

15 years of human biomonitoring in Flanders Surveillance feeding policy and research



GEBOORTEGEWICHT EN CHEMISCHE STOFFEN TIJDENS DE ZWANGERSCHAP

Eva Govarts
Vlaamse Instelling voor Technologisch Onderzoek (VITO)

HUMAN BIOMONITORING (HBM)

“A method for assessing human exposure to chemicals by measuring the chemicals, their metabolites or reaction products in human tissues or specimens, such as blood or urine”



Air pollution
PAHs, benzene

Phthalates



Pesticides



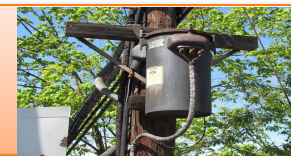
Cotinine



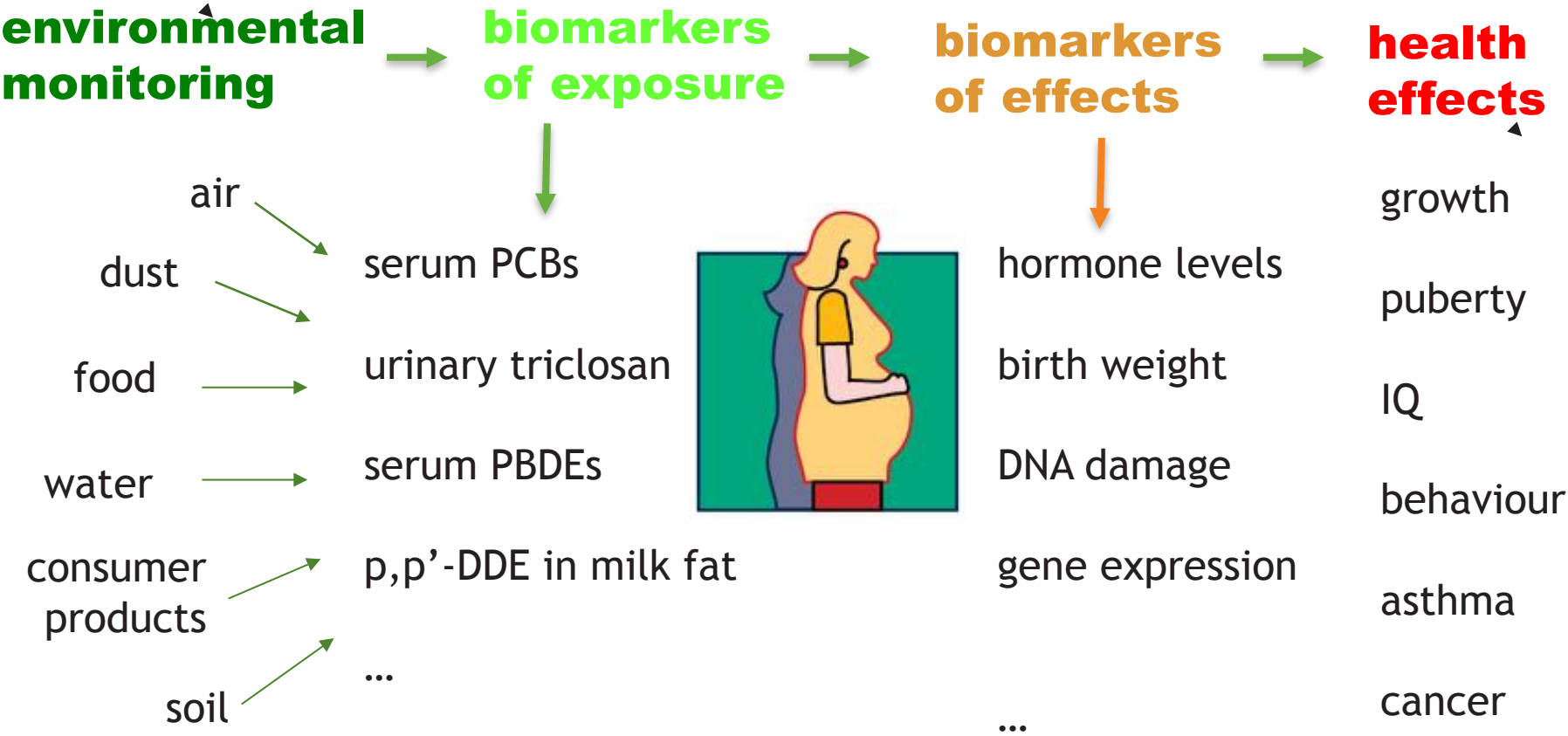
Heavy metals



PCBs



HBM: LINKING ENVIRONMENTAL EXPOSURE TO HEALTH EFFECTS



BACKGROUND: PRENATAL EXPOSURE AND BIRTH OUTCOMES

International Literature



Environmental Research

Volume 109, Issue 5, July 2009, Pages 559–566



Levels of hexachlorobenzene (HCB) in breast milk in relation to birth weight in a Norwegian cohort ^{*}

Merete Eggesbø^{a,b,*}, Hein Stigum^a, Matthew P. Longnecker^c, Anuschka Polder^c, Magne Aldrin^d, Olga Basso^e, Cathrine Thomsen^a, Janneche Utne Skaare^{a,f}, Georg Becher^a, Per Magnus^g

Science of the Total Environment 466–467 (2014) 770–776



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journal homepage: www.elsevier.com/locate/scitotenv



Prenatal exposure to hexachlorobenzene (HCB) and reproductive effects in a multicentre birth cohort in Spain ^{☆☆☆}

Mikel Basterrechea^{a,b,c,*}, Aitana Lertxundi^{b,c,d}, Carmen Iñiguez^{b,e,f}, Michelle Mendez^{b,g}, Mario Murcia^{b,e}, Imanol Mozo^{b,d}, Fernando Goñi^{b,c,h}, Joan Grimalt^{b,i}, Marieta Fernández^j, Mònica Guxens^{b,g}, On behalf of the INMA project

ehp ENVIRONMENTAL HEALTH PERSPECTIVES

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REVIEW

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Environ Health Perspect; DOI:10.1289/ehp.1307893

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth

Paula I. Johnson,¹ Patrice Sutton,¹ Dylan S. Atchley,¹ Erica Koustas,² Juleen Lam,² Saunak Sen,² Karen A. Robinson,^{4,5,6} Daniel A. Axelrad,⁷ and Tracey J. Woodruff⁸



Environmental estrogen (DES)
(Newbold et al., 2007, *Repro.Tox*)

BACKGROUND: PRENATAL EXPOSURE AND BIRTH OUTCOMES

International Literature: FLEHS studies



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RESEARCH ARTICLE

Expressi
Matern

Sylvie Remy

Nicolas van Lar

Published: Mar

Environ Health Perspect. 2009 Jan;
Published online 2008 Oct 8. doi: 10.1289/ehp.1103757
Research
Children's Health



Environ Health Perspect. 2012 Feb; 120(2): 162–170.

PMCID: PMC3279442

Published online 2011 Oct 13. doi: 10.1289/ehp.1103757

Review

**Intrauterine Expos
during the First 3**

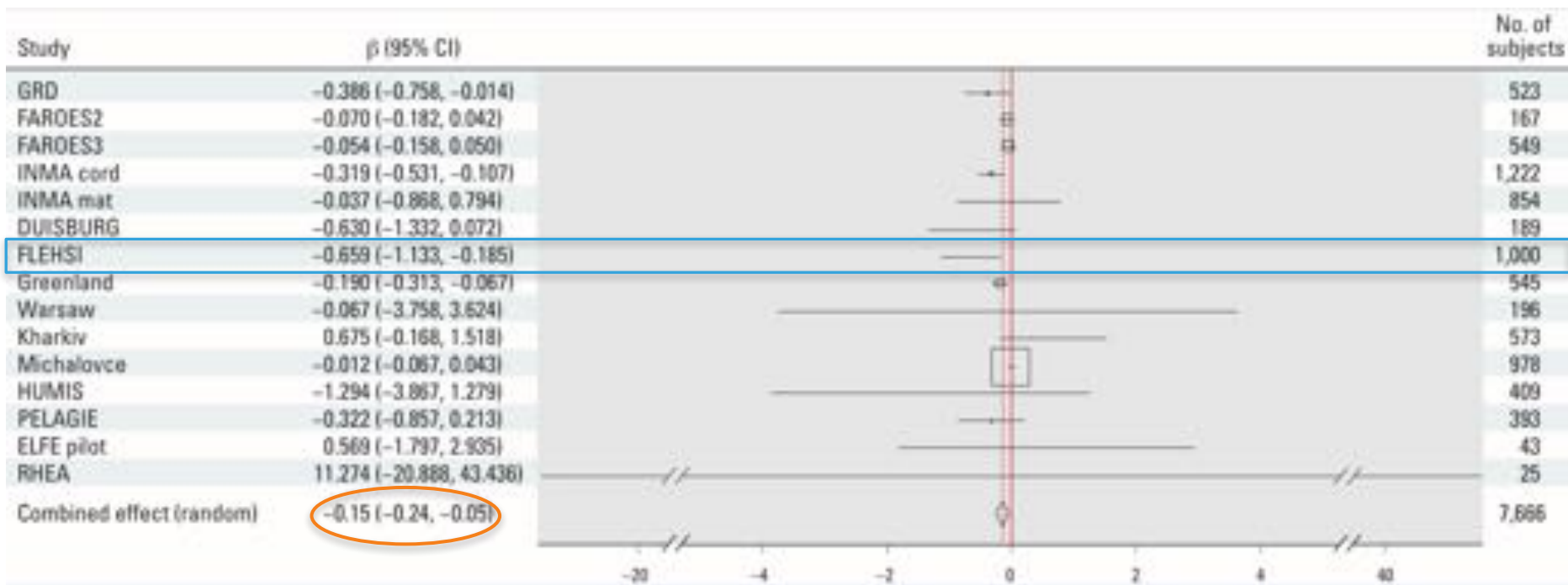
[Stijn L. Verhulst](#),¹ [Vera Nelen](#),
[Schoeters](#),^{3,4} and [Kristina Des](#)

Birth Weight and Prenatal Exposure to Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyldichloroethylene (DDE): A Meta-analysis within 12 European Birth Cohorts

[Eva Govarts](#),¹ [Mark Nieuwenhuijsen](#),^{2,3,4} [Greet Schoeters](#),^{1,5} [Ferran Ballester](#),^{2,6,7} [Karolien Bloemen](#),¹ [Michiel de Boer](#),⁸ [Cécile Chevrier](#),^{9,10} [Merete Eggesbo](#),¹¹ [Mònica Guxens](#),^{2,3,4} [Ursula Krämer](#),¹² [Juliette Legler](#),¹³ [David Martinez](#),^{2,3} [Lubica Palkovicova](#),¹⁴ [Evdiki Patelarou](#),¹⁵ [Ulrich Ranft](#),¹² [Arja Rautio](#),¹⁶ [Maria Skaalum Petersen](#),¹⁷ [Rémy Slama](#),^{18,19} [Hein Stigum](#),¹¹ [Gunnar Toft](#),²⁰ [Tomas Trnovec](#),¹⁴ [Stéphanie Vandentorren](#),²¹ [Pål Weihe](#),¹⁷ [Nynke Weisglas Kuperus](#),²² [Michael Wilhelm](#),²³ [Jürgen Wittsiepe](#),²³ [Jens Peter Bonda](#),^{20,24} and and OBELIX/ENRIECO²⁵

META-ANALYSIS EHP SINGLE POLLUTANT MODELS

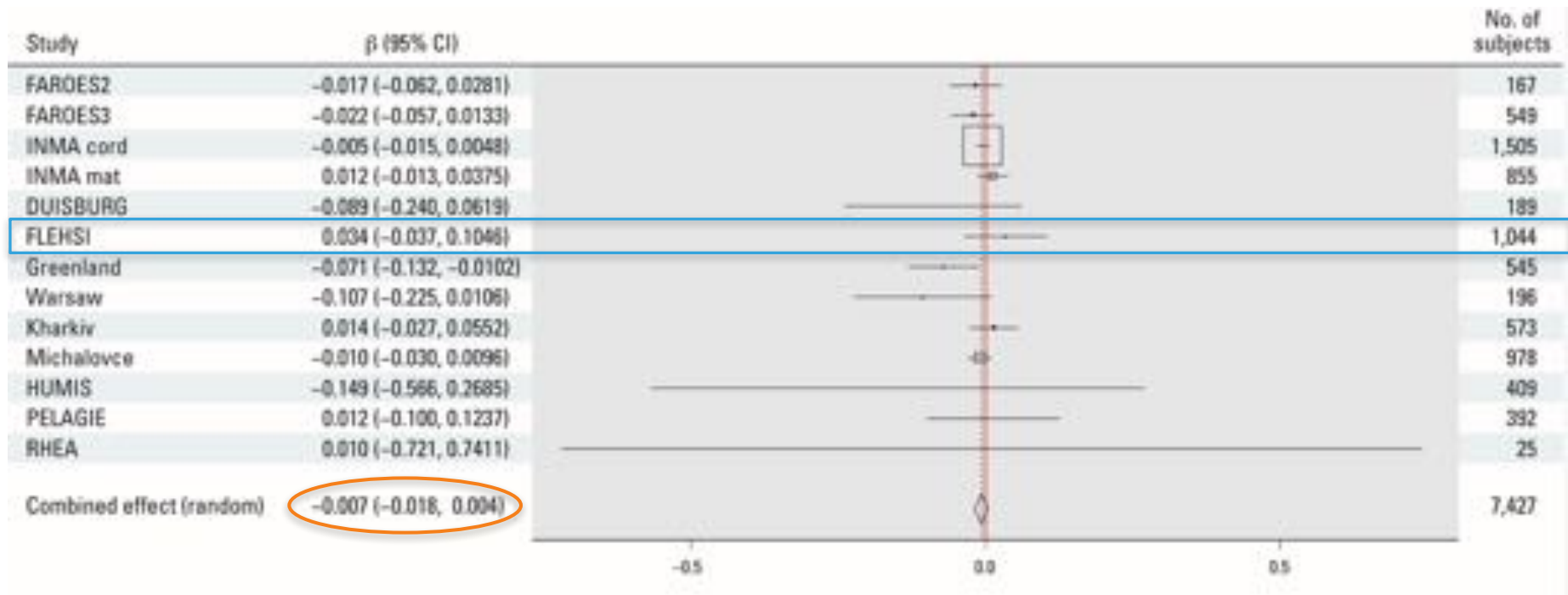
Association PCB 153 (ng/L) with birth weight



Govarts et al. 2012

META-ANALYSIS EHP SINGLE POLLUTANT MODELS

Association p,p' -DDE (ng/L) with birth weight



Govarts et al. 2012

MULTIPOLLUTANT EXPOSURE

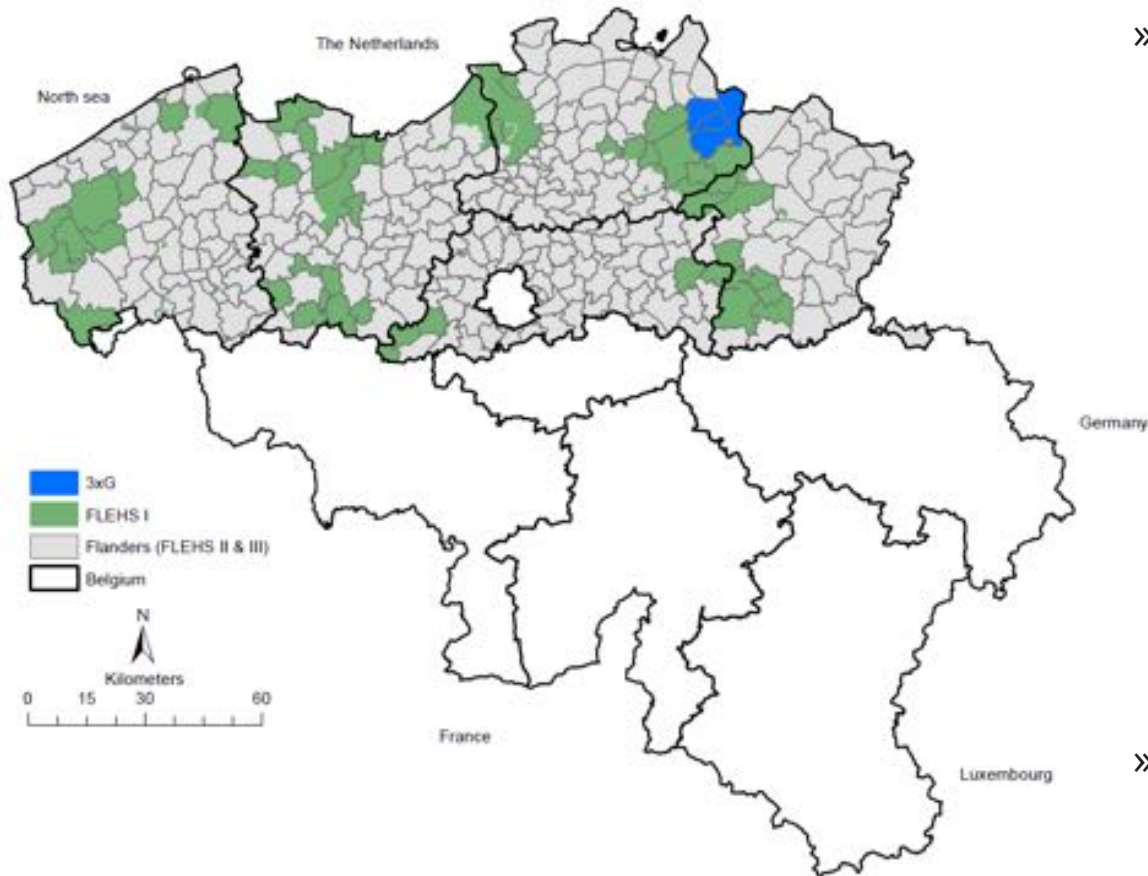
Objective: investigate association between prenatal exposure to a mixture of environmental chemicals and birth weight

- » Until now in literature: mostly single pollutant models
- » Real life: Humans are exposed to thousands pollutants during their life time



STUDY POPULATION

Four Flemish birth cohorts



» Flemish Environment and Health Study (FLEHS)

» I

» 2002-2004

» N = 1196

» II

» 2008-2009

» N = 255

» III

» 2013-2014

» N = 281

» 3xG

» Dessel, Mol & Retie

» 2011-2015

» N = 301



STUDY POPULATION

Pooled database of four Flemish birth cohorts

- » Birth outcome: birth weight
- » Common set of exposure biomarkers (cord blood):
 - » PCB138, PCB153, PCB180
 - » p,p'-DDE, HCB
 - » lead, cadmium
- » Covariates/confounders: cohort, gestational age, maternal age, maternal pre-pregnancy BMI, parity, smoking during pregnancy and sex of the newborn
- » N = 1579



STUDY POPULATION

| Characteristics | % |
|--------------------------|------|
| Age mother (years) | |
| <27 years | 24.7 |
| [27-30[years | 26.9 |
| [30-[33 years | 27.6 |
| ≥33 years | 20.9 |
| Pre-pregnancy BMI | |
| <18.5 years | 5.2 |
| [18.5-25[years | 68.1 |
| [25-[30 years | 18.8 |
| ≥30 years | 8.0 |
| Parity | |
| 0 | 53.7 |
| 1 | 30.8 |
| ≥2 | 15.5 |
| Smoking during pregnancy | |
| no | 85.8 |
| yes | 14.2 |
| Sex of the newborn | |
| boy | 51.6 |
| girl | 48.5 |

Study population characteristics (N=1579)

| Characteristics | Min | P25 | P50 | P75 | Max |
|-------------------------|------|------|------|------|------|
| Birth weight (g) | 1245 | 3140 | 3420 | 3700 | 5575 |
| Gestational age (weeks) | 31 | 39 | 39 | 40 | 42 |

| Exposures | %>LOQ | Median |
|-----------------------|-------|--------|
| PCB138 (ng/g lipid) | 79% | 15.8 |
| PCB153 (ng/g lipid) | 88% | 26.5 |
| PCB180 (ng/g lipid) | 87% | 18.0 |
| p,p'-DDE (ng/g lipid) | 99% | 91.5 |
| HCB (ng/g lipid) | 73% | 16.9 |
| cadmium (µg/L) | 73% | 0.07 |
| lead (µg/L) | 98% | 9.7 |

Different statistical tools used to explore multipollutant exposure + comparison with results from single pollutant exposure

- » Single pollutant
 - » Linear regression

- » Multipollutant
 - » Elastic net (ENET)
 - » Penalized regression model

 - » Graphical Unit Evolutionary Stochastic Search (GUESS)
 - » Bayesian variable selection approach
 - » Seeks for models that optimally predict the health outcome

 - » Deletion-Substitution-Addition algorithm (DSA)
 - » Iterative linear regression model search algorithm
 - » Selects model by minimizing RMSE



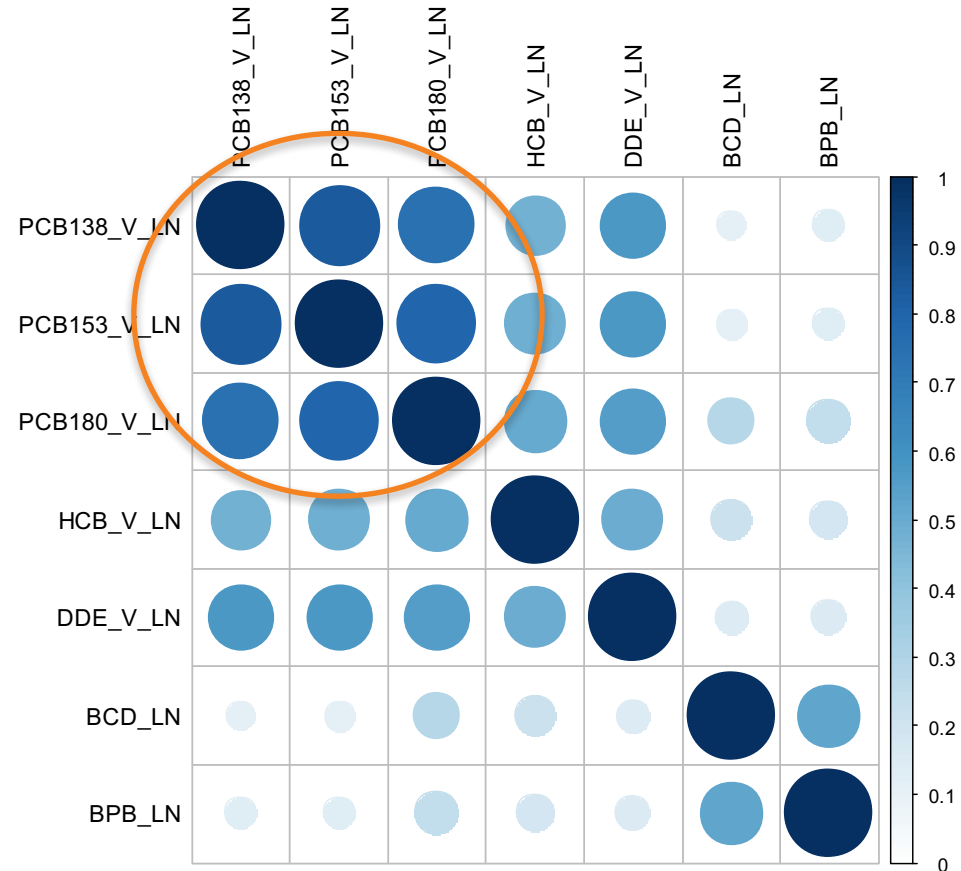
RESULTS

Single pollutant regression models

| Exposures | Estimate* (95% CI) | p-value |
|-----------------------|-----------------------|---------|
| PCB138 (ng/g lipid) | -45 (-74; -16) | 0.002 |
| PCB153 (ng/g lipid) | -55 (-83; -27) | 0.0001 |
| PCB180 (ng/g lipid) | -77 (-114; -40) | <0.0001 |
| p,p'-DDE (ng/g lipid) | 12 (-15; 33) | 0.44 |
| HCB (ng/g lipid) | -10 (-36; 16) | 0.46 |
| cadmium (µg/L) | -6 (-22; 10) | 0.45 |
| lead (µg/L) | 9 (-17; 35) | 0.52 |

*Increase (+) or decrease (-) in birth weight (g) for 1 unit \uparrow in ln-transformed exposure. Model is adjusted for cohort, gestational age, maternal age, maternal pre-pregnancy BMI, parity, smoking during pregnancy and sex of the newborn.

Pearson correlation matrix



RESULTS/DISCUSSION

Multipollutant approaches: preliminary results

- » ENET was not sensitive enough to pick up the signal. No exposure variables were retained.
- » GUESS and DSA algorithm identified **PCB153, PCB180 and p,p'-DDE** as contributing to the observed association of multipollutant exposure with birth weight

- » PCB138 not retained

 PCB 153 and PCB 180 most critical PCB metabolites in this mixture

- » p,p'-DDE retained, works in the opposite direction

 antagonistic effect?

CONCLUSION - POLICY RELEVANCE

- » Assessing health risks of combinations of exposure biomarkers reflects better real world situations



science gives information to policy makers about real situation

- » Findings will allow more effective risk assessment



critical chemical in a mixture ??



priority for policy actions

ACKNOWLEDGEMENTS

» Partners



» Mothers and maternity hospitals, ...



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