

Placental levels of halogenated organic compounds and cord immune markers



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Pregnancy Environment and Child Health (PEACH)

Cohort of mother-infant pairs

- Michigan State University (2003-2005)
- University of South Carolina (2006-2007+)

Exposure to halogenated organic compounds (HOC) *in utero* or via *breastfeeding*

- Polychlorinated biphenyls (PCBs),
- Dichlorodiphenyl dichloroethylene (DDE)
- Polybrominated diphenyl ethers (PBDEs).



Pregnancy Environment and Child Health (PEACH)

Outcomes:

- Immune markers (cytokines, immunoglobulins)
- Infectious (middle ear infections)
- Allergic manifestation in childhood (asthma, & eczema)

Exposure comparison

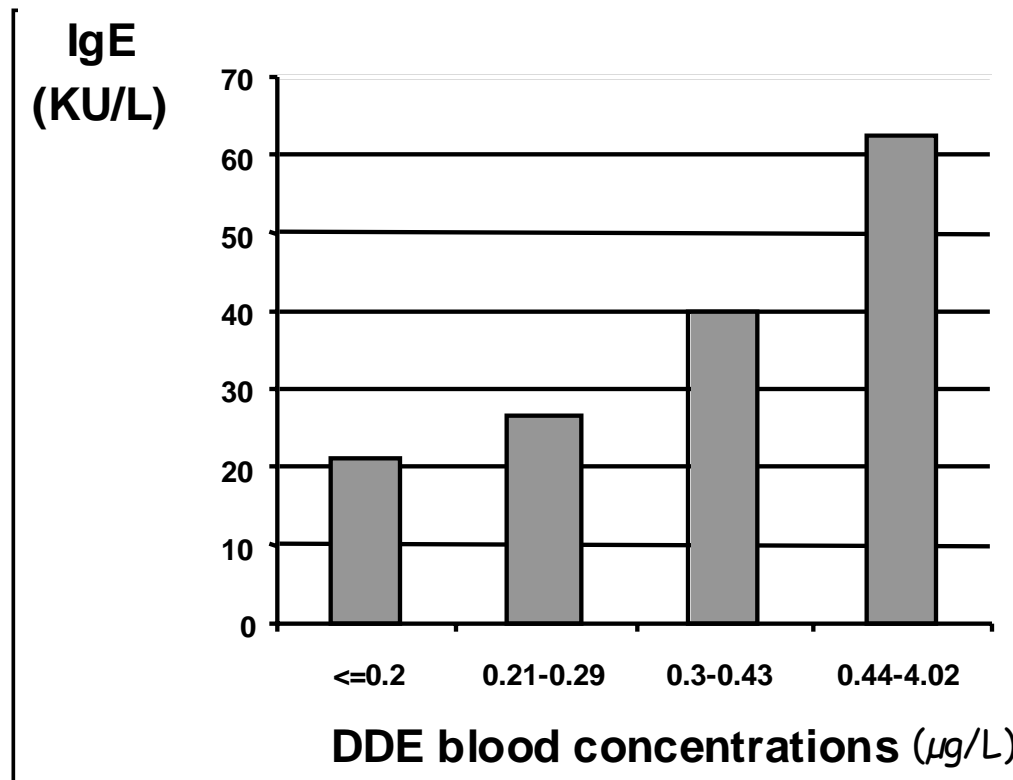
OSSM (Organochlorines and sex steroid metabolism) study:

- Female adult offspring of Michigan fisher
- Comparison of HOC exposure

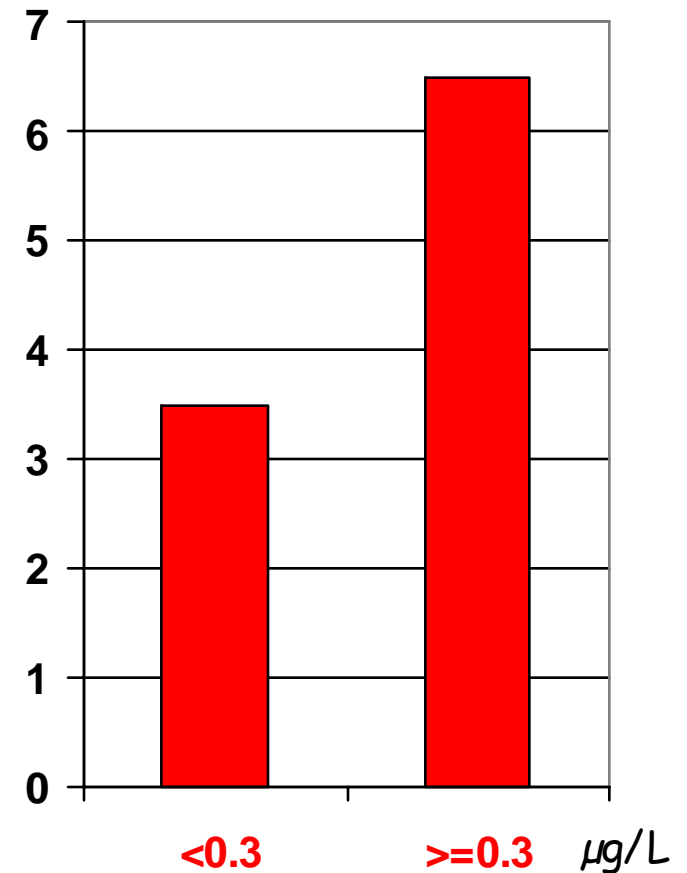
DDE blood concentrations in children were related to having increased IgE concentrations and a threefold risk of having asthma.

Karmaus et al., Arch Environ Health, 2001

IgE level and DDE concentration



Prevalence of asthma and DDE concentration



Findings supported by a Spanish group:

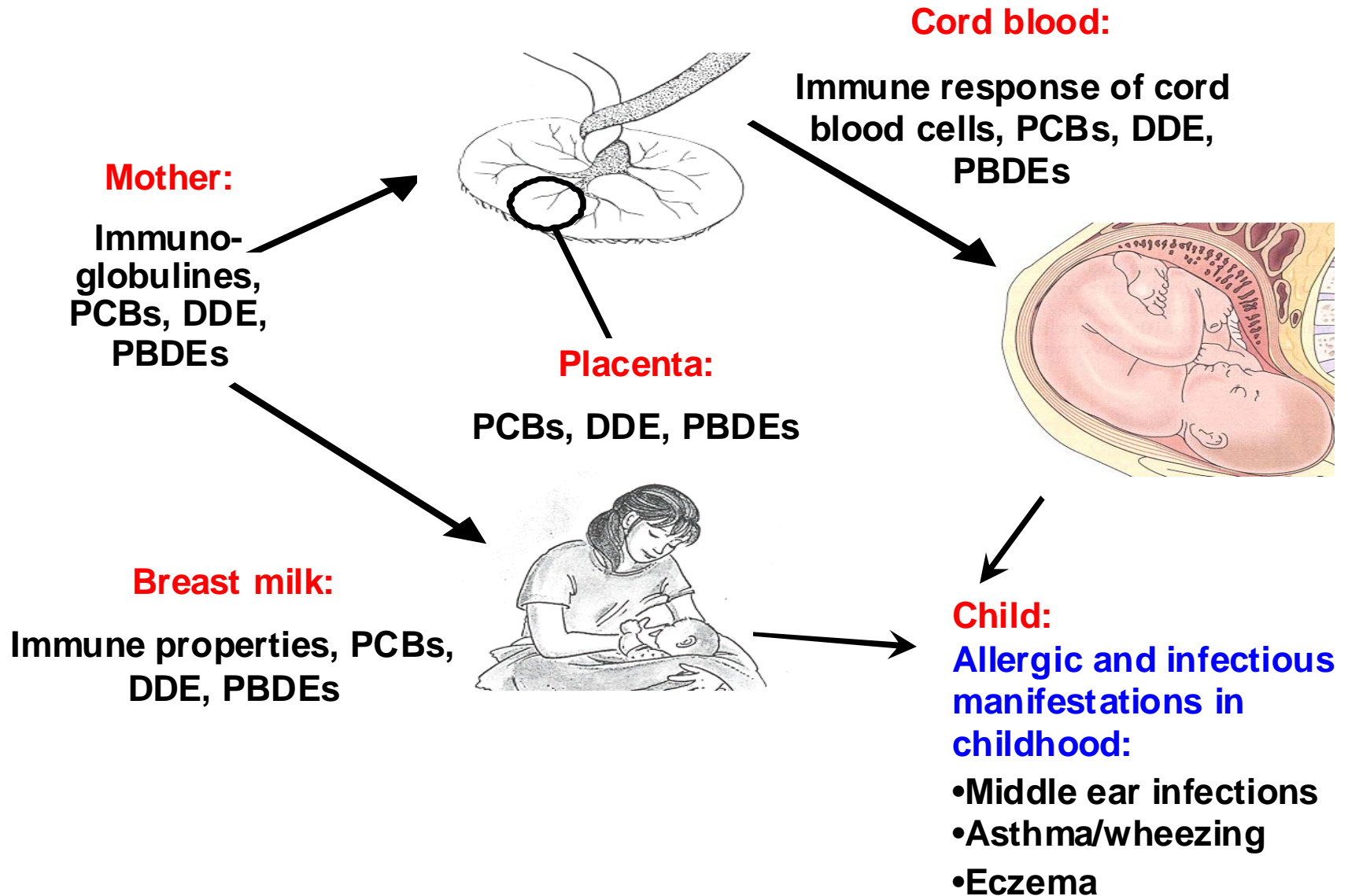
- Wheezing at 4 years of age increased with DDE concentration at 4 years

Sunyer et al., Environ Health Perspect, 2005

- Diagnosed asthma and persistent wheezing were associated with DDE at birth.
- Breastfeeding protected against diagnosed asthma and wheezing.

Sunyer et al., Clinical & Experimental Allergy, 2006

Exposures and outcomes



Population



- Primipara
- Age 18 and older
- No multiple births
- No diabetes, thyroid or adrenal disorders
- Less than 20 weeks gestation

All ethnic and racial groups are included.

Current population: - Michigan: n=52
Serum samples: n=35
Placental samples: n=36
Breast milk samples: n=25
- South Carolina: n~80

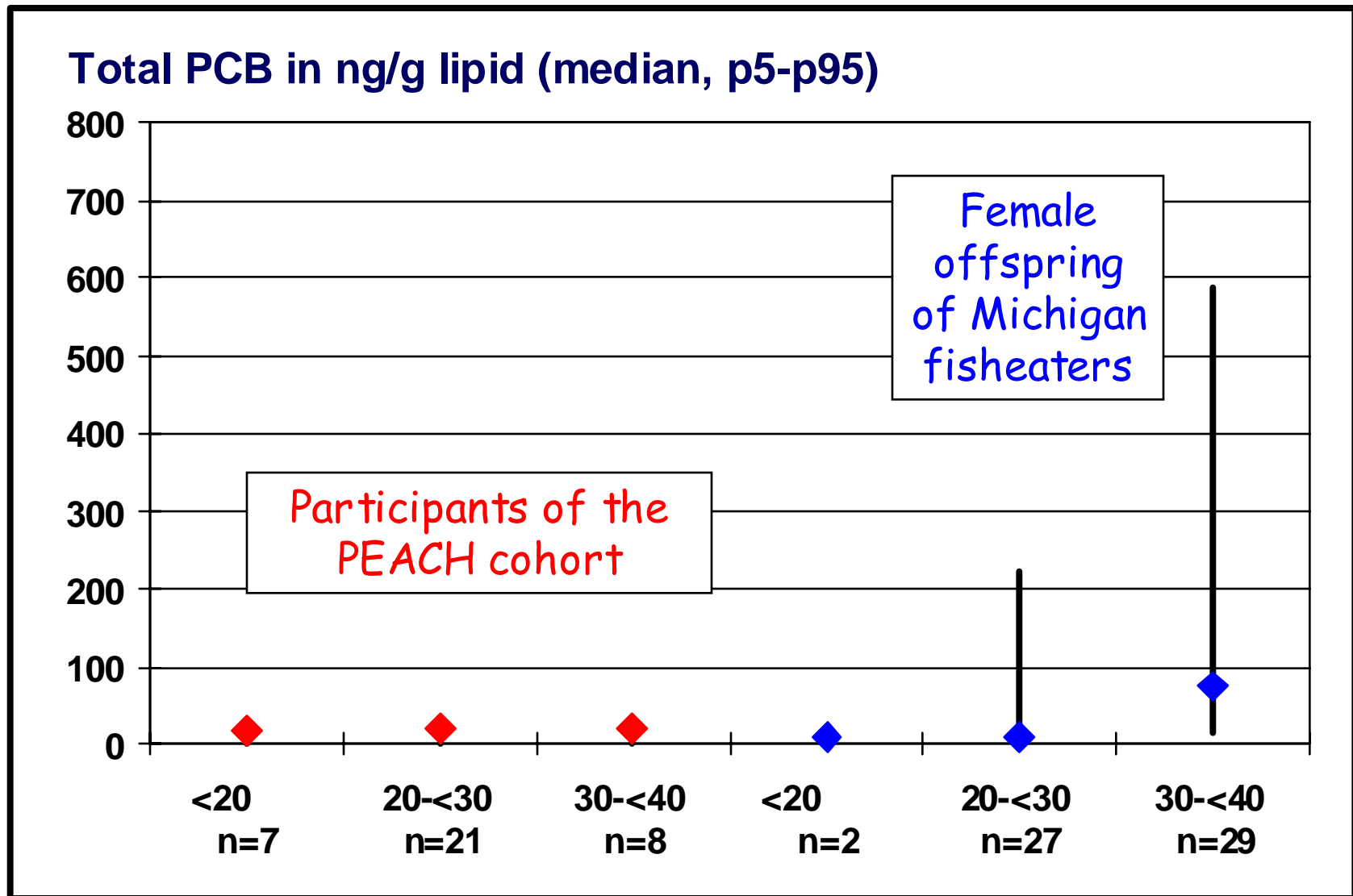
Exposure to halogenated organic compounds (HOC)

- Polychlorinated biphenyls (PCBs)
- p,p'-dichlorodiphenyl dichloroethylene (DDE)
- Polybrominated diphenylethers (PBDEs)
(sum of the congeners 28, 47, 77, 85, 99, 100, 153, 154, 183)

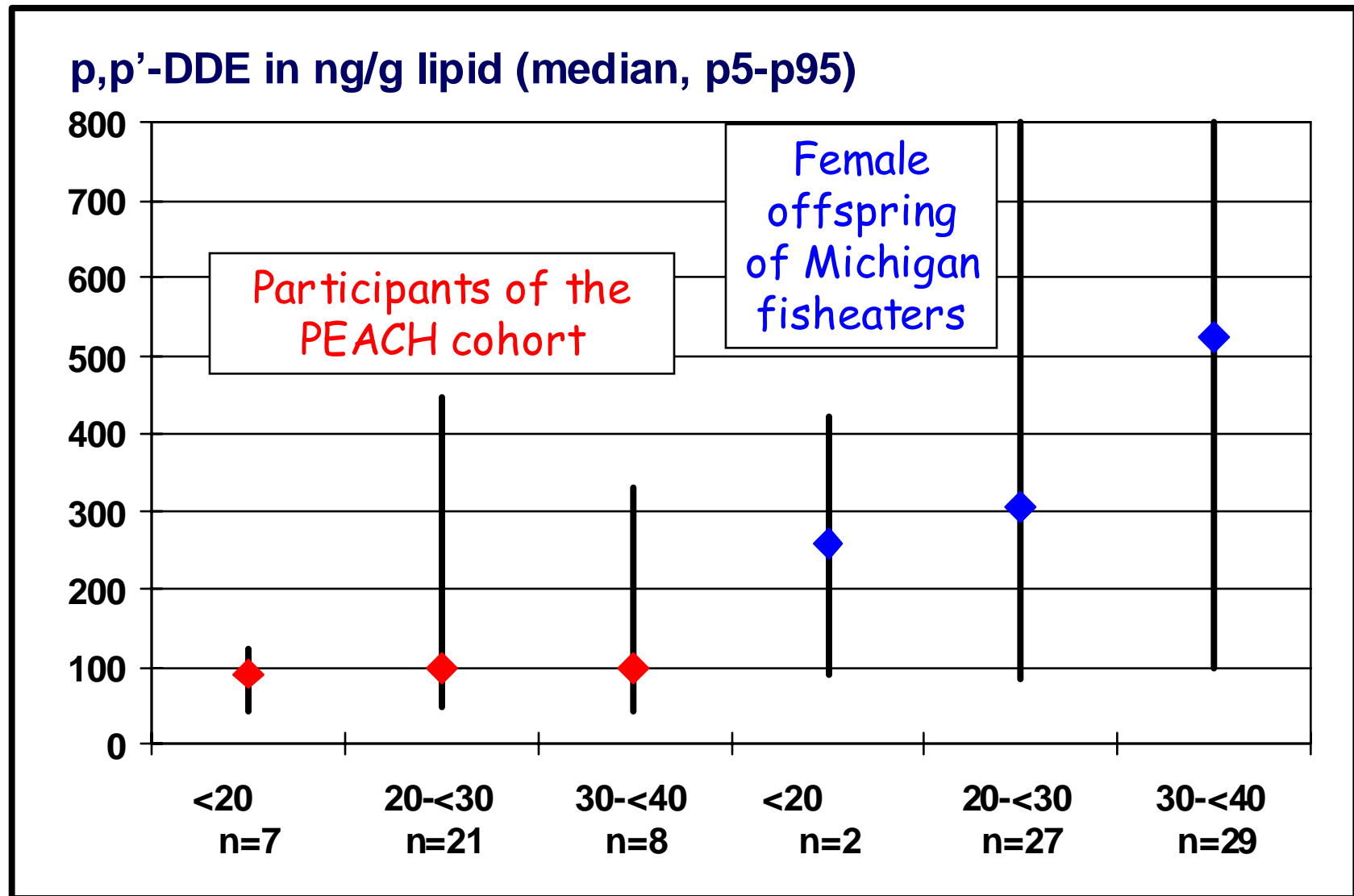
expressed as ng/g lipid

- Maternal serum
- Placental tissue
- Breast milk (first 4 weeks)

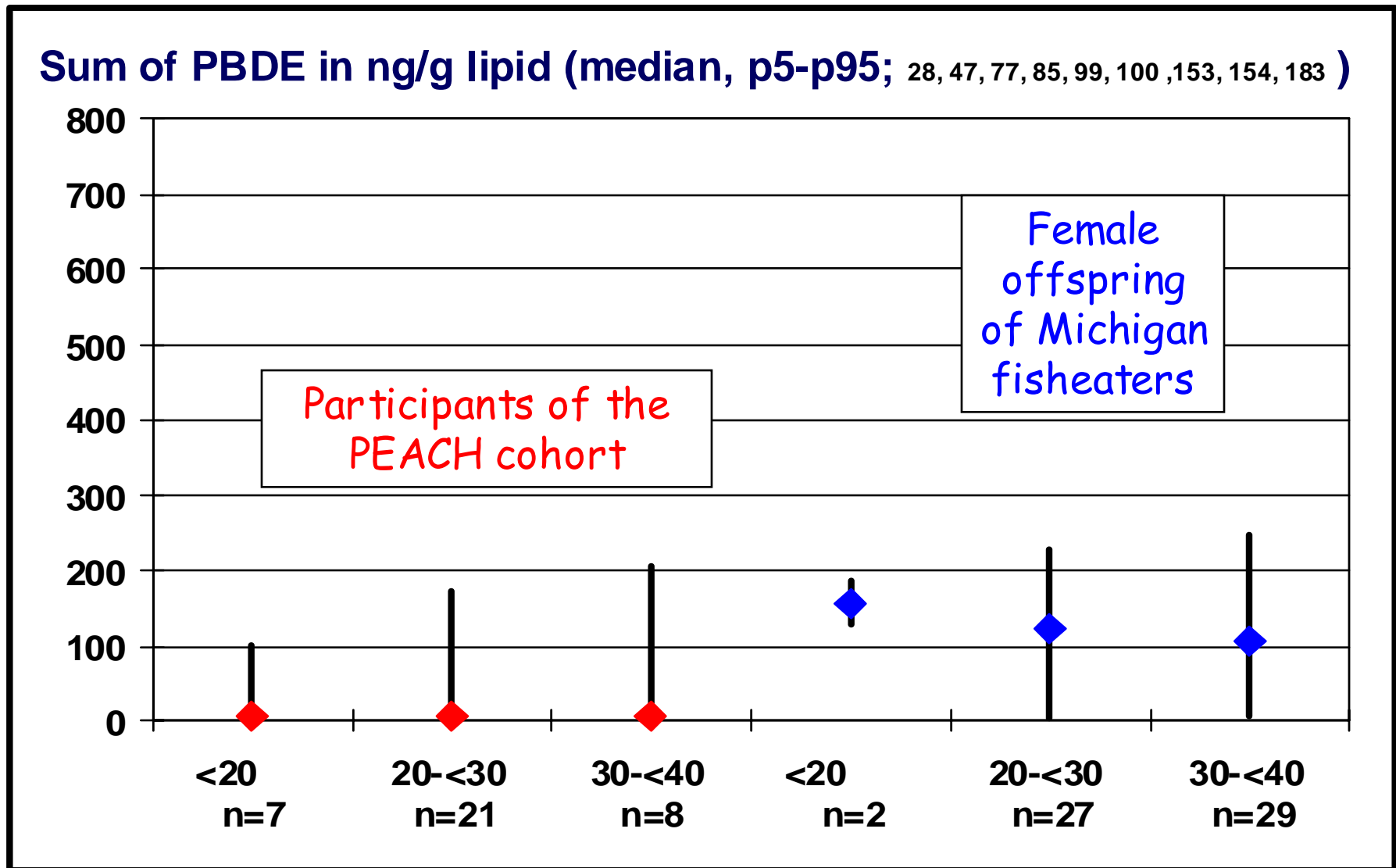
Comparison of PCB exposure - Serum



Comparison of p,p'-DDE exposure - Serum

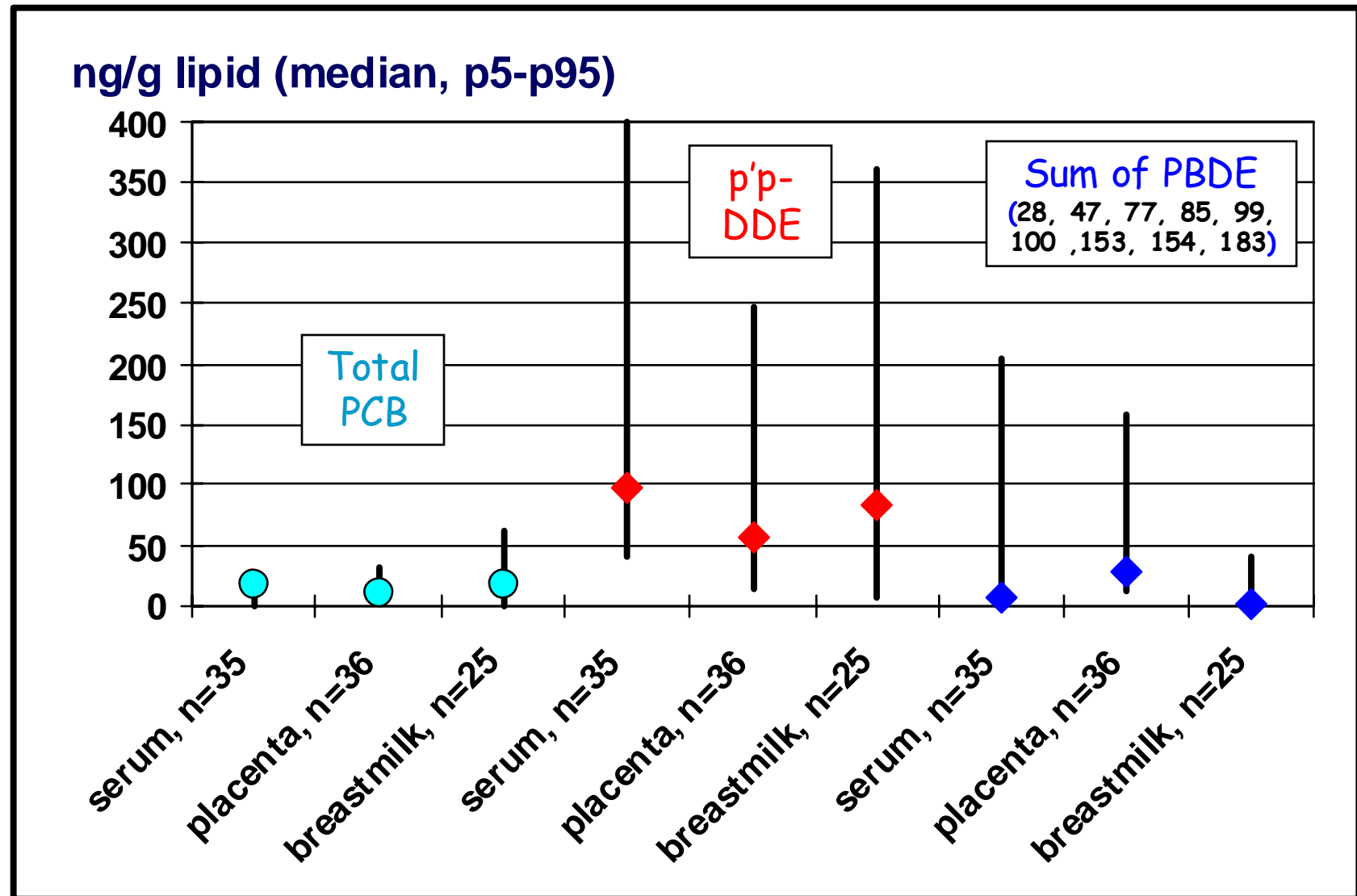


Comparison of PBDE exposure - Serum



HOC exposure - serum, placenta, breast milk

Participants of the PEACH study in Michigan



Comparison of p,p'-DDE exposure levels

Mean levels of DDE found in **breast milk**:

Michigan PEACH cohort:

303 ng/g lipid

Caucasian women in Canada:

336 ng/g lipid (Dewailly et al. 1993)

Finish and Danish women:

77 and **137** ng/g lipid, respectively (Shen et al. 2007)

Australian women:

217-378 ng/g (Mueller et al. 2007)

Comparison of p,p'-DDE exposure levels

Mean levels of DDE found in placentas:

Michigan PEACH cohort:

77.9 ng/g lipid

Spanish women:

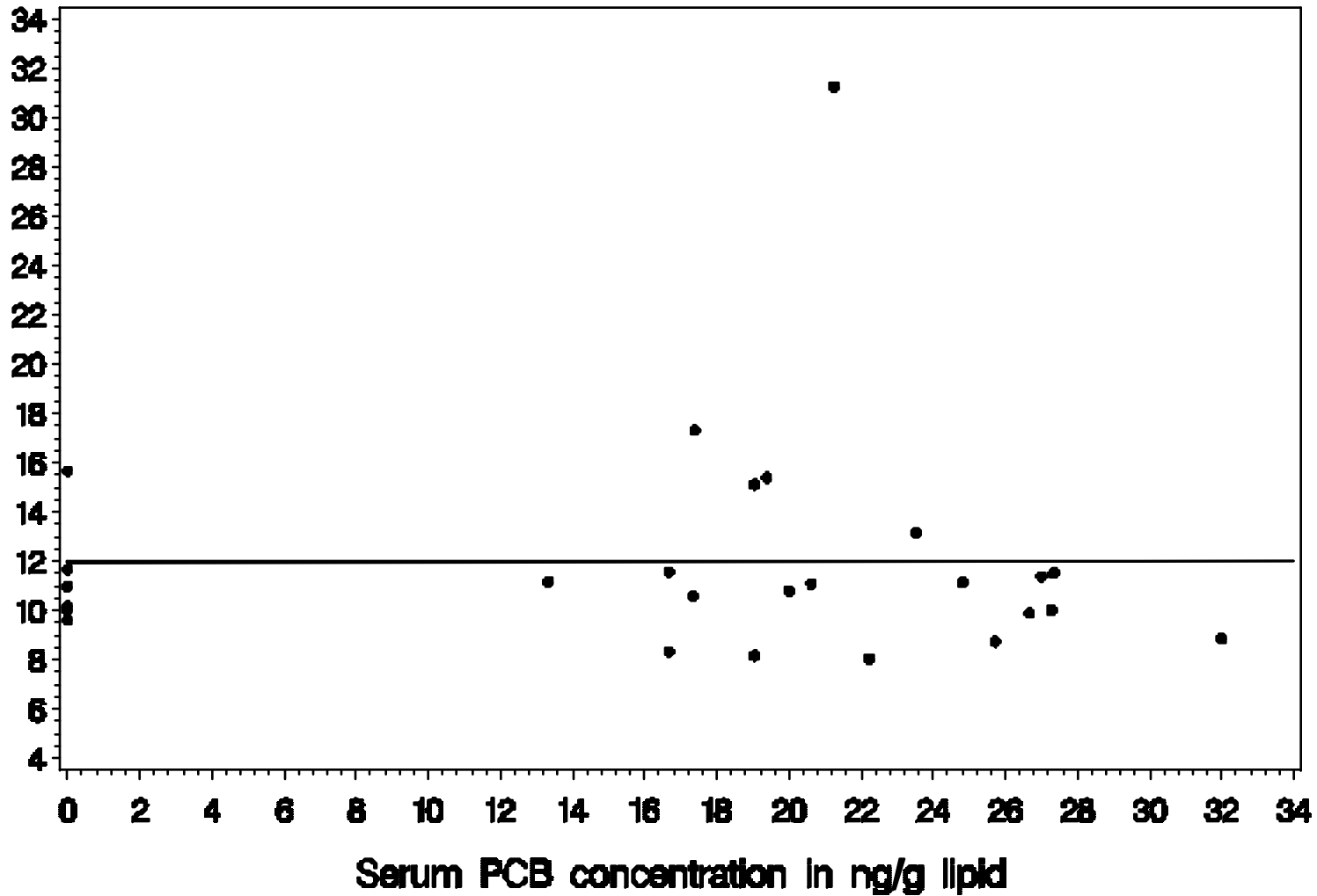
76.6 ng/g lipid (Lopez-Espinoza 2007)

Finish and Danish women:

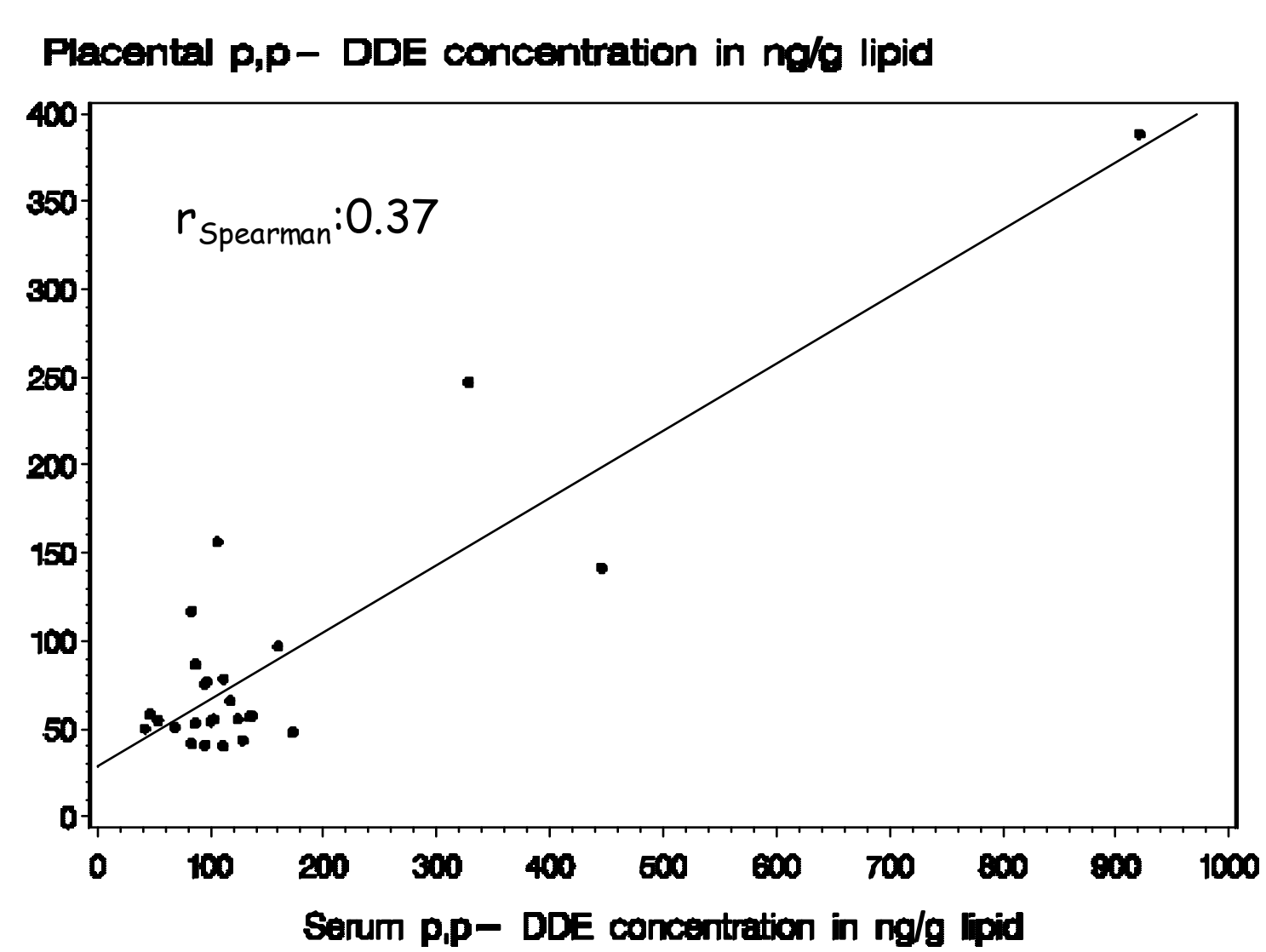
21 and 47 ng/g lipid , respectively (Shen et al. 2007)

There is no association between serum and placental PCB concentrations.

Placental PCB concentration in ng/g lipid

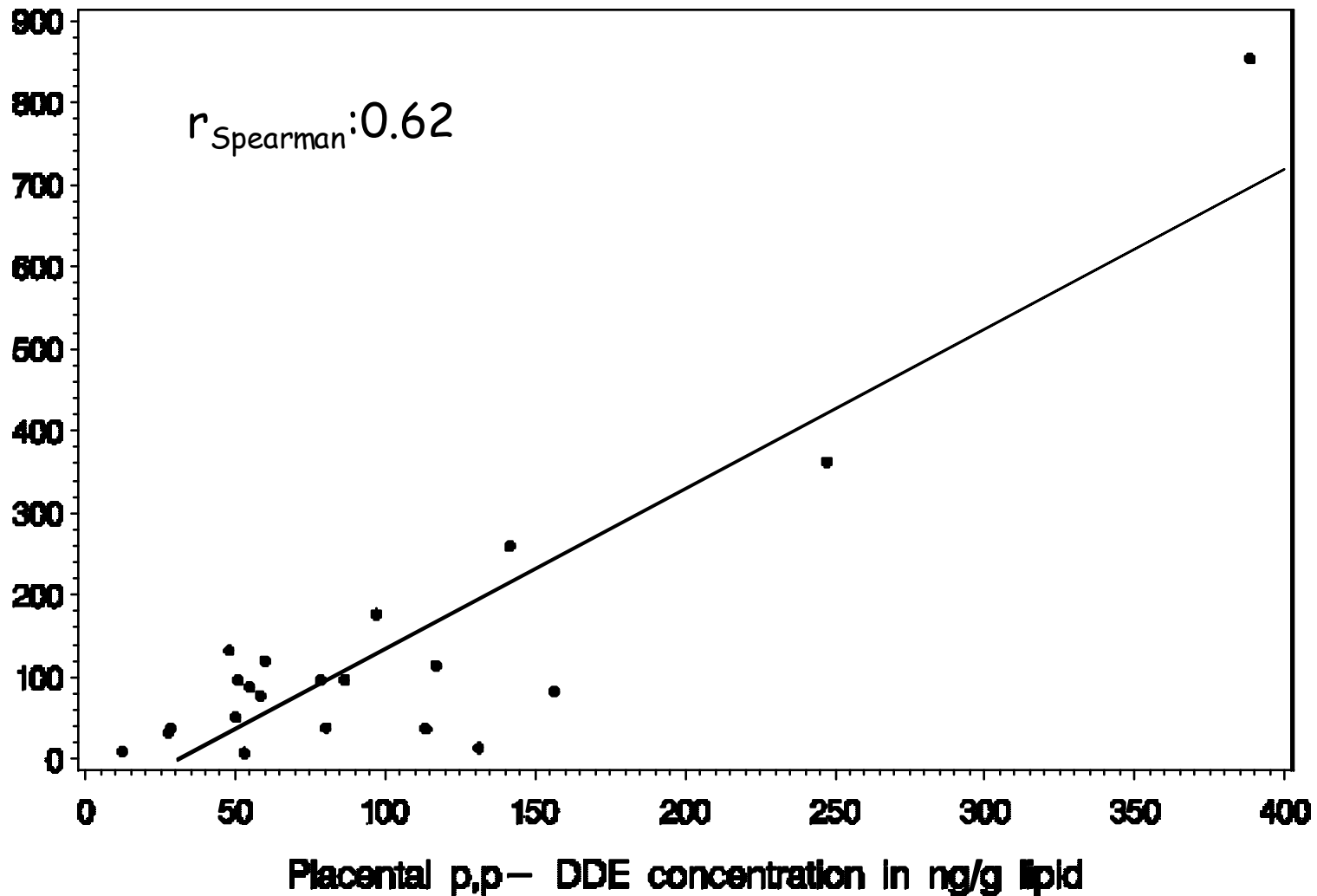


Serum and placental p,p'-DDE levels are related.



Placental and breast milk p,p'-DDE concentrations are correlated.

p,p- DDE concentration in ng/g lipid in breast milk



Conclusion - 1

- HOC levels in Michigan seems to be comparable to levels measured in Canada and Australia, but seems to be higher than those in Scandinavia.
- Maternal serum HOC concentrations do not or only weakly predict placental and breast milk concentrations.
- Placental and breast milk levels are closer related.
- Tissue metabolic activity is suggested to alter HOC concentrations.

HOC and immune development

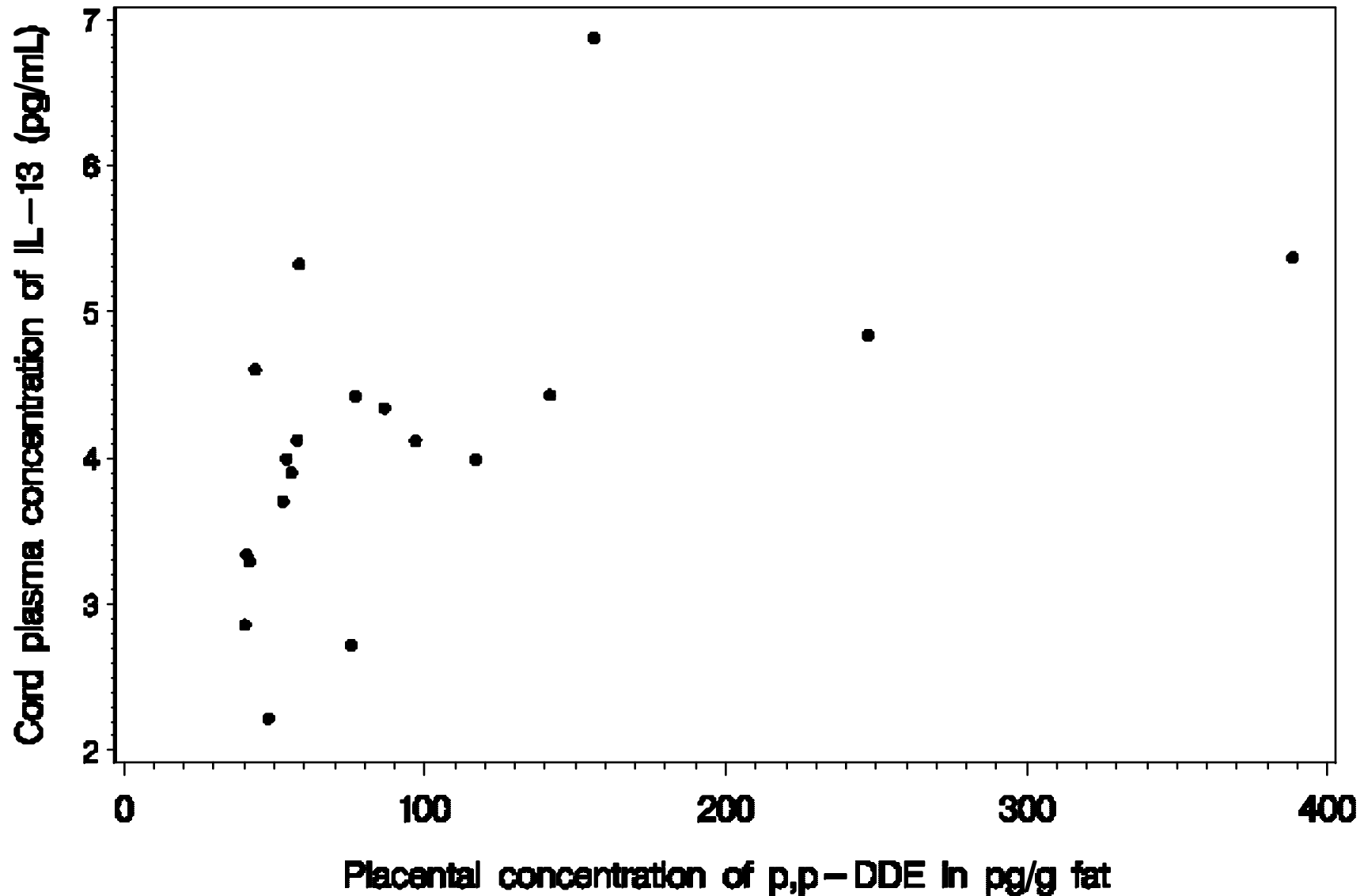
1. Immune responses can be primed during intra-uterine development (endocrine control).
2. Intra-uterine exposure to halogenated organic compounds (HOC) may alter immune responses detected in cord blood.
3. HOC are considered to act via endocrine disruption.
4. Cord blood immune responses are predictive of infections and allergic manifestation in childhood.
5. Intra-uterine HOC exposure may be related to infections and allergic manifestations.

Cord blood immune markers

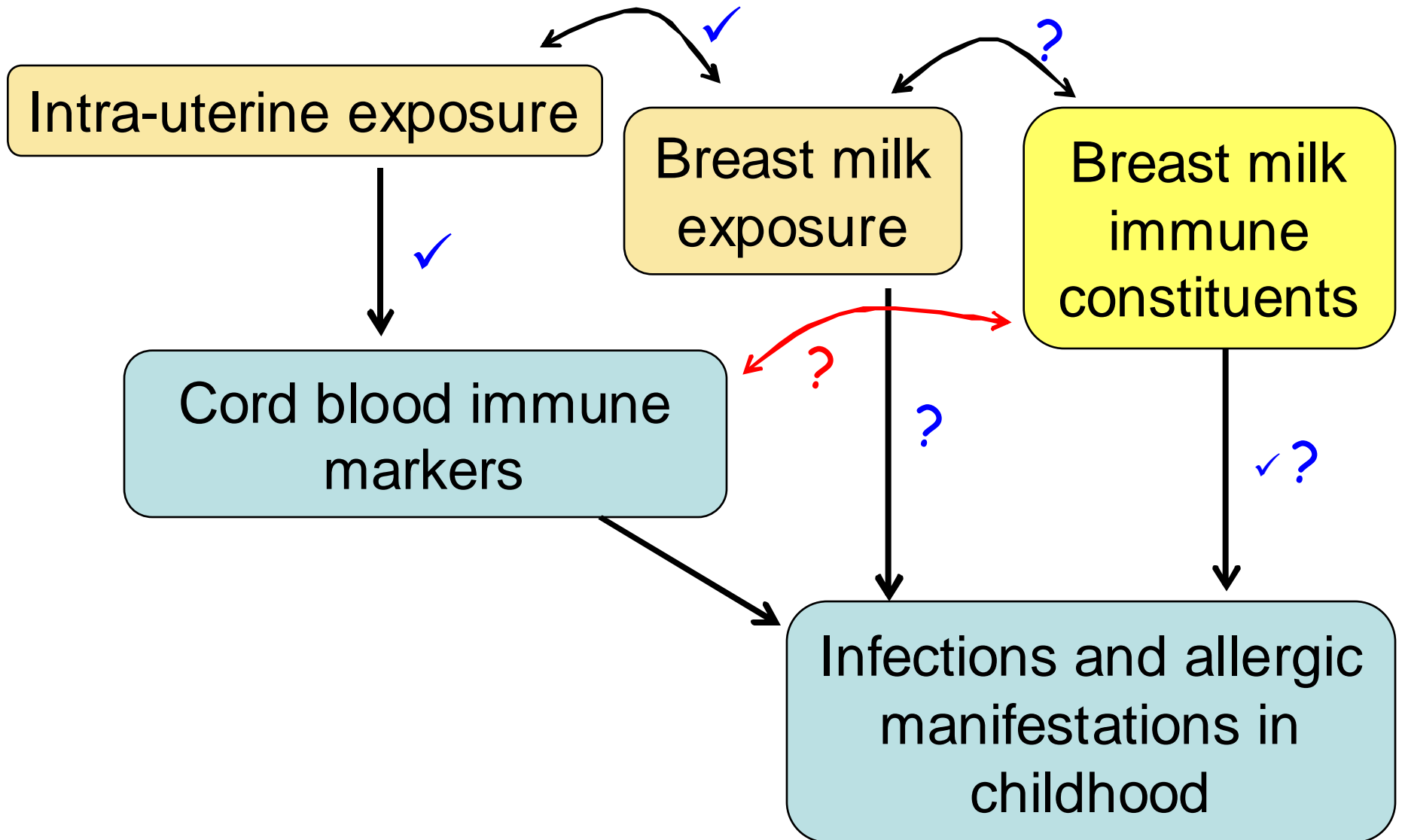
- Interleukin-4 (IL-4)
 - Interleukin-13 (IL-13)
 - Interferon- γ (INF- γ)
 - IL-4 / INF- γ
 - IL-13 / INF- γ
- Th2 cytokines
- Th1 cytokine
- Correction for an overall increase of cytokines at birth.

Placental p,p-DDE and IL-13 in cord serum

Brooks et al., *Pediatric Allergy and Immunology*, 2007



"Causal web" of early HOC exposure and immune responses



Conclusion - 2

1. Investigations of intra-uterine programming of infections and allergic disorders are in the early stages of development.
2. Several studies indicate that cord serum immune markers are affected by intra-uterine exposures such as HOC and smoking.
3. Persisting expression of genes (gene \times environment interactions, epigenetics) may explain the enduring effect of intra-uterine exposures.

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