Web of Science(ISI)

Example of Ongoing Child Cohorts

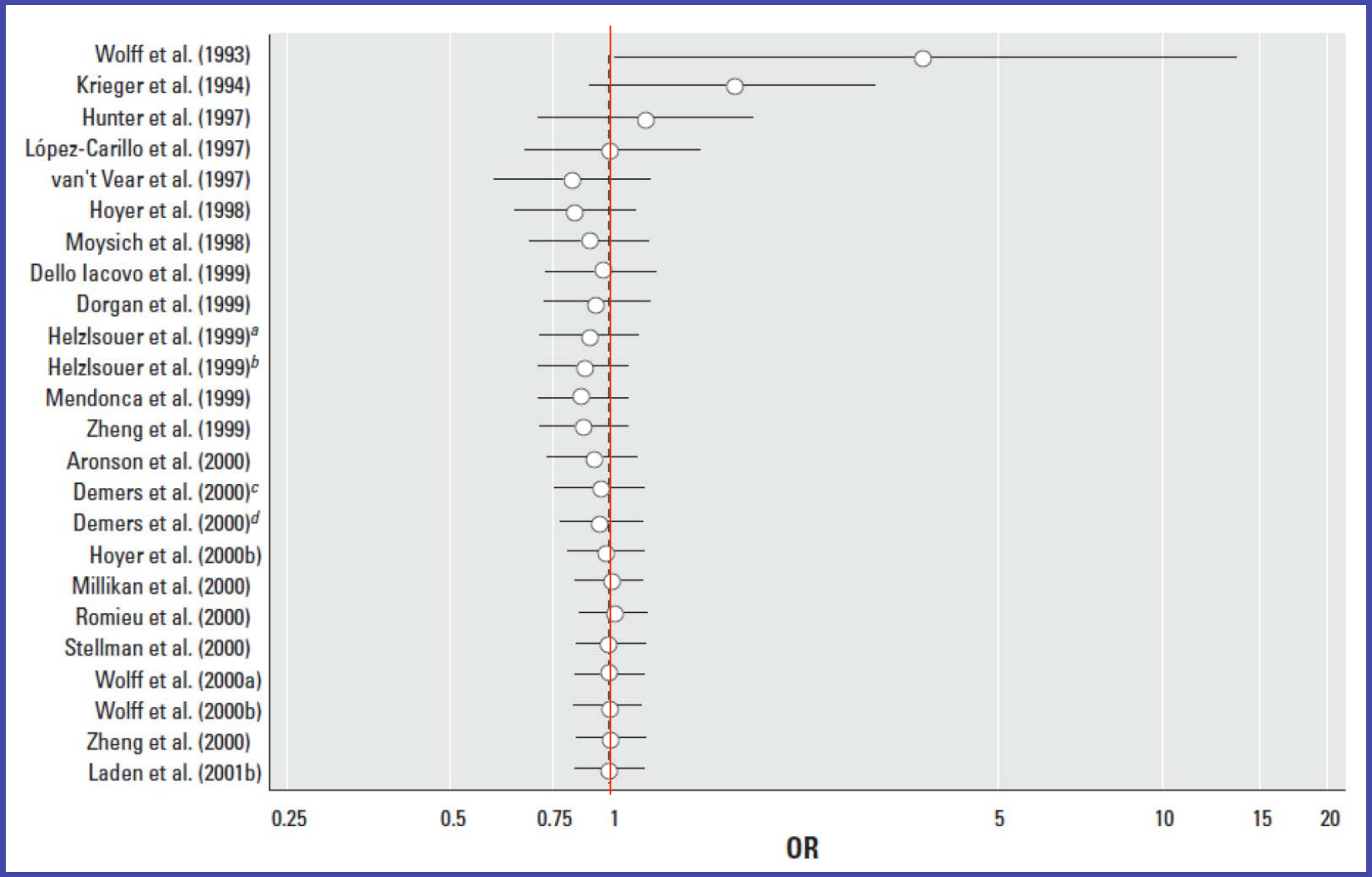
Place	Size	Enrollment
Hokkaido	20,000	2002-2005
Tohoku	1,300	2001-2003
Seiiku	1,600	2003-2005
Denmark	100,000	1996-2002
Finland	12,000	1966
France	5,000	2004-
Netherlands	10,000	2002-
Norway	100,000	1999-
Spain	3,500	2001-
U. K.	14,000	1991-1992
U. S. A.	100,000	2006-

Cognitive Outcomes of Human PCB Studies

	n	Outcome(cognitive)	Age		Exposure	Median(ug/g lipid)*
Collaborative Perinatal Project 1959-1965	732	WISC	7y	→→	Prenatal serum SumPCBs	140
North Carolina Cohort 1978-1982	712	McCarthy Scale	3-5y	→→	Breast Milk PCBs	80
Michigan Cohort 1980-1981	313	Fagan	7m	→	CordBlood PCBs, BreastMilk PCBs	120
		McCarthy Scale	4y	→	CordBlood PCBs, BreastMilk PCBs	
		WISC-R	11y	→	Prenatal PCBs	
Dutch Cohort 1990-1992	418	K-ABC	42m	→	Prenatal PCBs	100
Oswego Cohort 1991-1994	309	Fagan	6m	→	Cord blood PCBs, 7-9ChlorinePCBs	40
			12m	→	Cord blood PCBs	
German/Dusseldorf 1993-1995	171	Fagan	7m	→→		
		K-ABC	42m	→	Breast Milk PCB(138,153,180)	140

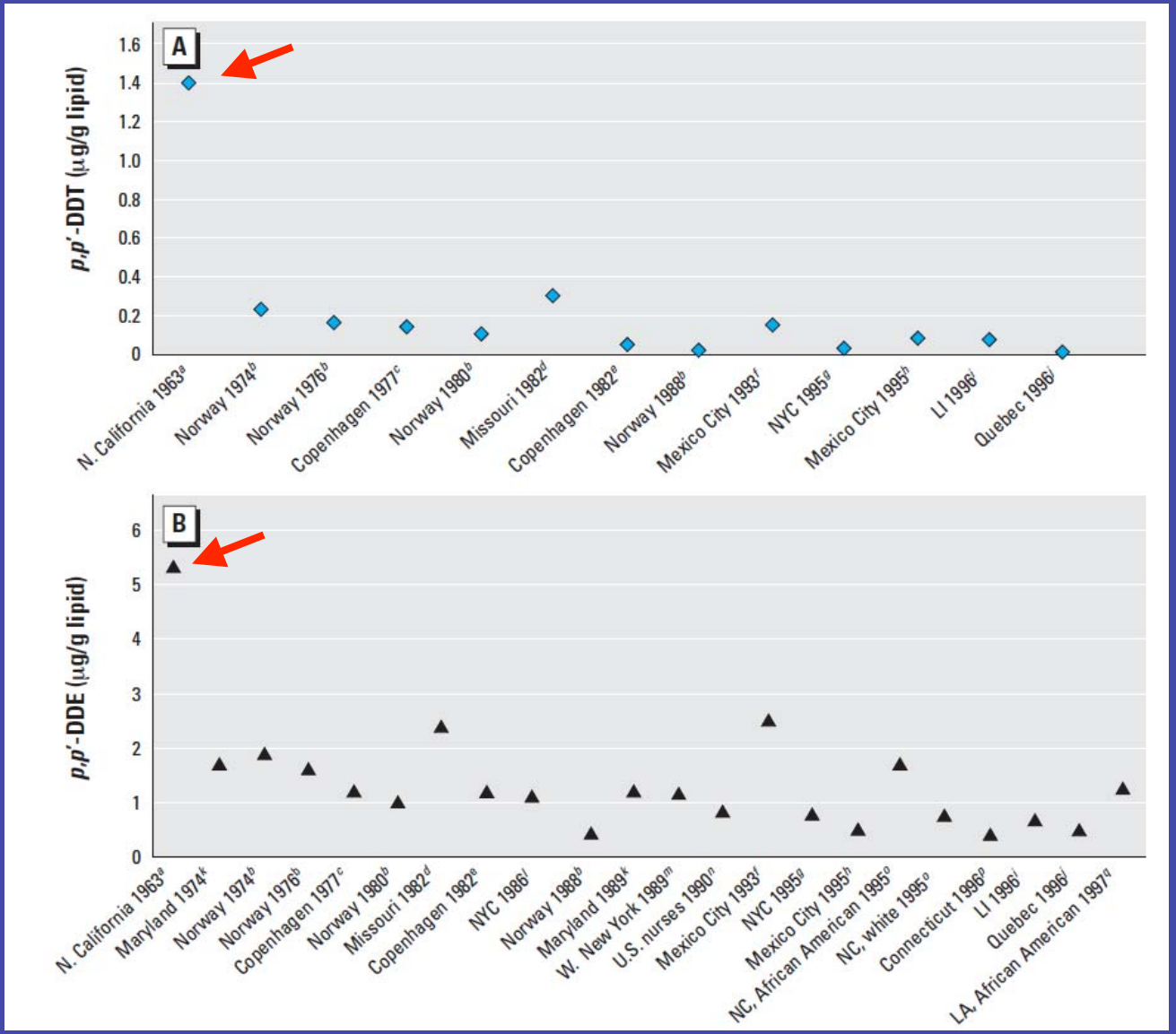
* PCB153 concentration in serum estimated by Longnecker et al. 2003

Breast cancer-DDT, DDE



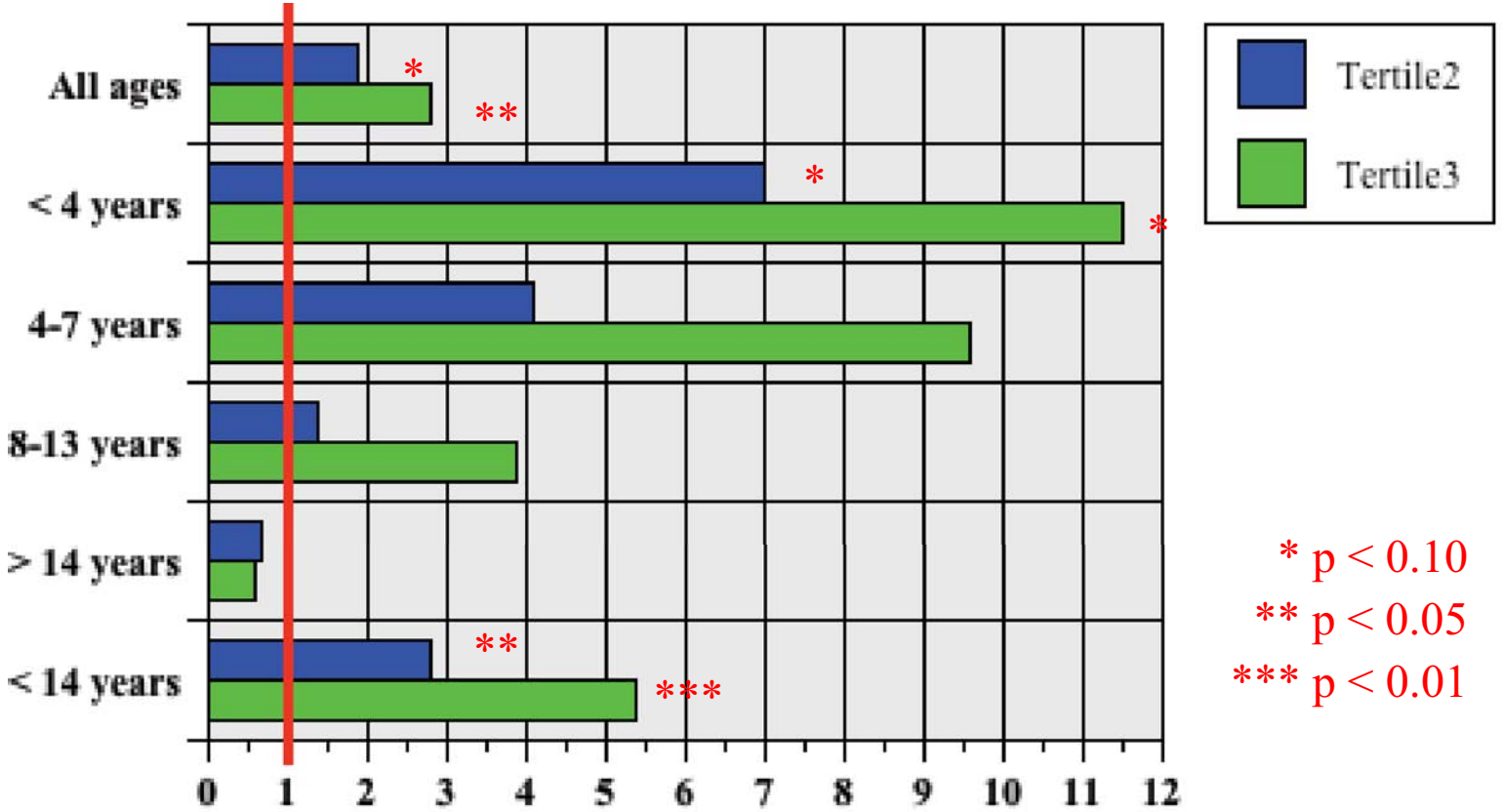
Lopez-Cervantes et al., 2004

DDT exposed at young



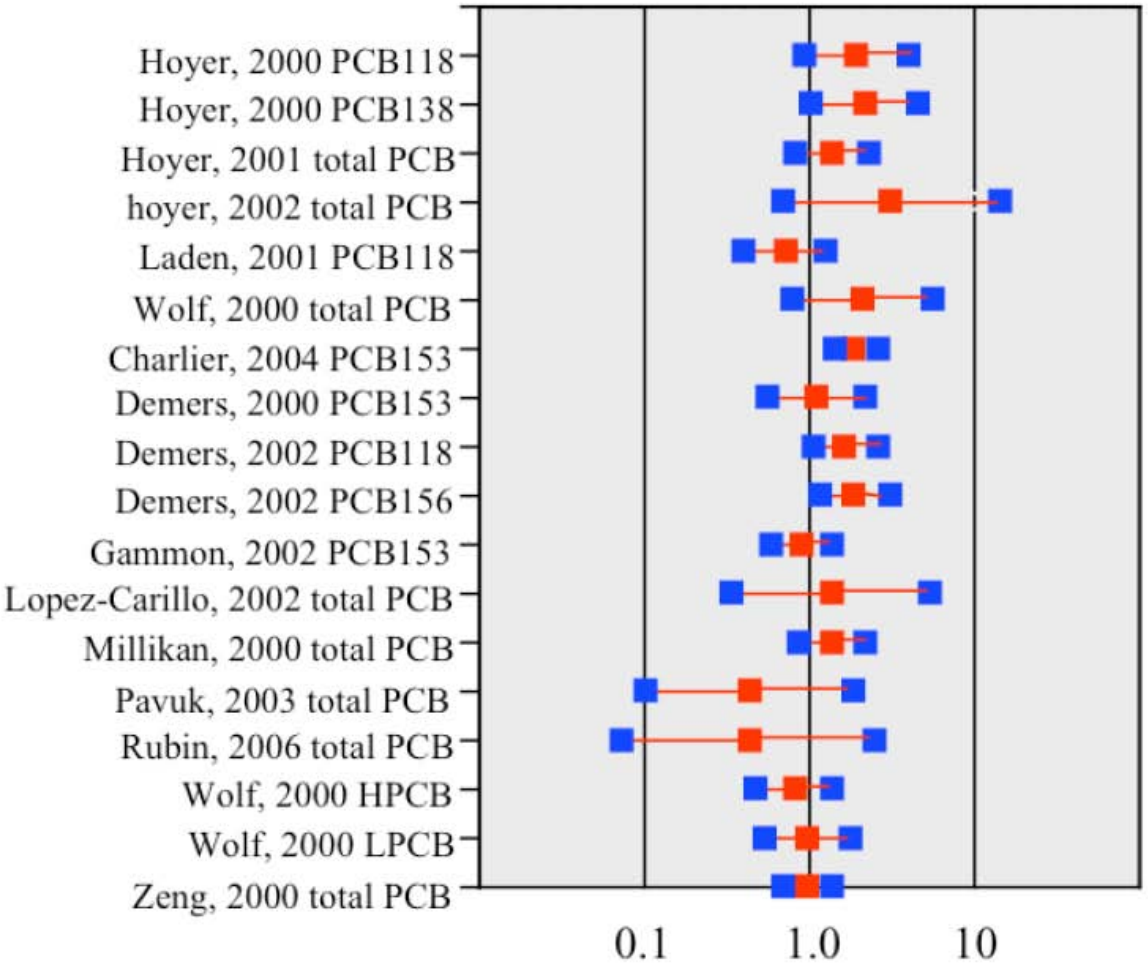
(Cohn et al. 2007)

p, p'-DDT Association with Breast Cancer Stratified by the Age at 1945



(Cohn et al. 2007)

Example of Recent PCB-Breast Cancer Epidemiologic Studies

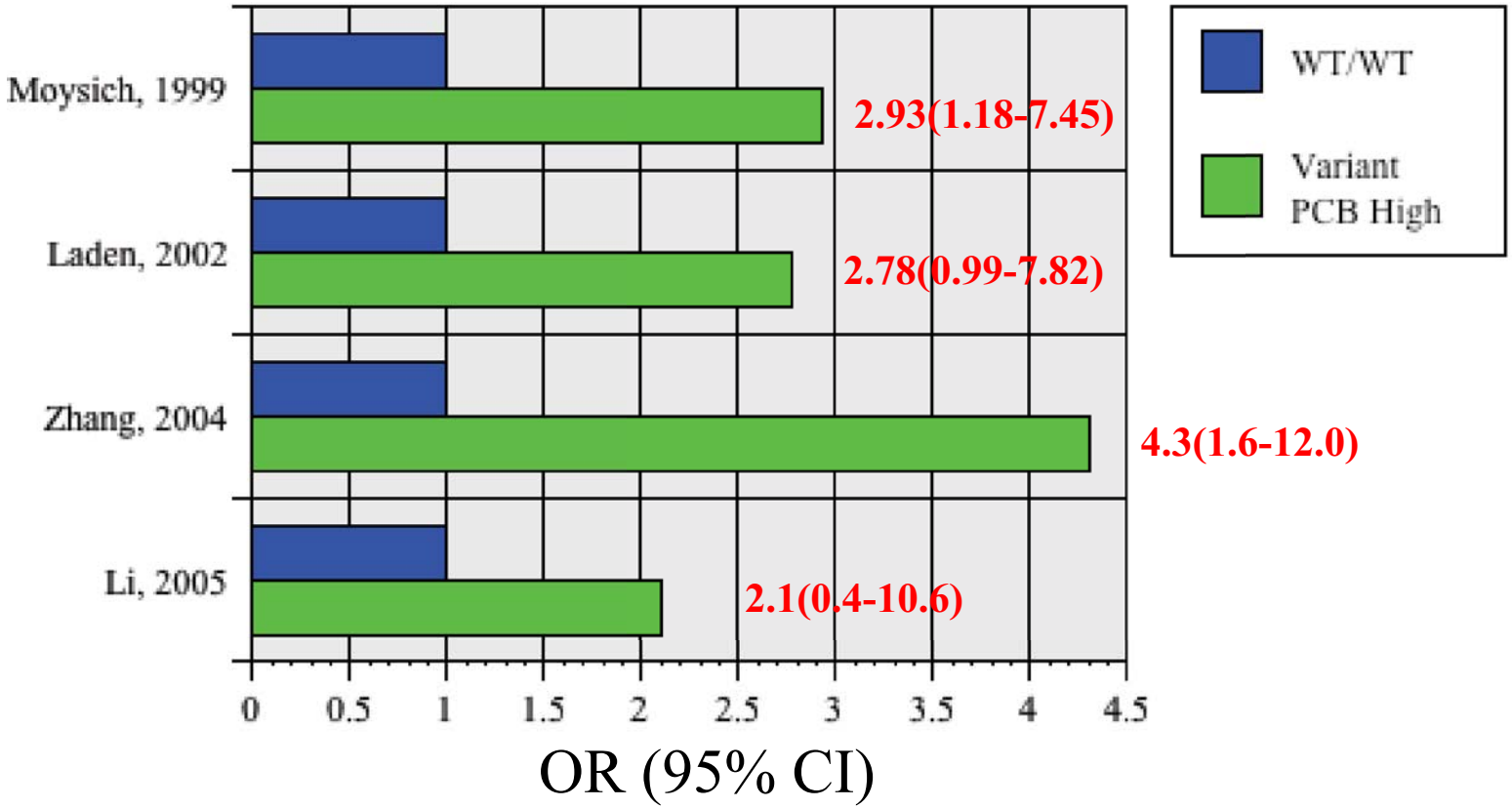


Odds Ratio and 95% CI

Data from Brody et al. 2007

Breast Cancer-PCBs, SNP

CYP1A1-m2 polymorphism

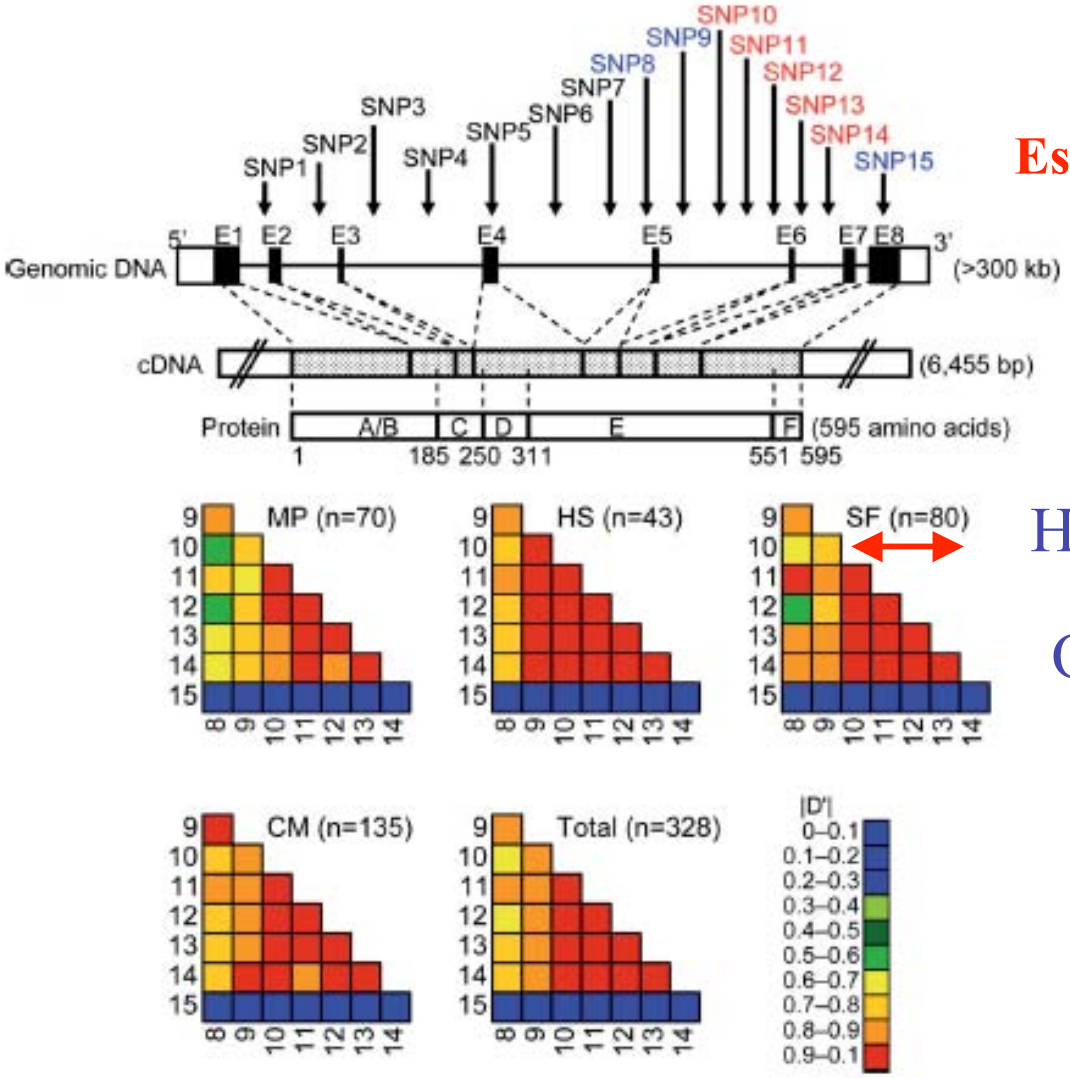


Polymorphism and Reproductive Disorder

AHRR Pro185Ala

- Micropenis (Fujita et al., 2002, Soneda et al., 2005)
- Endometriosis (Tsuchiya et al., 2005)
- Spermatogenesis in infertile men (Watanabe et al., 2004)

Example of Genomic Susceptibility- Male Genital Organ Disorders



Estrogen Receptor α (ESR1)

Haplotype Block

OR: hypospadias 13.75

cryptorchidism 9.0

Watanabe et al. 2007

Genome Epidemiology using Informatics