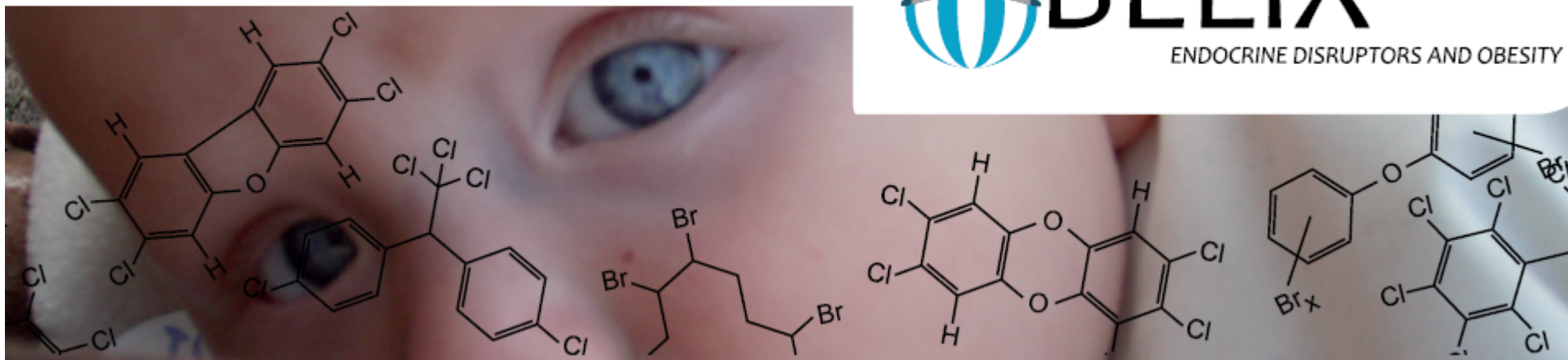


EDC Strategy, CHE partnership call, June 18, 2014



ENDOCRINE DISRUPTORS AND OBESITY



Prenatal exposure to EDCs and obesity:
combining toxicology and epidemiology

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Institute for Environmental Studies, VU University
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Obesity on the Rise

- Prevalence increasing in children adolescents, adults worldwide
- Risk factors
 - Diet
 - Physical activity
 - Genetics
 - Exposure to chemicals?



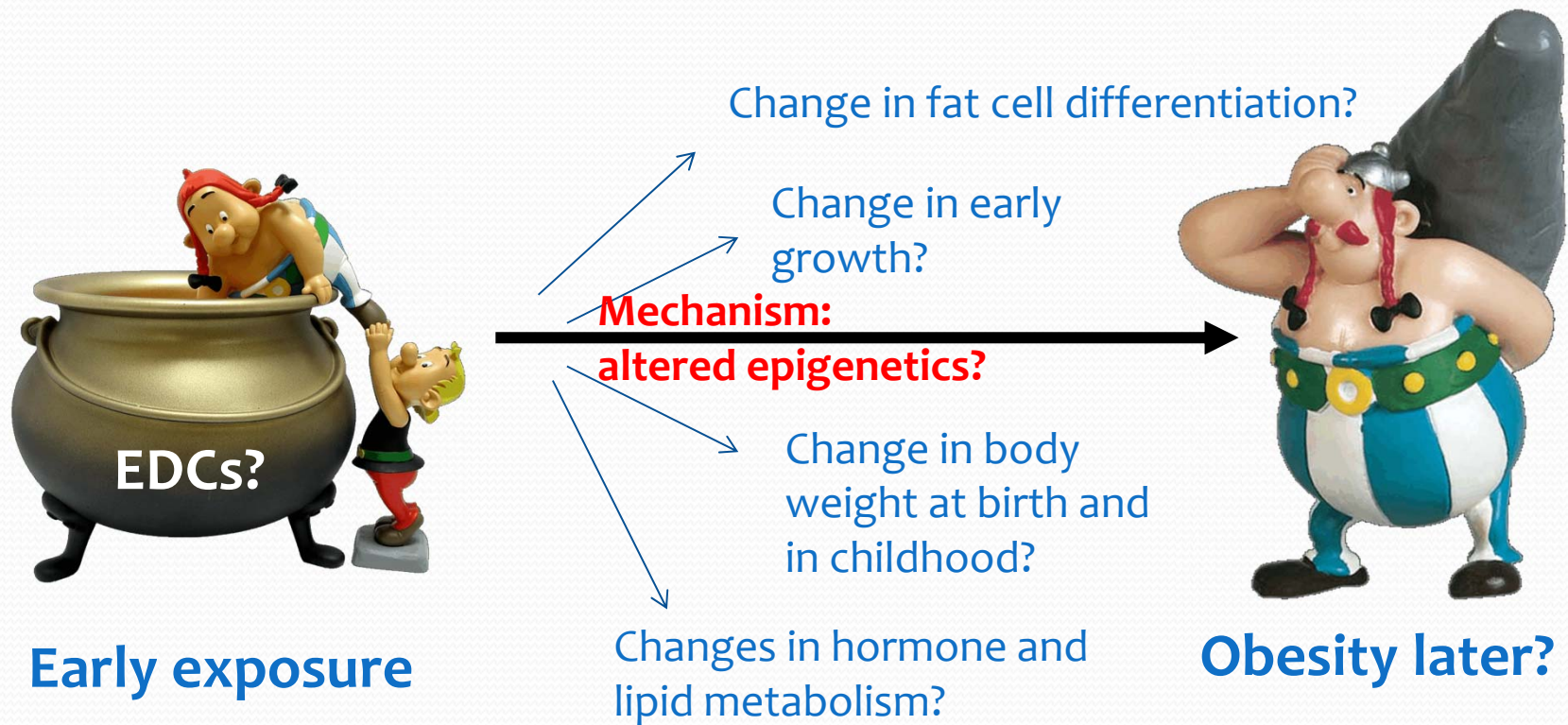


**OBesogenic Endocrine disrupting chemicals:
Linking prenatal exposure to the
development of obesity later in life**

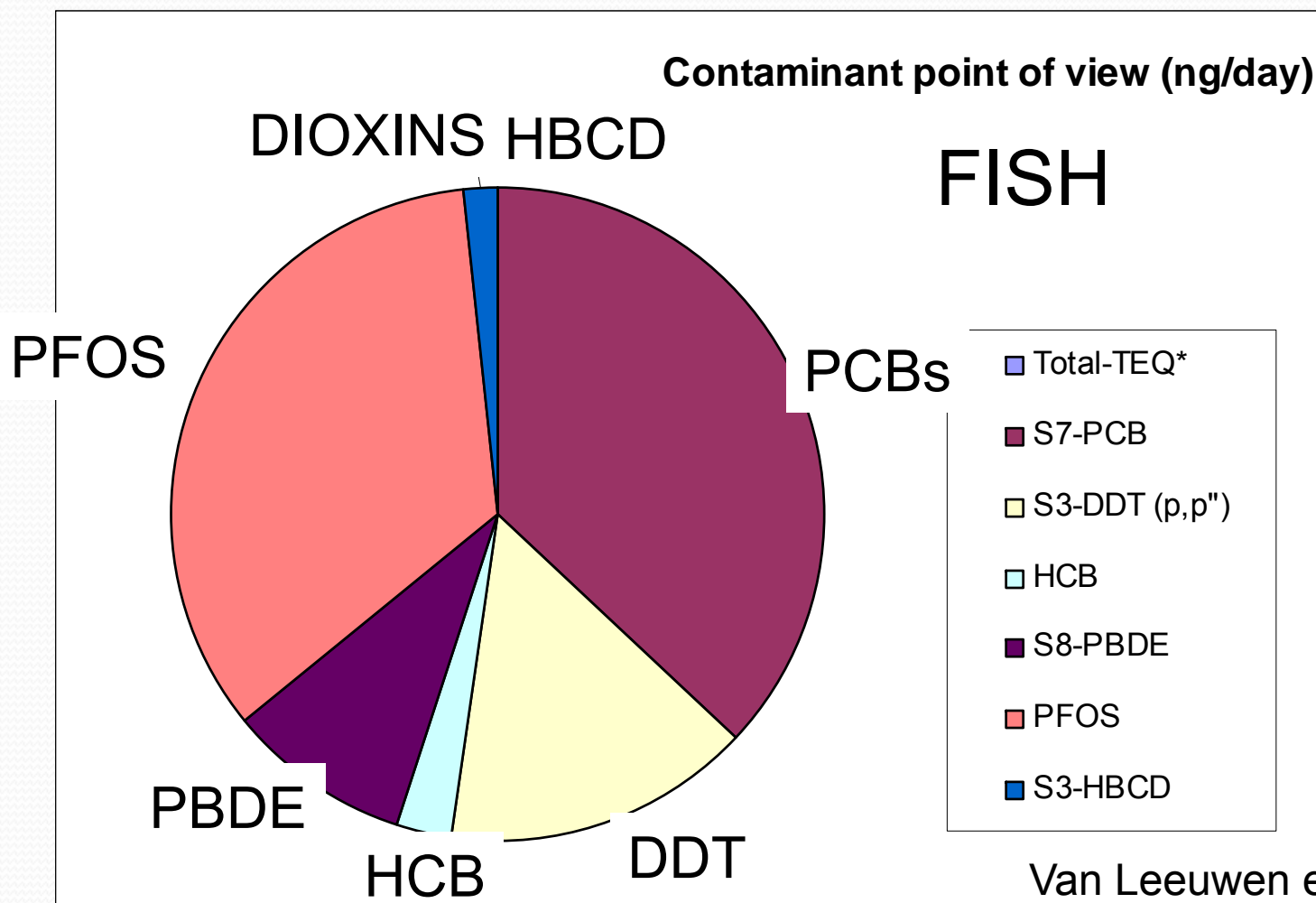
- European Commission FP7 funded research project
- Project duration: May 2009 – November 2013
- 7 research institutes throughout Europe (NL, BE, FR, SK, NO)

OBELIX research question

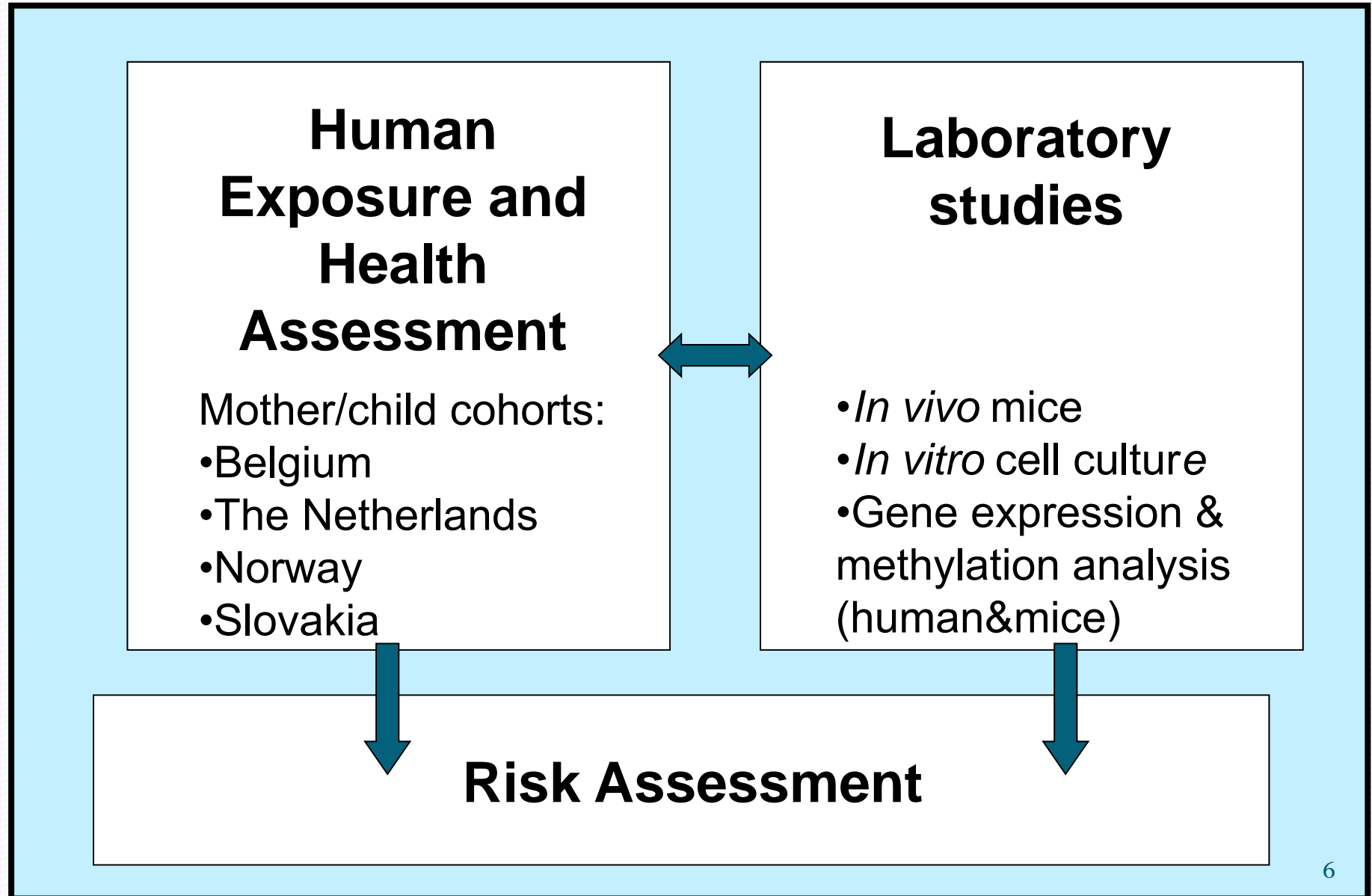
- Does exposure to endocrine disrupting chemicals (EDCs) early in life play a role in the development of obesity later in life?



EDCs studied in OBELIX are present in maternal diet



OBELIX approach



THE OBELIX & ENRIECO COHORTS

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ARMENIA

IRAN

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SPAIN

ITALY

CROATIA

BOSNIA & HER.

SERBIA

BULGARIA

TURKEY

SYRIA

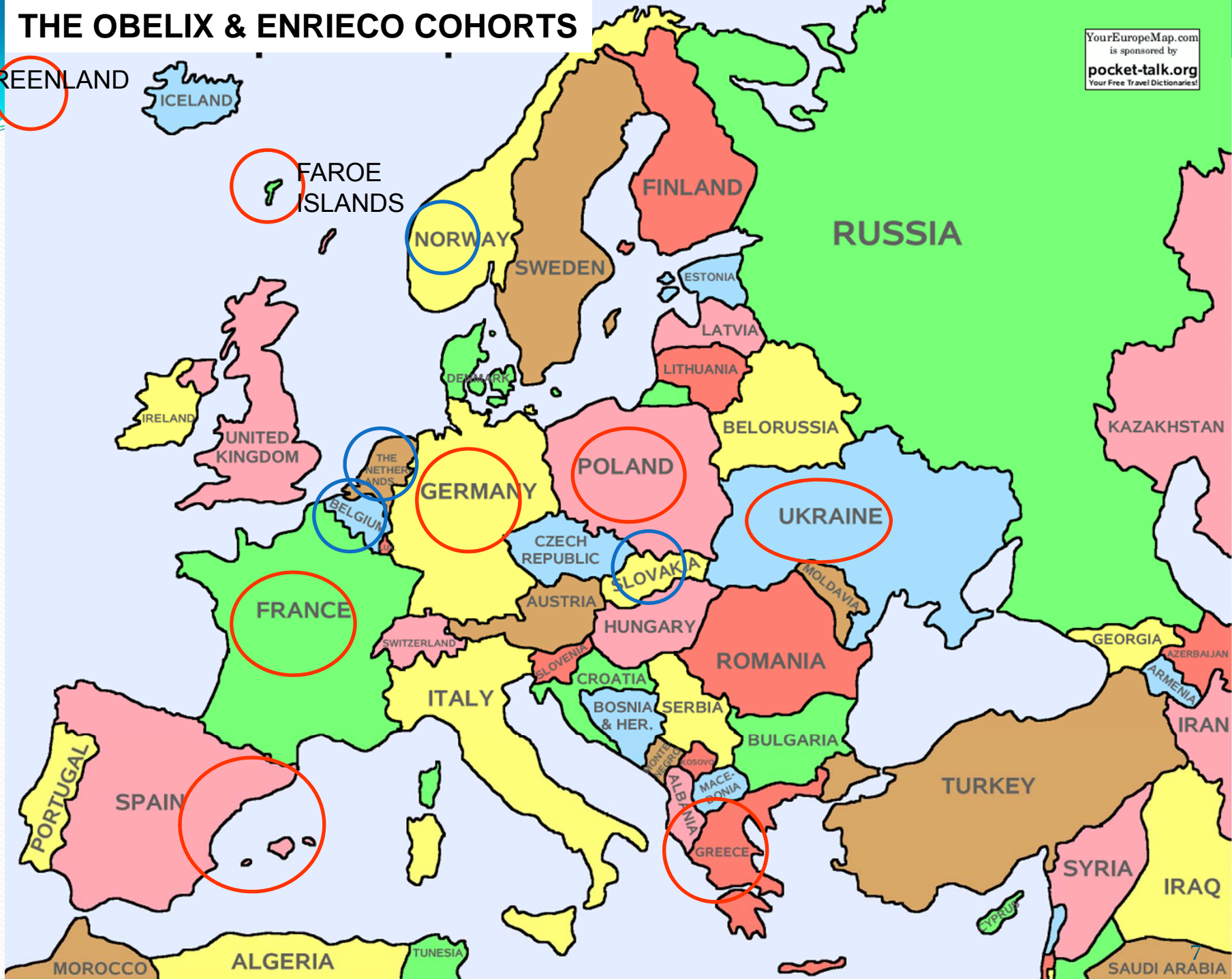
IRAQ

MOROCCO

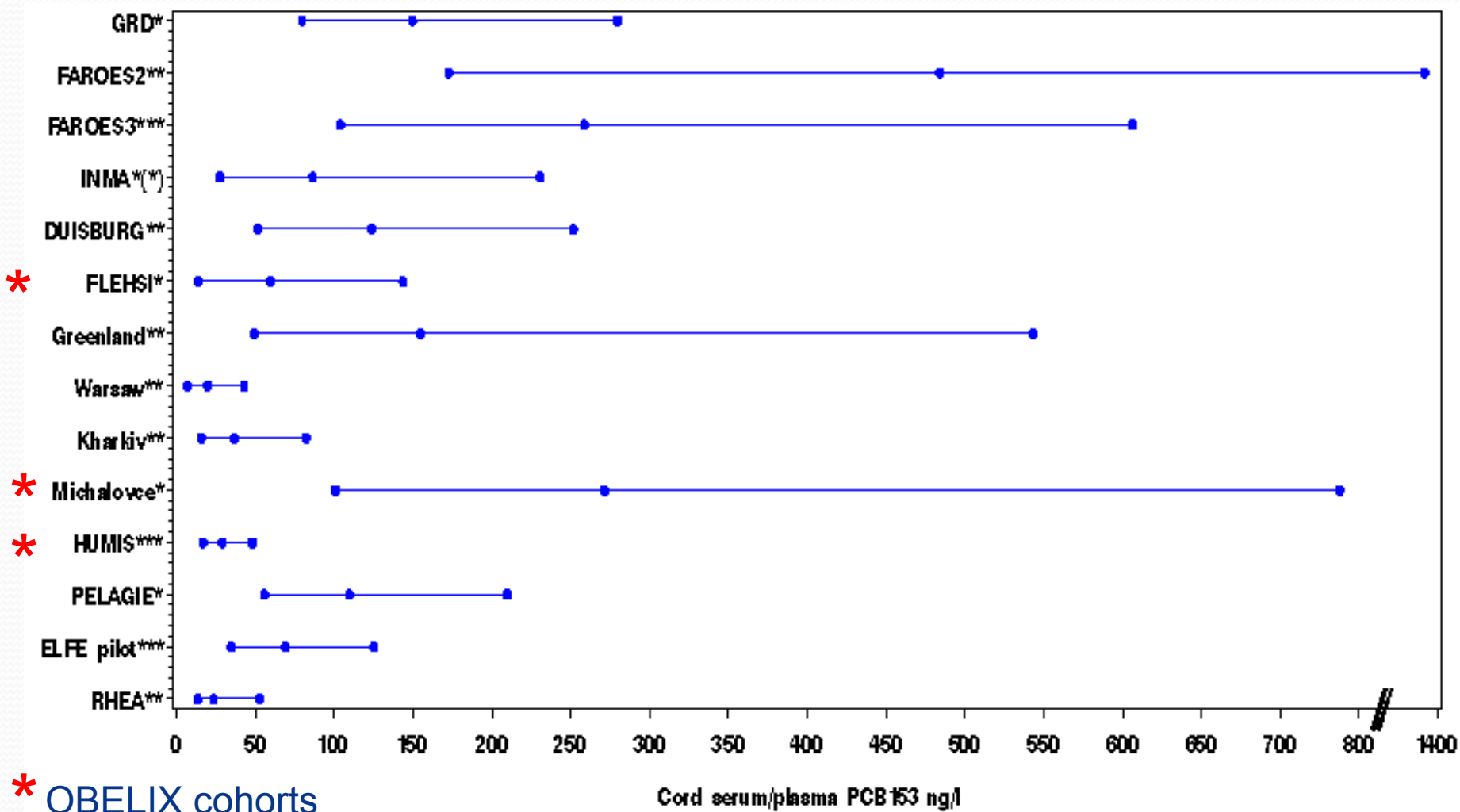
ALGERIA

TUNESIA

SAUDI ARABIA

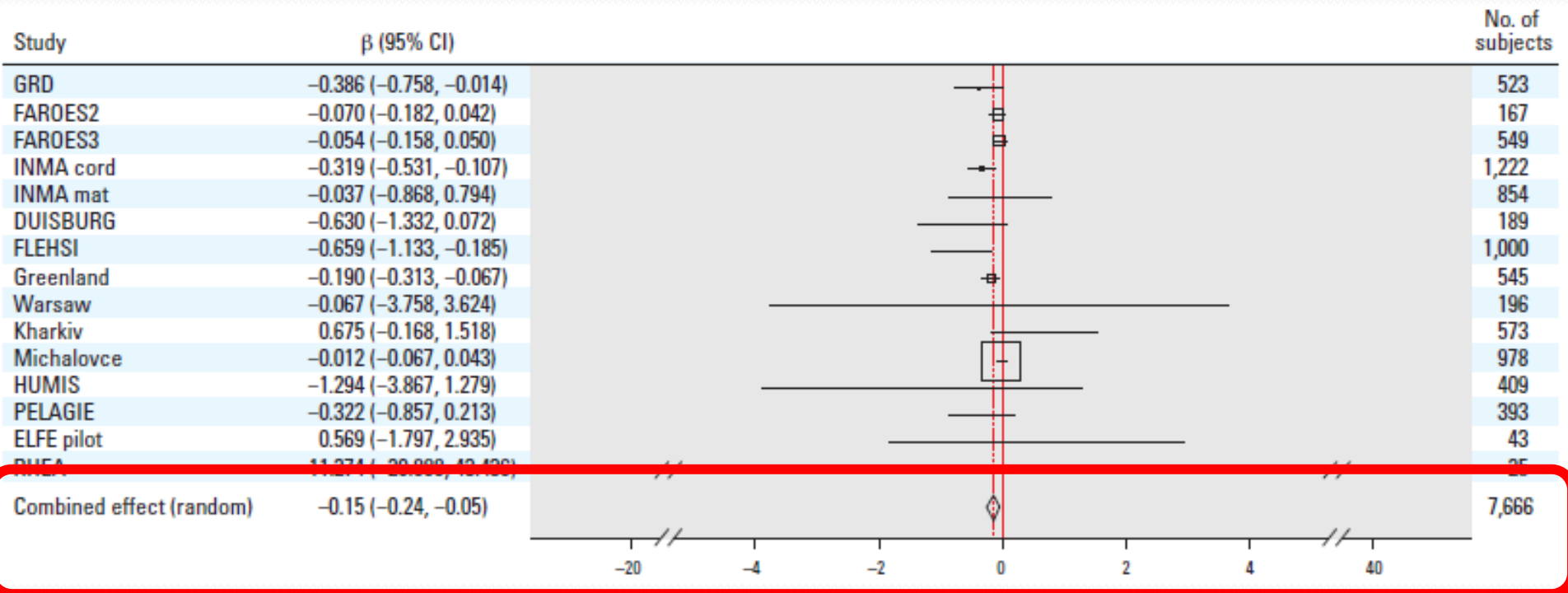


OBELIX-ENRIECO cohorts: prenatal PCB 153 exposure in European children



Govarts et al, 2012, *Environ. Health Perspectives*

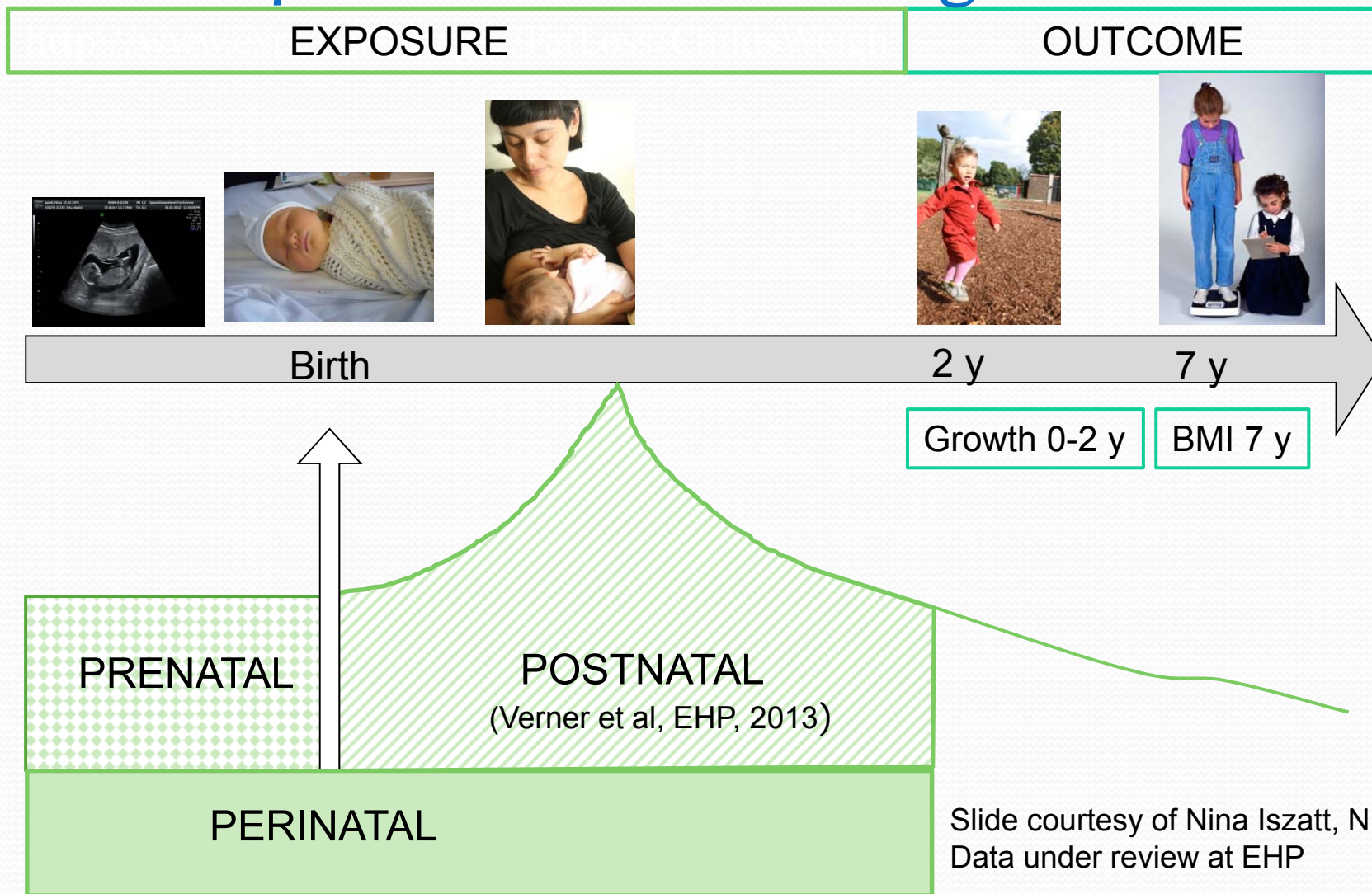
Meta-analysis prenatal PCB 153 and birth weight



Birth weight declined by 150g (95% CI 50-250 g) per 1 μ g/L increase in PCB 153 cord serum concentration

Govarts et al, 2012, *Environ. Health Perspectives*

Perinatal exposure to EDCs and growth/BMI

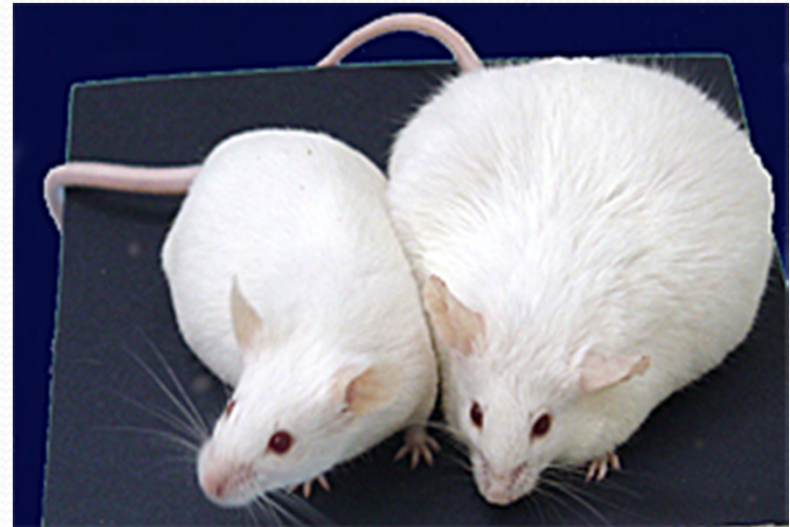


Slide courtesy of Nina Iszatt, NIPH, Data under review at EHP

@negative association with growth 0-2 y *positive association with growth 0-2y
 #positive association with BMI 7 y (preliminary)

Laboratory studies

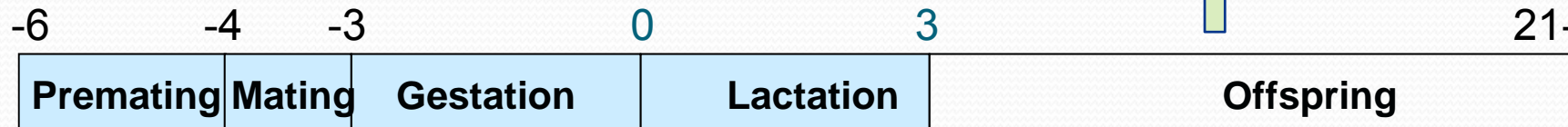
- *In vivo* mice
- *In vitro*
- Epigenetic mechanisms



Prenatal exposure to synthetic estrogen (DES) (Newbold et al., 2007, *Repro.Tox*)

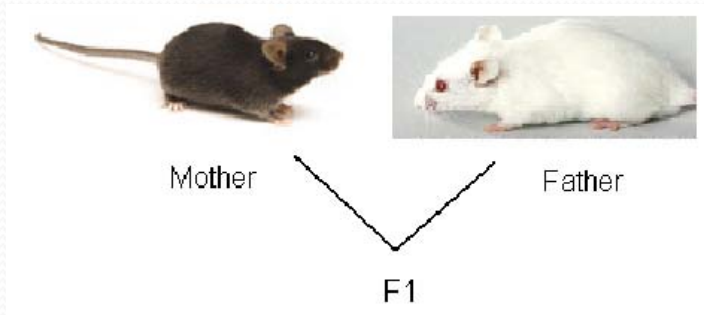
Experimental study design

weeks



(Maternal) dietary exposure

Mouse strain: C57BL/6J * FVB



- body weight
- fat pad weight
- histopathology
- food consumption
- spontaneous locomotor activity
- serum lipid and endocrine profile
- glucose tolerance test
- internal dose

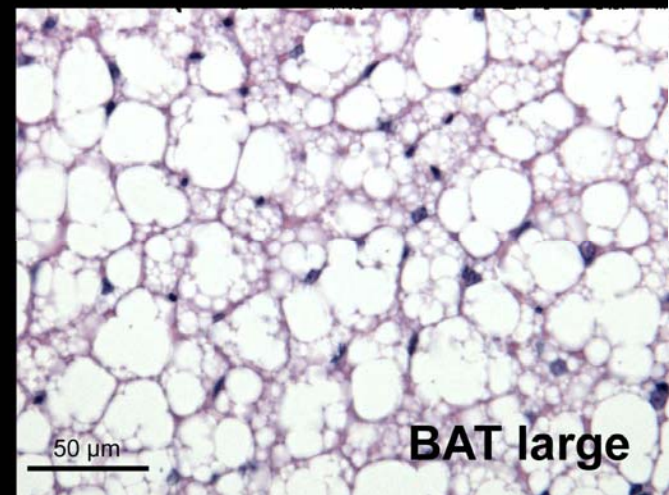
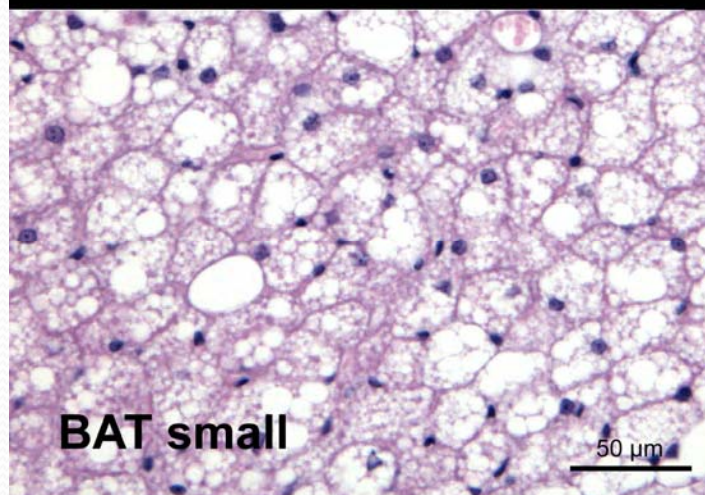
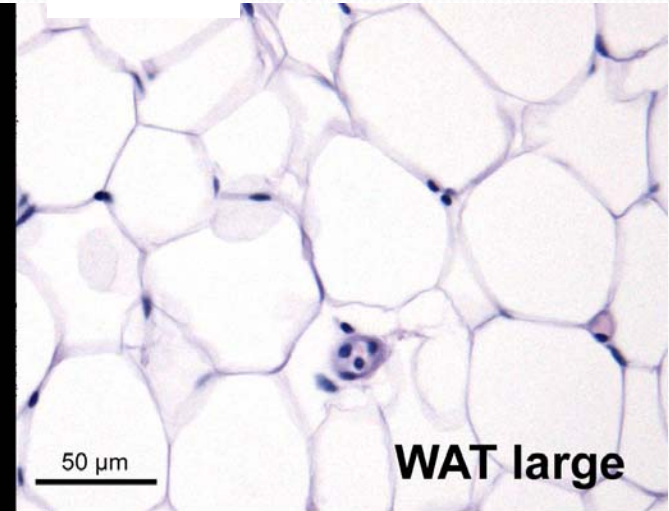
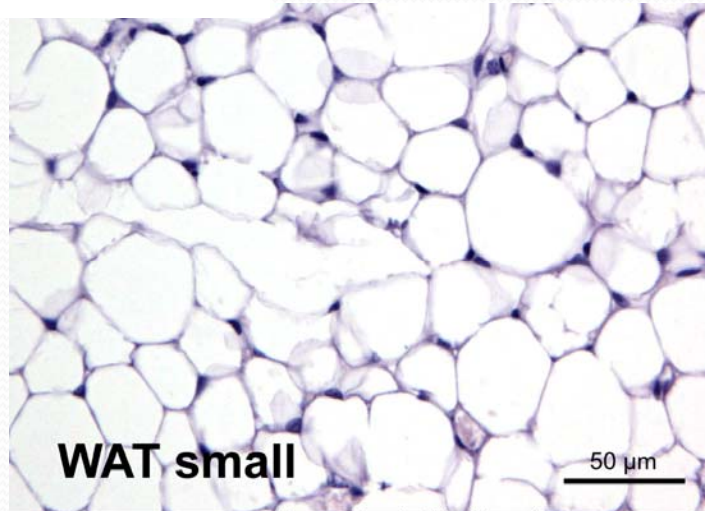
Early life exposure to BPA affects adipocyte size in white and brown adipose tissue

control

BPA

Males

3000 $\mu\text{g}/\text{kg}/\text{day}$



Risk assessment: are current chemical standards in food protective enough?

	Critical effect in animal studies		OBELIX BMDL	EFSA BMDL	OBELIX TDI	EFSA TDI	human exposure
			Benchmark dose lower limit		Tolerable daily intake level EFSA: European Food Safety Authority		Estimated by EFSA
BPA	↓ fat pad wt females	μ/k/d	292	3300	0.28	5	0.2-1.1
PFOA	↓ fat pad wt females	μ/k/d	46	300	0.23	1.5	0.002-0.006
TCDD	↑ fat pad wt females	p/k/d	453	25	>2	2	0.5-2
	↓ fat pad males		130	25	>2	2	0.5-2
PCB153	↑ glucagon females	μ/k/d	1042*	1200*	86#	44-214#	0.010-0.045
DEHP	↑ FFA males	μ/k/d	4390	5000	44	50	2.5-26

*critical body burden in μg/kg bw #margin of BB

OBELIX summary

Perinatal exposure to some EDCs (DDE, dioxin-like chemicals) early in life is associated with increased growth and weight in children.

In laboratory studies, EDC exposure early in life changes lipid and hormone metabolism long after exposure has stopped. Effects on body weight (both increases and decreases) were found. In vitro studies show that EDCs stimulate the differentiation of fat cells.

OBELIX discussion

- Effects in animals show clear gender specificity
- Divergent effects of pre- and postnatal exposure in children
- Mechanisms: generated new hypotheses
 - changes in DNA methylation related to EDC exposure
- Interactions with other risk factors?
- Long term consequences of changes in growth and BMI early in life?
- Exposure to mixtures?
- Are current TDIs protective enough? Need to include metabolic disruption as a relevant endpoint of endocrine disruption



European Commission

THANKS TO THE



BELIX

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