Kovine, arzen in selen pri izbrani slovenski populaciji: rezultati EU projektov PHIME in DEMOCOPHES

Milena Horvat, Janja Snoj Tratnik, Darja Mazej, Majda Pavlin, A. Miklavčič, Alfred B. Kobal

Institut Jožef Stefan, Ljubljana

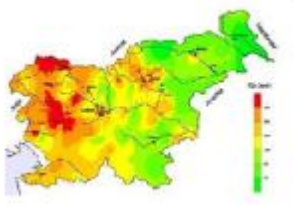
M.Kersnik, A. Briški, J. Osredkar

UKCL, Ljubljana

Vsebina

- Uvod
- Opis študij PHIME in DEMOCOPHES/COPHES
- Povzetek rezultatov
- Primerjava s slovenskim biomonitoringom

Okolje, v katerem živimo



Porazdelitev živega srebra na ozemlju Slovenije.

Izpostavljeni smo različnim vplivom, tudi kemikalijam, ki prihajajo iz:

- zraka,
- hrane in pitne vode,
- tal in vode,
- izdelkov za osebno nego,
- obleke in pohištva,
- detergentov in čistil,
- kajenja.

V telo vstopajo preko dihal, kože in z zaužitjem ter se prerazporedijo po tkivih.

Vpliv na zdravje

Kemikalije so v okolju lahko obstojne, hlapljive in mobilne. Če se razpršijo po velikih geografskih območjih, so prebivalci izpostavljeni **nizkim odmerkom** onesnaževanja.

- V telesu ustvarijo **ravnovesje** med telesnimi tekočinami in tkivi.
- Kopičijo se v tkivih in **povzročajo škodljive spremembe** (tkiva z visoko vsebnostjo maščob, kosti, lasje, drugi organi).
- Učinki se lahko pokažejo šele **dolgoročno**.

Občutljive skupine

- Nosečnice in ženske v rodni dobi,
- novorojenčki, otroci in mladostniki,
- kronični bolniki,
- starejši nad 70 let,
- socialno šibkejši.

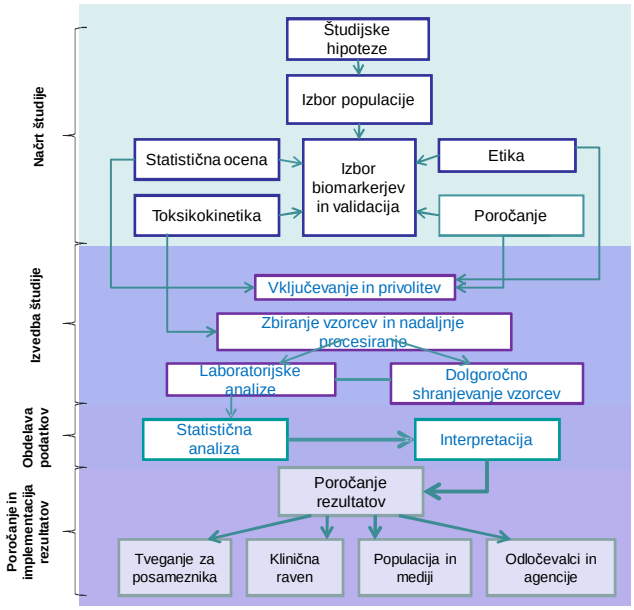
Biomonitoring

= merjenje in spremljanje sprememb v organizmih, tkivih, tekočinah, celicah ali biokemijskih procesih, ki nastanejo zaradi izpostavljenosti organizma kemikalijam.

Biomonitoring v ljudeh

= merjenje koncentracije kemikalij v krvi, urinu, slini, semenski tekočini, izdihanem zraku, materinem mleku, laseh, nohtih ali tkivih.

Stopnje Izvajanja HBM



HUMANI BIOMONITORING V EVROPI

harmonizirani pristop

Institut "Jožef Stefan", Ljubljana, Slovenija

HBM v Eropi

Raziskava DEMOCOPHES v Sloveniji

Pilotna raziskava humanega biomonitoringa v Evropi

Milena Horvat, Darja Mazej, Janja Snoj Tratnik, Ester Heath, Tina Kosjek, Selma Sehić, A.B. Kobal
Odsek za znanosti o okolju, Institut Jožef Stefan, Ljubljana

8

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

HBM v Evropi

Action 3 of the EHAP - 2004

- *We will develop a coherent approach to human biomonitoring in Europe*
  - ESBIO FP6 2006
  - Council Conclusions 2007
  - Paris Conference 2008
  - COPHES/DEMOCOPHES 2009
  - Berlin & Brussels Conferences 2010
  - Council conclusions 2010
  - Budapest symposium 2011

Commitment to act – 2010

- *We will contribute to develop a consistent and rational approach to human biomonitoring as a complementary tool to assist evidence-based public health and environmental measures, including awareness-raising for preventive actions*

9

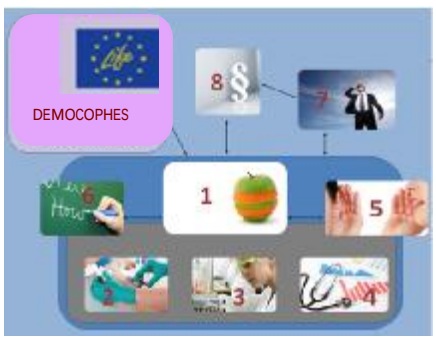
HUMANI BIOMONITORING V EVROPI

Podobnosti – razlike – skupni interesi

FP7 financira Evropska komisija

- Razvoj okvira HBM
- Razvoj protokolov
- Analiza rezultatov na nivoju Evrope
- Priporočila & zaključki

Dec 2009-Nov 2012



Life+ financiranje (50 % EU + 50 % država članica)

- otroci in njihove mame
- okrog 3600 sodelujočih
- Cd, ftalati, kotinin v urinu
- živo srebro v laseh
- (bisfenol A v urinu)

Sept 2010-Okt 2012

Koordinacija in harmonizacija humanega biomonitoringa v Evropi

HUMANI BIOMONITORING V EVROPI

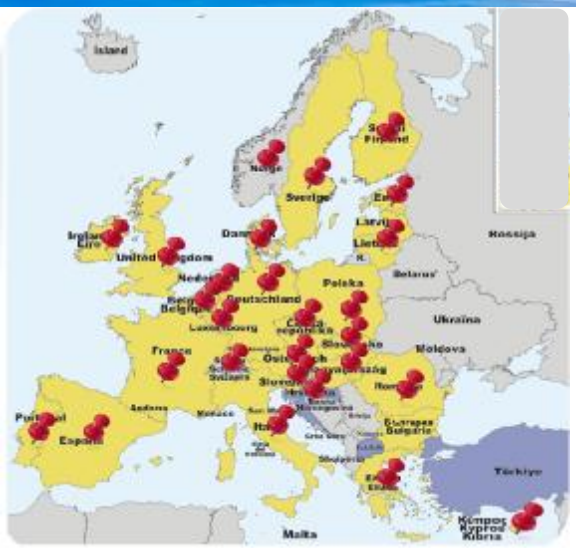
COPHES partnerji

24 EU članic + Norveška, Hrvaška, Švica

DEMOCOPHES partnerji:

17 držav: BE, CY, DE, DK, PL, RO, SI, ES, HU, SE, UK, PT, CZ, SK, LU, IE, CH

NO, FR, AT, HR vključene kot *ad hoc* partnerji

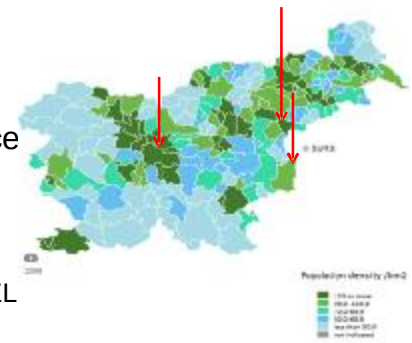


11

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

1) Izbira populacije

Cilj : 60 + 60 parov mati/otrok
dodatno za Slovenijo – oče



–mestno okolje LJUBLJANA
(gostota prebivalcev cca 1000/km2)

–podeželsko okolje ŠMARJE PRI JEL
(gostota prebivalcev <100/km2)

Način nabora – preko šol
→dogovor s petimi šolami

OŠ Vodmat, OŠ Tone Čufar, OŠ Poljane
OŠ Šmarje pri Jelšah, OŠ Bizeljsko

12

2) Izbira analitov

- **OBVEZNI** glede na EU protokol
  - Hg v laseh
  - Cd, ftalati, kotinin in kreatinin v urini
- **DODATNI** za Slovenijo
  - BPA, parabeni in triklosan v urinu
  - Hg v urinu in krvi
  - Pb, Cd in Se v krvi

13

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

Institut "Jožef Stefan", Ljubljana, Slovenij

Raziskava DEMOCOPHES v Sloveniji

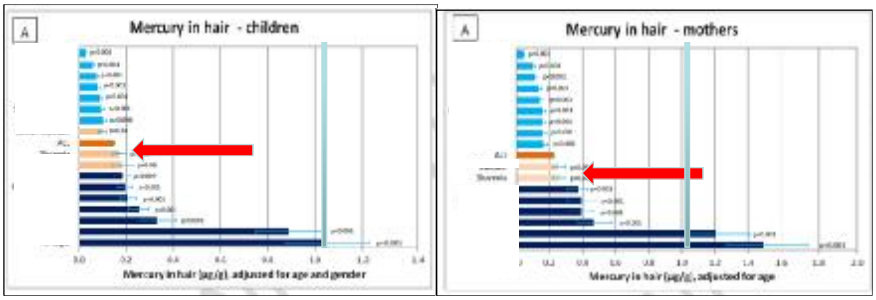
REZULTATI

Hg, Pb, Cd, As, Se

14

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

Rezultati Hg - Evropa

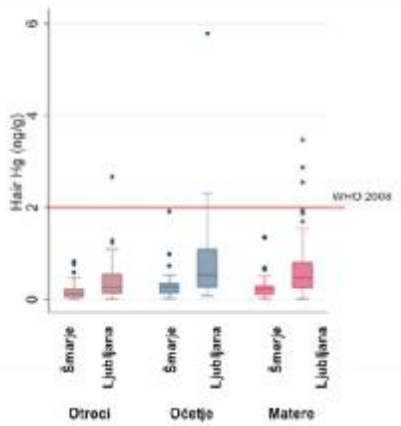


Živo srebro v laseh (µg/g)				
		N	GM	P90
Slovenija	Otroci	120	0,169	0,678
	Matere	120	0,263	0,848
EU	Otroci	1836	0,145	0,800
	Matere	1839	0,225	1,200

15

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

REZULTATI Hg - Slovenija



16

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

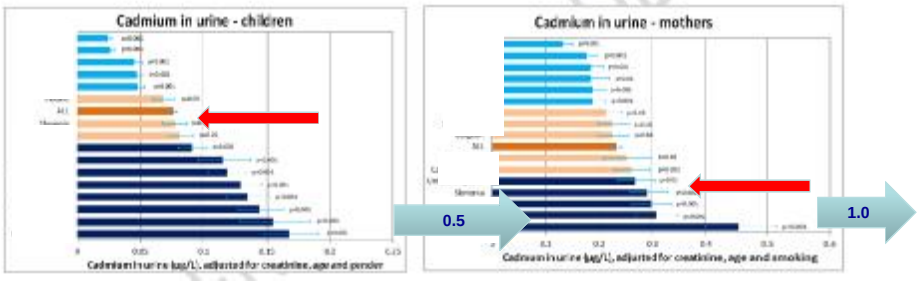
Vplivni faktorji: Hg v laseh

EU (1800 parov mati/otrok)	Slovenija (155 parov mati/otrok)
- starost	- starost mater
- uživanje rib in morske hrane	- uživanje rib
- nivo izobrazbe	- nivo izobrazbe
	- mestno okolje
	- očetje
	- razbitje termometra
	- ukvarjanje s spajkanjem doma

17

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

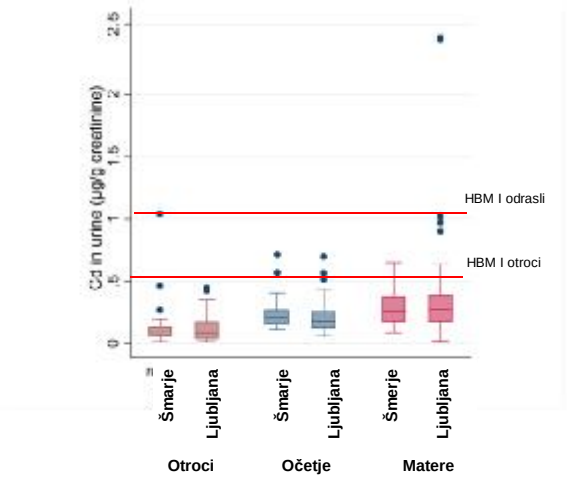
Rezultati Cd - Evropa



Cd v urinu (µg/g kreatinina)				
		N	GM	P90
Slovenija	Otroci	120	0,067	0,156
	Matere	120	0,231	0,434
EU	Otroci	1698	0,070	0,220
	Matere	1685	0,196	0,620

18

REZULTATI Cd - Slovenija



19

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

Vplivni faktorji: Cd v urinu

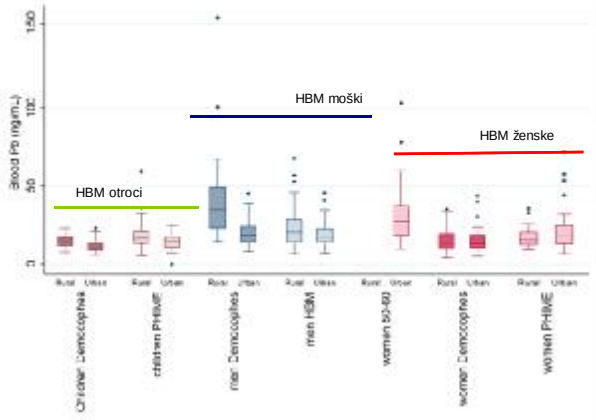
EU (1800 parov mati/otrok)	Slovenija (155 parov mati/otrok)
- kreatinin	- kreatinin
- kajenje	- kajenje
- starost	- matere
- nivo izobrazbe	- mestno okolje samo pri otrocih
- javni vodovod v primerjavi z zasebnimi viri in ustekleničeno vodo	- uživanje divjačine pri materah
	- otroci, kjer se doma ukvarjajo s spajkanjem

20

HUMANI BIOMONITORING V EVROPI

harmonizirani pristop

REZULTATI svinec - Slovenija



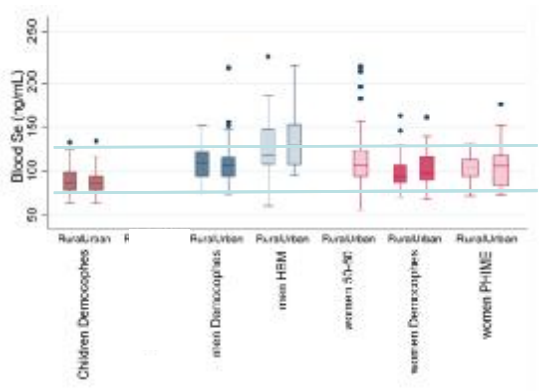
- očetje najvišje vrednosti med vsemi opazovanimi skupinami
- med mestnim in podeželskim okoljem ni signifikantne razlike

21

HUMANI BIOMONITORING V EVROPI

harmonizirani pristop

REZULTATI selen - Slovenija



- očetje
- mestno okolje

22

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

ZAKLJUČKI (1/2)

- Prva raziskava izvedena v 17 Evropskih državah
- Primerjava EU podatkov z NHANES, Health Canada in nacionalnimi HBM
- Koncentracije znotraj varnih meja, razen pri nekaterih posameznikih;
- Močna korelacija koncetracij med otrokom in materjo – *življenski stil in okolje*;
- Mlajši otroci (6-8 let) imajo višje koncetracije kot starejši (9-11 let)
- Velike variacije koncetracij v biomarkerjih znotraj posamezne države in med državami
- Možna identifikacija virov izpostavljenosti – ukrepi za zmanjšanje izpostavljenosti

HUMANI BIOMONITORING V EVROPI
harmonizirani pristop

ZAKLJUČKI (2/2)

- primerljivi rezultati z Evropo
- izpostavljenost slovenske populacije v relativno varnih mejah
- izpostavljenost preiskovanim kemikalijam slovenske populacije je primerljiva s povprečjem v Evropi
- razpoznavnost vira izpostavljensoti in možnost svetovanja za zmanjšanje izpostavljenosti
- možna širitev preiskave na druge kemikalije (*na primer pesticidi, herbicidi in ostale agrokemikalije in njihovi razgradni produkti*)

HUMANI BIOMONITORING V EVROPI

harmonizirani pristop

ZAHVALA

- Vsem sodelujočim družinam
- Šolam (OŠ Vodmat LJ, OŠ Tone Čufar LJ, OŠ Poljane LJ, OŠ Šmarje pri Jelšah, OŠ Bizeljsko)
- Sodelavcem na projektu (*Majda Pavlin, Damjana Nikovski, Ana Miklavčič, Vesna Fajon, Urška Kristan, Petra Planinšek, Barbara Korc, Darja Gramec, Julija Vit Urbanija, Lidija Poteko,....*)
- Za finančno podporo Evropski komisiji preko LIFE+ projekta Democophes in projekta 7. okvirnega programa COPHES ter ARRS v okviru raziskovalnega programa P1-0143

25

PHIME

Public health impact of long-term, low-level mixed element exposure in susceptible population strata

Slo

WP

WP **e**
trer

WP

WP I:3

Longitudinal cohort study of prenatal exposure to mercury in the Mediterranean region

Co-workers

Fabio Barbone
Zdravko Spiric
Sheena Nakou
Giulia Modugno
Veronica Tognin
Adriano Cattaneo
Ana Miklavcic
Ana Milardovic
Anica Casetta
Caterina Flegar
Chiara Menegolli
Claudia Carletti
Claudia Carosi
D'Anna Little
Daniela Drigo
Darja Mazej
David Neubauer
Elena Flaugnacco
Elena Kos
Eleni Antonopoulou
Martina Cogaj
Maura Bin
Milena Horvat
Mladen Krsnik
Paola Fabbro
Paolo Collarile
Petra Cuderman
Oleg Petrovic
Igor Prpic
Sara Grafitti
Tamara Bomestar
Valentina Cogaj
Valentina Liut
Federica Bonifacio
Federica Pisa
Giorgio Tamburlini
Giuseppina D'Ottavio
Inge Vlasic Cicvaric
Jana Kodric
Janja Tratnik
Josko Osredkar
Karin Kuljnic Vlasic
Katia Sofianou
Lamia Channoufi
Laura Deroma
Liza Vecchi
Luca Ronfani
Marcella Montico
Marco Carrozzi
Maria Parpinel
Marika Mariuz
Francesca Valent
Francesca Castiglione
More .....

Objective

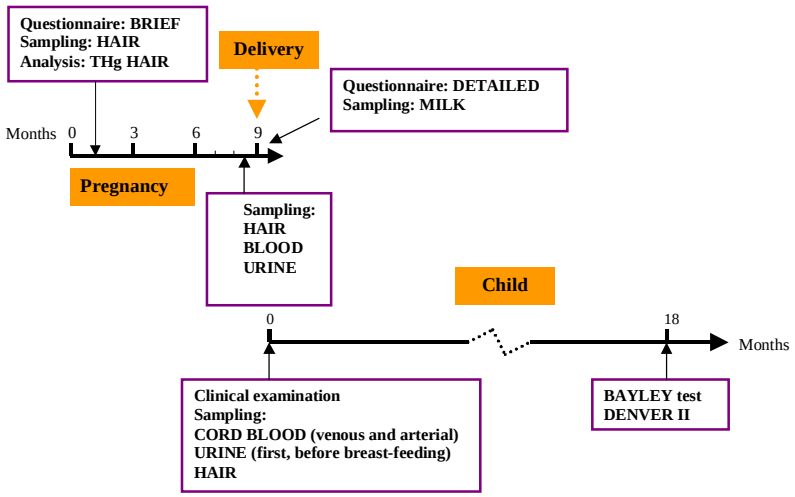
To assess the impact of low levels of methylmercury exposure through fish consumption during pregnancy on the neurodevelopment of children at 18 months

PHIME – MEDITERRANEAN STUDY AREAS

Northern Adriatic Cohort I and II

Eastern Aegean Cohort

WP1: 3 General study design



Number of subjects/samples

Country (target no. of subjects)	Croatia (200)	Greece (400)	Italy (750)	Slovenia (350)	Total (1700)
Hair (before, at)	234	457	859	582	2168
Hair (after)	196	-	762	353	1311
Cord blood	207	391	626	443	1667
Maternal blood	225	-	872	-	1097
Milk	125	52	603	290	1070
Cord tissue	215	-	46	333	261
Meconium	205	225	-	-	430
Urine (newborn)	184	66	-	-	250
Urine (before)	225	326	676	24	1227
Hair (at 18 months)	-	-	244	-	244
TOTAL					**9725**

Measurements

Sample	Analyte
Hair	Total Hg, MeHg (samples above 1 µg/g)
Maternal blood Whole blood Plasma Serum	 THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn polymorphism (Italy, Croatia) Se, Zn, PUFA Fe, Mg, Ca
Cord blood Whole blood Plasma Serum	 THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn, polymorphism (Slovenia, Greece) Se, Zn Fe, Mg, Ca
Milk	THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn
Cord tissue	THg, MeHg((samples above 1 µg/g of hair)
Meconium	THg, MeHg((samples above 1 µg/g of hair)
Urine	THg, Cd, creatinine

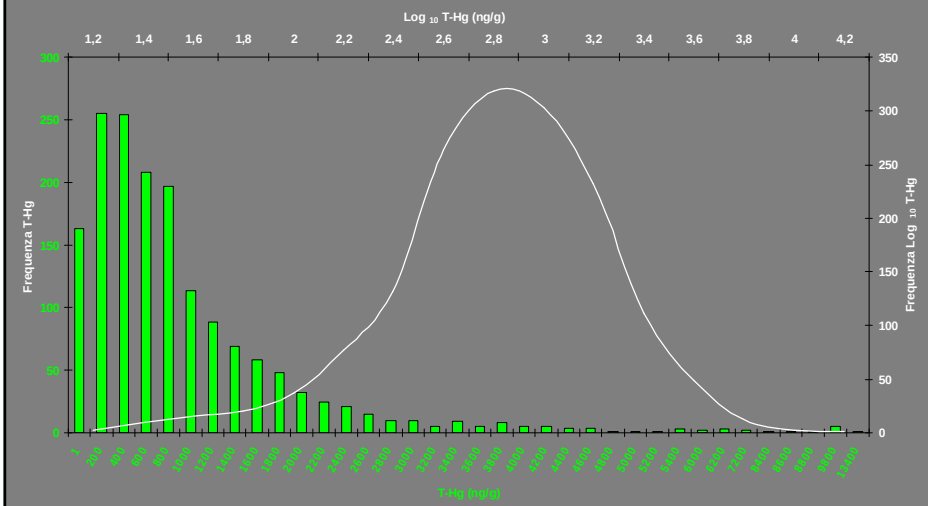
Measurements

Sample	Analyte
Hair	Total Hg, MeHg (samples above 1 µg/g)
Maternal blood Whole blood Plasma Serum	 THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn polymorphism (Italy, Croatia) Se, Zn, PUFA Fe, Mg, Ca
Cord blood Whole blood Plasma Serum	 THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn, polymorphism (Slovenia, Greece) Se, Zn Fe, Mg, Ca
Milk	THg, MeHg((samples above 1 µg/g of hair), Cd, Pb, As, Se, Mn, Cu, Zn
Cord tissue	THg, MeHg((samples above 1 µg/g of hair)
Meconium	THg, MeHg((samples above 1 µg/g of hair)
Urine	THg, Cd, creatinine

Outcome testing instruments

- Bayley Scales of Infant Development III
  - v Global test of cognitive development measures in 5 domains:
    - →Cognitive
    - →Language (expressive and receptive)
    - →Motor (gross and fine)
    - →Adaptive Behaviour
    - →Social skills
- Modified Checklist for Autism in Toddlers(M-CHAT)
- Supplementary Questionnaire-update on family information (occupational, living conditions) and medical history of child
- 7-day diet diary of child (Italy only)

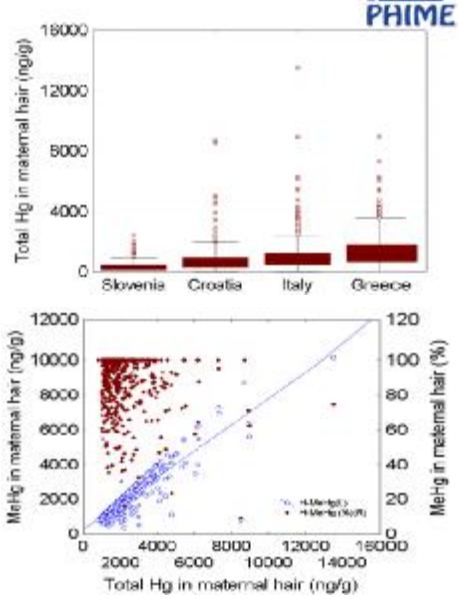
Frequency distribution of THg (ng/g) in maternal hair (n=1700)



THg and MeHg in maternal hair

H-THg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	574	234	891	454
Mean	377	851	1032	1440
SD	332	1088	954	1187
Min	15	16	17	55
Median	297	604	770	1122
Max	2439	8710	13520	8973
P10	73	137	316	369
P90	780	1806	2016	2764

H-MeHg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	28	49	323	247
Mean	1318	1997	1641	1858
SD	387	1337	952	1040
Min	576	928	356	485
Median	1268	1651	1370	1565
Max	2439	8710	10132	7300
P10	966	1038	1008	990
P90	1647	3323	2570	3190

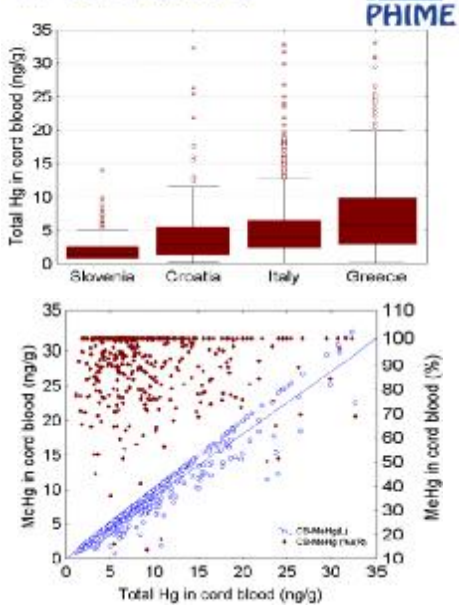


P10 – 10th percentile, P90 – 90th percentile

THg and MeHg in cord blood

CB-THg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	443	209	609	391
Mean	1.98	4.29	5.37	7.33
SD	1.73	4.44	4.69	5.83
Min	0.16	0.33	0.12	0.21
Median	1.52	2.94	3.93	5.81
Max	14.1	32.3	32.8	33.1
P10	0.46	0.94	1.33	1.68
P90	4.20	9.05	10.7	14.8

CB-MeHg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	14	47	226	207
Mean	6.77	9.01	7.33	9.23
SD	2.94	6.10	5.81	5.57
Min	3.04	0.88	1.15	0.90
Median	6.37	7.84	5.73	7.41
Max	14.1	32.3	54.8	30.8
P10	3.60	3.71	2.61	3.95
P90	9.82	16.7	13.8	16.8



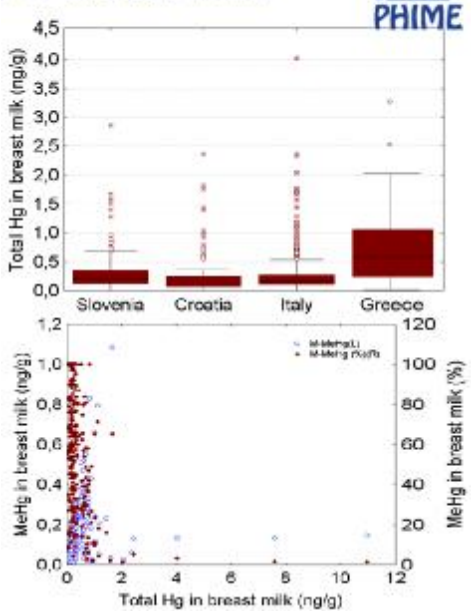
P10 – 10th percentile, P90 – 90th percentile

THg and MeHg in breast milk

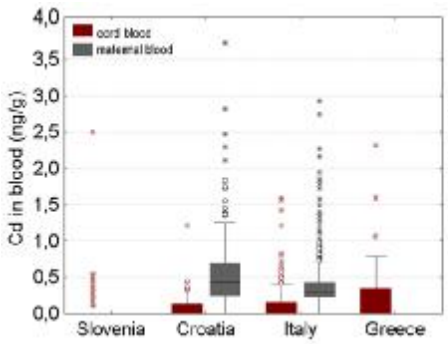
M-THg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	272	124	603	33
Mean	0.28	0.27	0.27	0.75
SD	0.30	0.38	0.33	0.77
Min	0.00	0.00	0.00	0.01
Median	0.21	0.15	0.18	0.60
Max	2.86	2.36	4.02	3.27
P10	0.06	0.03	0.07	0.06
P90	0.53	0.66	0.61	1.70

M-MeHg	*Slovenia*	*Croatia*	*Italy*	*Greece*
N	8	28	224	23
Mean	0.08	0.17	0.17	0.11
SD	0.04	0.11	0.14	0.08
Min	0.03	0.04	0.01	0.01
Median	0.07	0.15	0.13	0.08
Max	0.15	0.55	1.09	0.23
P10	0.04	0.05	0.04	0.02
P90	0.11	0.26	0.32	0.23

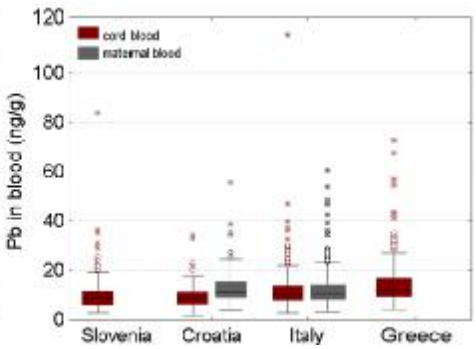
P10 – 10th percentile, P90 – 90th percentile



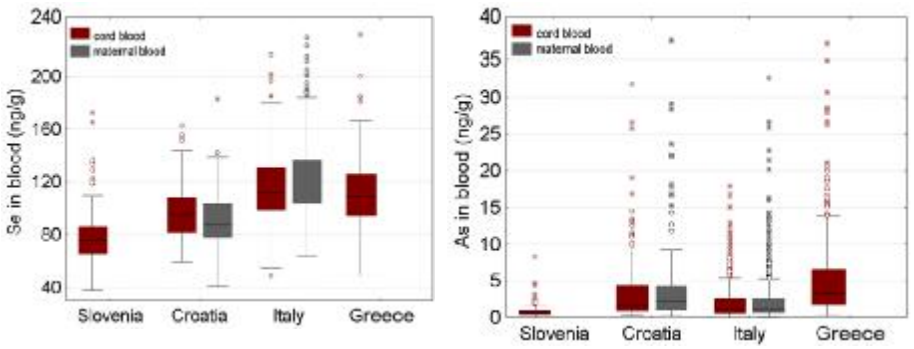
Cd in cord and maternal blood



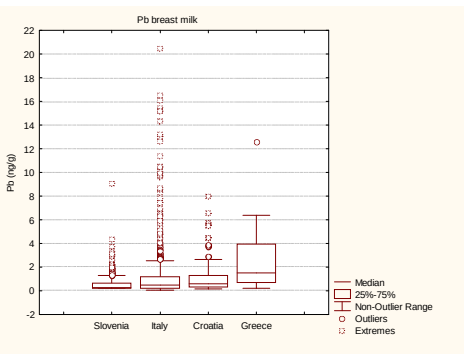
Pb in cord and maternal blood

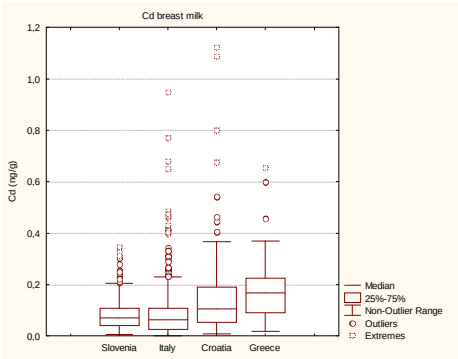


Se and As in cord and maternal blood

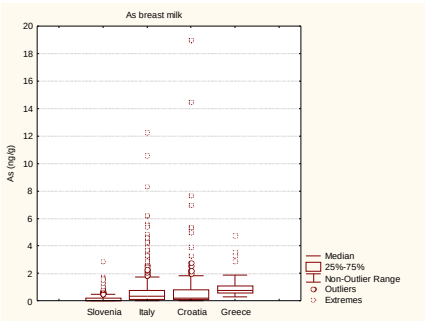


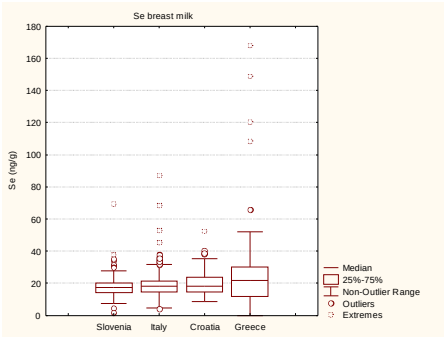
Pb and Cd in breast milk





As and Se in breast milk



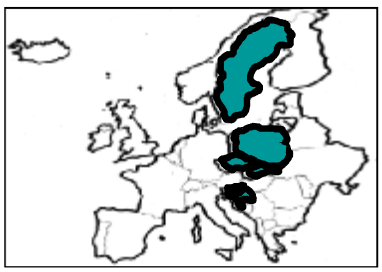


WP III:1 Human biomonitoring

Women 55-59 and children 7-11 years;

Cd, Pb and Hg in blood

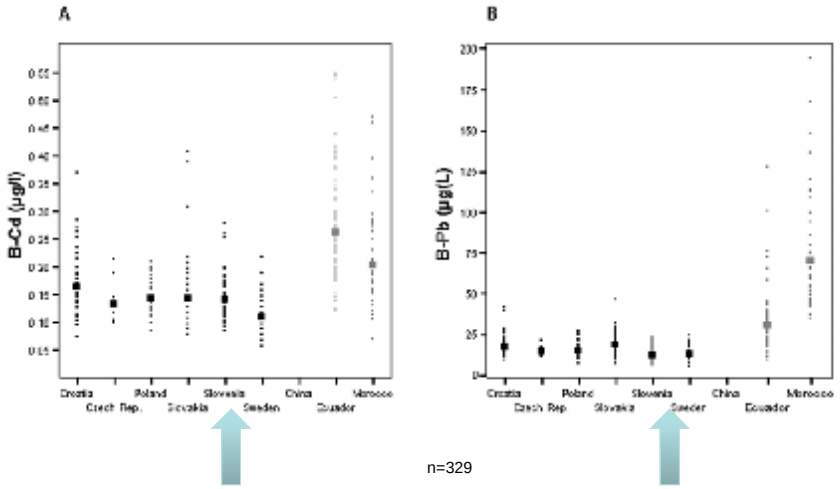
Croatia
Czech Rep
Poland
Slovakia
Slovenia (hair, urine, blood)
Sweden



Ecuador
Morocco
China - Beijing

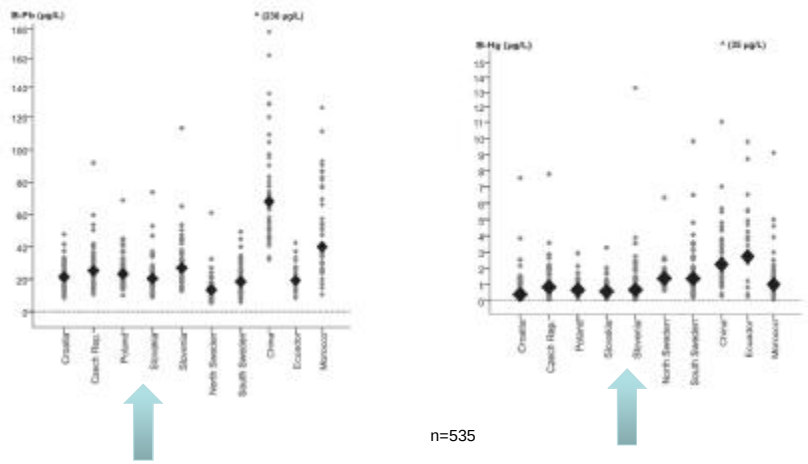
~50 in each group
Brief questionnaire

Cd and Pb in children's blood



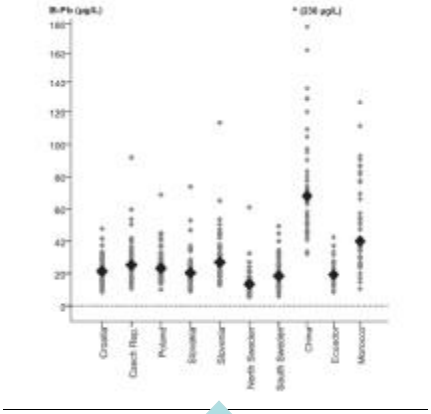
n=329

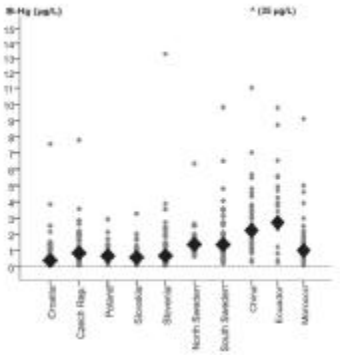
Cd and Pb in women's blood



n=535

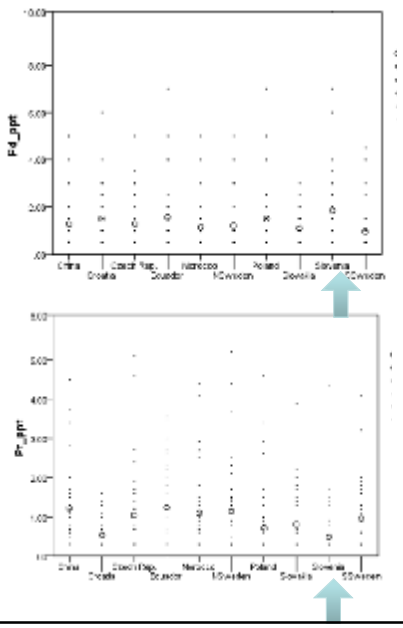
Cd and Pb in women's blood

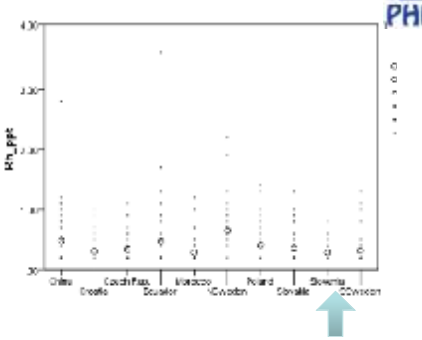




n=535

Catalytic converter elements Pt, Rd, Pd in blood





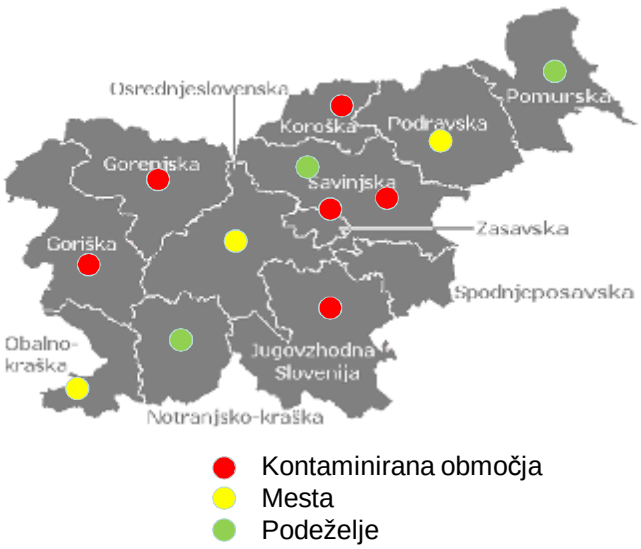
Single ng/L
Thousand times less than Cd, Hg and Pb.

After PHIME – What do we know about metals in Europe?

- **Cadmium and lead: Very small international differences.**
- **Mercury differs between countries (fish consumption, dental practice)**
- **'Hot spots' in Europe locally elevate the levels of toxic metals in children (adults unknown).**
- **Methylmercury exposure considerable in some Mediterranean regions.**
- **'Catalytic converter elements' (Pt, Pd, Rh) about 1000 times lower than Cd, Hg, Pb.**
- **No decreasing time trend for cadmium.**

- **Today's sources of lead exposure largely unknown.**

Slovenski HBM, 2008 - 2014



Hvala za pozornost!