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Organohalogens: A persisting burden in Slovenia?

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ABSTRACT

Persistent organic pollutants (POPs) represent a concern for the environment and human health due to their persistence and toxicity. Exposure in Slovenia is geographically differentiated because the country, as part of former Yugoslavia, has a history of industry and regional contamination and is – at the same time – known for its clean nature. The PCB pollution of the Krupa River drew the public's attention to the chemical burden of Slovenians, and the demand for studies has been rising since. We assessed the exposure of men (n = 548) and primiparous women (n = 536) to POPs in 12 regions of Slovenia as well as exposure pathways via questionnaires. Most PCDD/Fs, PCBs, and PBDEs could be determined in pooled samples of maternal milk at low concentrations (1.57 pg/gTEQ, 1.47 pg/gTEQ, and 1076 pg/g fat, respectively), but a much lower number of compounds could be measured above the LOQ in pooled men's plasma samples (PCDD/Fs 0.08 pg/gTEQ, PCBs 0.007 pg/gTEQ, ΣPBDE 920 pg/g), and only HCB, p,p'-DDE, ΣDDT, and the non-dioxin-like PCB congeners 138, 153, and 180 could be determined in individual samples of milk (concentration range 5–60 ng/g fat). In individual samples of men's serum, only p,p'-DDE and ΣPCB were detected at concentrations of 0.25 ng/g and 0.3 ng/g, respectively. Nonetheless, we were able to differentiate between polluted and unpolluted areas on a national level, with higher exposure levels in the PCB polluted region of Bela Krajina, the industrial region Zasavje, and the capital, Ljubljana. Despite low concentrations, determinants of exposure, such as age, proximity to roads, old building materials, private water supplies, and consumption of alcohol, fish, meat, and eggs that have previously been observed only at higher levels could still be identified. Furthermore, levels of PCBs and PBDEs were highly correlated suggesting common exposure sources and pathways, whereas PCDD/Fs were correlated to a lesser extent. The calculated ratio between DDT and DDE in maternal milk samples was decreasing with the year of sampling, suggesting no ongoing exposure to DDT. The study findings suggest low exposure of men and lactating women to legacy pollutants in Slovenia, which gave rise to the hypothesis that Slovenia's geographical location might provide shelter from the long-range transport of POPs via Westerly winds. This hypothesis remains to be confirmed within future studies.

1. Introduction

Persistent organic pollutants (POPs) can be characterised by their resistance to environmental degradation, their ability to bioaccumulate, and their potential threat to the environment, wildlife, and human health (Angerer et al., 2007; Curtean-Bănăduc et al., 2020; Govaerts et al., 2018; Islam et al., 2018; Nawab et al., 2020; Rawn et al., 2012; Warenik-Bany et al., 2019). Subjected to restriction and monitoring since 2001, POPs include organochlorine pesticides (OCPs), industrial chemicals, and unintentionally produced by-products. Even though some POPs have been prohibited since the 1970s, they are still present in the environment and detectable in different matrices, including human samples (Fång et al., 2015; Schwarzenbach et al., 2010).

In Slovenia, assessment of exposure to POPs is of interest due to the country's legacy of industrial activity and local PCB pollution. Between 1962 and 1983, a capacitor manufacturer disposed of PCB contaminated oil in the karstic region of Bela krajina (Pezdirc et al., 2011), where it

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Abbreviations

BAT	best available techniques
BDE	brominated diphenyl ether
DDT	dichlorodiphenyltrichloroethane
dl – PCB	dioxin-like PCB
H6CDD/F	hexachlorodibenzo-p-dioxin/furan
H7CDD/F	heptachlorodibenzo-p-dioxin/furan
HCB	hexachlorobenzene
HCE	heptachlor epoxide
MM	maternal milk
ndl–PCB	non-dioxin-like PCB
OCDD/F	octachlorodibenzo-p-dioxin/furan
OCP	organochlorine pesticide
PCDD/Fs	polychlorinated dibenzop-dioxins and polychlorinated dibenzofurans
p,p'-DDE	dichlorodiphenyldichloroethylene
PBDE	polybrominated diphenyl ether
PCB	polychlorinated biphenyl
PeCDD/F	pentachlorodibenzo-p-dioxin/furan
PMM	pooled maternal milk
POPs	persistent organic pollutants
PP	pooled men's plasma
S	men's serum blood samples
SD	standard deviation
TCDD/F	tetrachlorodibenzo-p-dioxin/furan

contaminated the spring of the Krupa River (Fig. 1). Monitoring has been carried out since the pollution became known, and reported values from the 1980s are as follows: 55 ng/g in sediment, 0.3 μg/g in water, 117 μg/g in fish, and 155 ng/g in human blood of the local population (Jan and Tratnik, 1988). The literature is in general agreement on the most important exposure sources for humans. As POPs biomagnify up the food chain they accumulate at the highest trophy levels such as predator species in aquatic and terrestrial environments. Thus, diet, especially meat and fish consumption, is the main contributor to exposure of humans to legacy pollutants and studies report positive correlations among POPs with similar half-lives in the human body (Bjerregaard-Olesen et al., 2017; Porta et al., 2008). Lifestyle factors influencing the metabolism of pollutants, such as alcohol intake and smoking, have been associated with POP concentrations as well (Arrebola et al., 2010; Porta et al., 2008).

The most crucial windows of vulnerability to the effects of POPs are prenatal and neonatal developmental stages. Because maternal history is known to alter POP concentrations in the mother's body (Miyashita et al., 2015), primiparous women were chosen as one study population. The temporary physiological state of these women is of further interest for the interpretation of the study results, as pregnancy induced changes in metabolism include rapid elimination of drugs and pollutants from the body. As highlighted in a review study by Porta et al. (2008), further studies on POP exposure of populations are needed. Men of the same age group were additionally included in this study, which was part of the first national human biomonitoring survey in Slovenia.

Human biomonitoring is an effective means of directly assessing the chemical burden of a population instead of estimating it; it allows comparisons among countries and the identification of time trends of exposure, as done by Fång et al. (2015) who evaluated exposure to POPs globally. As such, it successfully supplements ambient environmental monitoring (Angerer et al., 2007). However, POP concentrations measured below the level of quantification in individual blood samples have been repeatedly reported. Thus, sample pooling is a common strategy for overcoming these limitations (Rawn et al., 2012).

Among the restricted global persistent contaminants, PCDD/Fs, PCBs, PBDEs, and OCPs were included in the national human biomonitoring project. The aim of the study was to collect data on exposure of the general population (men) and primiparous women to POPs and to determine geographical differences among 12 regions classified into rural, urban, and potentially polluted/industrial areas. Additionally, we searched for correlations between questionnaire data and POP concentrations in individual samples of maternal milk (MM) and individual samples of men's serum (S, male participants). Pooled men's plasma (PP, male participants) and pooled maternal milk (PMM) were included for better detection and comparison between regions. We hypothesised that elevated POP concentrations are concentrated in industrial regions rather than in rural environments in Slovenia and that the legacy of the

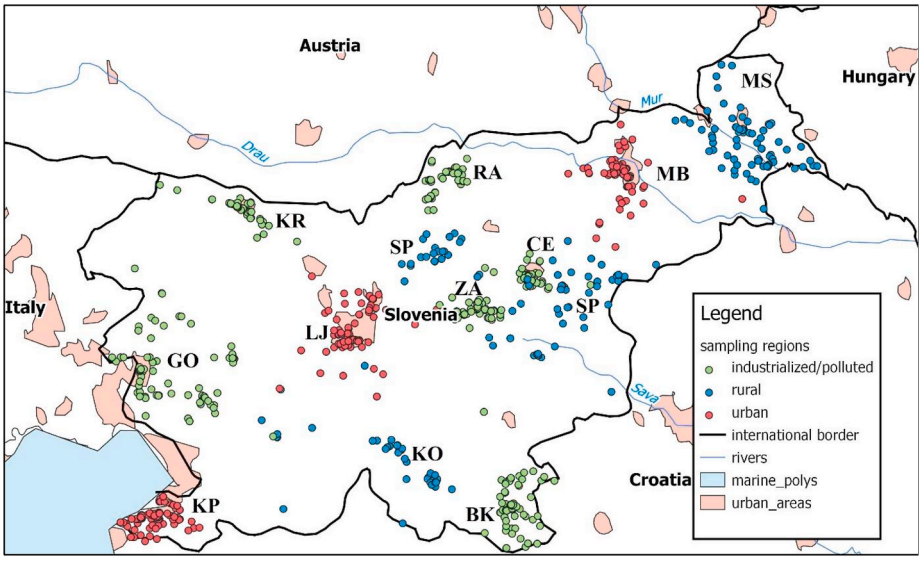

Fig. 1. Sampling regions (Natural Earth quick start for QGIS). Dots represent approximate sampling locations for data protection. Study areas: BK = Bela krajina, LJ = Ljubljana, KO = Kočevje and Cerknica, CE = Celje, GO = Posočje and Idrija, KP = Koper, KR = Jesenice, MB = Maribor, MS = Pomurje, Ra = Mežica valley, SP = Savinjsko-Posavska, ZA = Zasavje.

PCB pollution of the Krupa River in Bela krajina is still measurable.

2. Material and methods

2.1. Study population and design

A detailed description of the study population, design, and questionnaire data has been published elsewhere (Snoj Tratnik et al., 2019). Briefly, 536 primiparous women and 548 men (18–49 years of age) were recruited from 12 regions classified as rural (KO = Kočevje and Cerknica, MS = Pomurje, SP = Savinjsko-Posavska), urban (LJ = Ljubljana, MB = Maribor, KP = Koper), and potentially polluted/industrial areas due to past/present industrial activities, and/or geological presence of metals (RA = Mežica valley, GO = Posočje and Idrija, KR = Jesenice, ZA = Zasavje, CE = Celje, BK = Bela krajina) (Fig. 1) during two sampling campaigns. The pilot phase (2008–2009) included three regions (Ljubljana, Kočevje and Cerknica, and Bela krajina). Other regions (Celje, Posočje and Idrija, Koper, Jesenice, Maribor, Pomurje, Mežica Valley, Savinjsko-Posavska, Zasavje) were included in the follow-up study (2011–2014). Recruitment of women was done in the third trimester of pregnancy via maternity hospitals and schools as well as gynaecologists and their respective partners were invited to participate in the study at any point. Important criteria for inclusion were continuous residency in the area for at least 5 years with no active exposure sources nearby, no occupational exposure, good health of all participants including the child, an unproblematic pregnancy, breastfeeding, and availability for sampling during 8 weeks post-partum. The study design is in line with the WHO protocol on human biomonitoring (WHO, 2007), following the recommended procedures on recruitment, questionnaires, interviews, sampling, chemical analyses, compound selection, and ethics and as such ensures reliability and comparability with other studies. The protocol recommends the use of pooled samples of maternal milk to assess exposure levels of priority POPs equally defined in the document. Additionally, it recommends the exclusion of participants with occupational exposure of active exposure sources in close proximity of the residence. A detailed questionnaire was included in the sampling campaign; it covered information on lifestyle, employment, health, residency, and diet as suggested by the WHO protocol on HBM (WHO, 2007). The population characteristics are summarised in supplementary Table A.1. The National Medical Ethics Committee of the Republic of Slovenia granted approval of the pilot study (number of accordance 42/12/07) and the follow-up study (number of accordance 53/07/09).

2.2. Pooled samples

Samples of maternal milk and men's plasma were obtained from 12 sampling regions (Fig. 1) and pooled into 50 PMM and 33 PP samples according to the respective sampling location. Within each sampling region, sample pools were formed based on the residence of participants, considering industrial activity, emission sources, and geography (relief, wind direction). The final number of samples per pool was largely restricted by project funding and by variations in participation per location (supplementary Table A.2). Pooled samples were prepared and analysed for PCDD/Fs, dl-PCBs, and PBDE as described below.

2.3. Laboratory analysis

Table 1 provides an overview of all the analytes and matrices included. Samples were analysed at the National Laboratory of Health, Environment, and Food, located in Maribor. A detailed version of the analytical methods is provided in the supplementary material.

2.3.1. Fat extraction

Fat was extracted from human milk (PMM, MM) using Sodium Oxalate ($Na_2C_2O_4$) and acetone for protein participation, and hexane for extraction.

Table 1
Overview of analytes measured in different matrices.

Pooled maternal milk (PMM)	Pooled men's plasma (PP)	Individual samples of maternal milk (MM)	Individual samples of men's serum (S)
PCDD/Fs	PCDD/Fs		
		PCBs: 28, 52, 101, 138, 180, 153, ΣPCB	PCBs: 28, 52, 101, 138, 180, 153, ΣPCB
PCBs: 105, 114, 123, 126, 156, 157, 167, 169, 189, 77, 81, 118	PCBs: 105, 114, 123, 126, 156, 157, 167, 169, 189, 77, 81, 118		
PBDEs	PBDEs		
		OCs[a]	OCs[a] isodrin
		δ - HCH α -, β – endosulfan (sulfat)	

[a] ΣDDT, p,p'-DDT, o,p'-DDT, p,p'-DDE, o,p'-DDE, p,p'-DDD, o,p'-DDD, HCB, aldrin, endrin, dieldrin, α -, β -, γ – HCH, heptachlor, chlordane, cis-HCE, trans-HCE.

2.3.2. Sample preparation and analysis of PCDD/Fs, dl-PCBs, and PBDEs (maternal milk and men's plasma)

The methodologies applied for the analysis of PCDD/Fs, dl- PCBs, and PBDEs followed the United States Environmental Protection Agency (EPA) methods (EPA 1613, 1668A, and 1614, respectively) that have been presented in detail elsewhere (Horvat et al, 2010, 2015), and a detailed description is provided in the supplementary material.

To summarise briefly, isotopically labelled internal standard was added to all samples. The extracts were cleaned up using a multiple-step protocol, micro-concentrated and analysed using a high-resolution gas chromatograph coupled with high-resolution mass spectrometer (HRGC/HRMS) and isotope dilution quantification. LOQs were 0.05 pg/g for tetra to hepta PCDD/F and 0.1 pg/g for octa PCDD/F, dl-PCBs, and PBDE expressed as whole weight for men's plasma samples and on the basis of fat basis for PMM samples.

2.3.3. Quality control for PCDD/Fs, dl-PCBs, and PBDEs (maternal milk, men's plasma)

Laboratory method blanks were used in every batch and subtracted from the results. To all samples isotopically labelled ^{13}C standards were added at the earliest point of sample processing. Target analyte quantification was performed via isotope dilution. Injection standards were used in every sample extract prior to instrumental analysis, and the concentrations of the surrogates were determined as percent recoveries, which were compliant with standard prerequisites.

2.3.4. Sample preparation of men's serum and maternal milk for analysis of OCPs and ndl-PCBs

For MM samples, fat extracts were used as described in Section 2.3.1. Men's S samples were mixed with 5% formic acid in acetonitrile and centrifuged. The centrifugate was added to a dispersive solid phase reagent. The resulting suspension was centrifuged again and extracted twice with hexane. MM fat extracts and concentrated dried men's S extracts were loaded to the conditioned SPE cartridge, eluted with hexane:dichloromethane and hexane:dichloromethane, and reduced for gas chromatographic analysis.

An Agilent Technologies 6890N GC equipped with two 60 m × 0.25 mm x 0,25 μm capillary columns with slightly different polarities and two ^{63}Ni electron-capture detectors (ECD-ECD) was used. The operating conditions are described in detail in the supplementary material.

For MM samples, limits of quantification (LOQs) were 0.01 mg/kg

for α-HCH, heptachlor epoxide, chlordane, and HCB, 0.015 mg/kg for endosulfan, heptachlor, aldrin, dieldrin, DDE, and β,γ,δ-HCH, and 0.02 mg/kg for endrin, endosulfan sulphate, DDT, DDD, and ndl-PCBs expressed per gram of fat. For men's S samples LOQs were 0.015 μg/kg for HCB, 0.2 μg/kg for α,β,γ-HCH, heptachlor, heptachlor epoxide, aldrin, dieldrin, isodrin, chlordane, and DDE, and 0.3 μg/kg for endrin, DDT, DDD, and ndl-PCBs.

2.3.5. Quality control for OCPs and ndl-PCBs (maternal milk, men's serum)

Real matrix blanks were used in every batch, where all analytes investigated were below the limits of detection (LOD). For quality assurance, internal standard PCB 209 was added to every sample. In every batch, a quality control (QC) sample (fortified blank sample) was analysed. The recoveries for every analyte were calculated. Fortifications used were interchanging from batch to batch throughout the entire range of the calibration curve – from low to high range.

Recoveries ranged from 52 to 114% (MM) and from 43 to 102% (men's S) with variations in QC samples not exceeding 25%. Median recoveries were 82% (MM) and 72% (men's S).

2.4. Emission inventory for Slovenia (2008–2014) and POP sources to air (PAHs, PCDD/Fs, HCB, PCB)

The Slovenian Environmental Agency is responsible for reporting air emissions for Slovenia. These data are gathered each year in Informative Inventory Reports for Slovenia (submission under the UNECE Convention on Long-Range Transboundary Air Pollution). Emissions to air have been reported for the following POPs: PAHs, PCDD/Fs, HCB, and PCBs. The emissions in g (E) are calculated as follows (Allende et al., 2016; Logar et al., 2016; Rode et al., 2010).

$$E = AD \times EF$$

E = emission (g).
AD = activity data (quantity of fuel combusted (t))
EF = emission factor per quality of fuel (g/t).

2.5. Statistical analysis

Questionnaire data were used to determine associations between analytical concentrations of POPs in individual samples with potential exposure sources. All statistical analyses were carried out in R Studio version 3.6.3. Correlations among analytes were evaluated via a correlation matrix using Spearman's correlation coefficient and Benjamini&Hochberg adjustment (Patil, 2018). Other correlations were tested separately using Spearman's correlation test (stats package) and confirmed using multiple linear regression modelling (confounders listed in Table A.7). Differences among groups were obtained via analyses of variance and covariance (ANOVA and ANCOVA) and the Wilcoxon test. Cluster analysis and principal component analysis (PCA) were carried out for pattern recognition of sample concentrations.

Values below LOQ were treated as LOQ/2. 2005 WHO toxicity equivalency factors (TEFs) (Van den Berg et al., 2006) were used to convert analytical concentrations of PCDD/Fs and dl-PCBs into toxic equivalents (TEQs). Analytes with 70% of the samples < LOQ were excluded from the statistical analysis and from the presentation of descriptive statistics. Concentrations were not normally distributed and log-transformed data were thus used to achieve normality. For PP samples, no information on lipid content was available, which made fat normalisation impossible. For S samples, no normalisation was performed because analyte concentrations did not correlate with lipid content (Hebert and Keenleyside, 1995).

2.6. Calculation of proposed reference values

Reference values (RVs) are statistical estimates of the upper margin of background exposure of populations. They were introduced as a tool in science-policy translations and communication to policy makers as they allow an understanding of the exposure burden of population and mirror successes and failures of regulatory actions (Buekers et al., 2018; Schulz et al., 2011). Preliminary RVs for PCDD/Fs, dl-PCBs, and PBDE were established for men and primiparous women (20–40 years of age) following the guidelines suggested by the international project on HBM in Europe (HBM4EU) and the German HBM commission (Govarts, 2018; Schulz et al., 2011). Values were calculated by rounding off the 95th percentile (P95) of measured concentrations within the 95th confidence interval of that value as suggested in the literature (Ewers et al., 1999; Schulz et al., 2011; Solberg, 1987a, 1987b). RVs for PCDD/Fs and dl-PCBs were based on calculated TEQs of the measured concentration. The data for calculation is presented in the supplementary Table A.5.

3. Results

Descriptive statistics of analytes and proposed RVs by sample matrix are presented in Table 2.

3.1. Polychlorinated dibenzodioxins/furans (PCDD/Fs) and dioxin-like-polychlorinated biphenyls (dl-PCBs)

Median concentrations for PCDD/F and dl-PCBs ranged from 0.05 pg/g fat to 24.5 pg/g fat and from 0.42 pg/g to 2700 pg/g fat in PMM samples, respectively. In PP samples, only 1,2,3,4,6,7,8 – H7CDD and 1,2,3,4,6,7,8,9 – OCDD could be detected in more than 30% of the samples with median concentrations of 0.05 pg/g and 0.1 pg/g, respectively. Dl-PCBs were detected in a median range between 0.15 pg/g and 9.8 pg/g (PP), respectively. In PMM and PP samples, 1,2,3,4,6,7,8,9 – OCDD was the largest contributor to ΣPCDD/Fs in PMM samples, followed by 1,2,3,4,6,7,8 – H7CDD and 2,3,4,7,8 – PeCDF (71%, 11%, 6%). In PP samples, among the two detected congeners, 1,2,3,4,6,7,8,9 – OCDD contributed more (67%). The largest contributions to ΣPCB had PCB 118 (PMM: 50% and PP: 55%), followed by PCB 156 in PMM (22%) and PCB 105 in PP (19%) and PCB 105 in PMM (11%) and PCB 156 in PP (14%).

The TEQ values are presented in Table 3 (and in more detail in supplementary Table A.4). The highest contribution to ΣPCDD/Fs TEQ came from 2,3,4,7,8-PeCDF (21%) in PMM samples and from 1,2,3,7,8-PeCDD (29%) in PP samples. Among PCB congeners, PCB 126 made the largest contribution to Σdl-PCBTEQs (36% PMM and 6% PP). ΣPCDD/F TEQs was 1.6 pg/gTEQ$_{2005}$ and 0.08 pg/gTEQ$_{2005}$ for PMM and PP, respectively, and Σdl-PCBTEQs was 1.5 pg/gTEQ$_{2005}$ (PMM) and 0.007 pg/gTEQ$_{2005}$ (PP). The calculated ΣPCDD/Fs + dl-PCBs TEQ was 3.04 pg/gTEQ$_{2005}$ in PMM samples and 0.09 pg/gTEQ$_{2005}$ in PP samples, where PCDD/Fs contributed 52% to ΣTEQ PCDD/Fs + PCBs in PMM and 92% in PP.

3.2. Polybrominated diphenyl ethers (PBDEs)

Median analytical concentrations of PBDEs in pooled samples ranged from 12 pg/g to 505 pg/g fat in PMM and from 0.25 pg/g to 6 pg/g in PP samples. Among PBDEs, BDE 47 contributed the most to ΣPBDE (46% in PMM, 70% in PP).

3.3. Organochlorine pesticides (OCPs)

Organochlorine pesticides were measured only in individual samples. Only HCB, p,p'–DDE, and ΣDDT metabolites could be detected in MM at median concentrations of 5 ng/g fat, 50 ng/g fat, and 60 ng/g fat, respectively. In S samples, only p,p'–DDE could be detected (median = 0.25 ng/g). Using LOQ/2 as a representative value for p,p'-DDT the mean p,p'-DDT:p,p'-DDE ratio was 0.1 in MM samples.

Table 2
Descriptive statistics of pooled samples of maternal milk (n = 50) and men's plasma (n = 33) and individual samples of maternal milk (n = 448) and men's serum (n = 520). CI = confidence interval. Reference values (RVs) for PCDD/Fs and dl-PCBs are presented in pg/g TEQ. Median TEQ values are presented in the supplementary Table A4.

	Pooled samples maternal milk (pg/g fat)									Pooled samples men's plasma (pg/g)								
	P25	Median	A. mean	P75	P95	range	SD	< LOD %	RV	P25	Median	A. mean	P75	P95	Range	SD	< LOD %	RV
1,2,3,4,6,7,8 - H7CDD	2.48	3.70	3.62	4.98	6.72	0.02–7.10	1.89	6	0.07[a]	0.02	0.05	0.06	0.05	0.08	0.02–0.70	0.12	73	0.001[a]
1,2,3,4,6,7,8 - H7CDF	0.17	0.45	0.60	0.99	1.57	0.02–2.10	0.54	22	0.02[a]								100	
1,2,3,4,6,7,8,9 - OCDD	17.0	24.5	25.9	32.8	51.6	0.10–68.0	13.3	2	0.02[a]	0.05	0.10	0.18	0.18	0.43	0.05–1.40	0.24	55	0.0001[a]
1,2,3,4,6,7,8,9 - OCDF								88									97	
1,2,3,4,7,8,9 - H7CDF								88									97	
1,2,3,4,7,8 - H6CDD	0.02	0.26	0.57	0.56	3.17	0.02–4.40	0.96	48	0.30[a]								97	
1,2,3,4,7,8 - H6CDF	0.05	0.73	0.72	1.10	1.86	0.02–2.50	0.63	30	0.20[a]								97	
1,2,3,6,7,8 - H6CDD	1.03	1.45	1.59	2.18	3.21	0.02–4.40	0.96	8	0.30[a]								88	
1,2,3,6,7,8 - H6CDF	0.27	0.70	0.78	1.10	1.71	0.02–3.50	0.64	22	0.18[a]								97	
1,2,3,7,8 - PeCDD	0.03	0.42	0.51	0.85	1.36	0.02–2.10	0.50	32	1.40[a]								88	
1,2,3,7,8 - PeCDF	0.05	0.11	0.15	0.23	0.43	0.02–0.53	0.14	42	0.01[a]								100	
1,2,3,7,8,9 - H6CDD								72									97	
1,2,3,7,8,9 - H6CDF								76									97	
2,3,4,6,7,8 - H6CDF	0.02	0.05	0.22	0.26	1.06	0.02–1.30	0.34	58	0.10[a]								97	
2,3,4,7,8 - PeCDF	1.40	2.15	1.91	2.50	3.00	0.02–3.20	0.82	6	0.90[a]								97	
2,3,7,8 - TCDD	0.05	0.13	0.24	0.37	0.77	0.02–1.20	0.28	42	0.80[a]								97	
2,3,7,8 - TCDF	0.02	0.05	0.13	0.14	0.54	0.02–0.68	0.18	64	0.05[a]								97	
PCB 105	483	565	722	760	1775	100–3600	563	0	0.05[a]	2.50	3.30	3.34	4.50	5.02	0.24–6.70	2.31	0	0.0002[a]
PCB 114	110	130	174	178	568	32.0–790	151	0	0.02[a]	0.20	0.29	0.36	0.42	0.83	0.11–1.10	0.23	0	0.00003[a]
PCB 123	32.3	37.5	43.2	52.0	79.0	5.30–140	23.7	0	0.003[a]	0.29	0.35	0.38	0.50	0.61	0.20–0.70	0.13	0	0.00002[a]
PCB 126	7.43	11.0	11.7	15.8	20.6	1.90–23.0	5.23	0	2.00[a]								97	
PCB 156	985	1200	1402	1575	3110	210–4200	732	0	0.10[a]	1.80	2.40	3.01	3.30	7.24	0.10–11.0	2.59	3	0.0002[a]
PCB 157	170	205	258	270	721	51.0–810	166	0	0.02[a]	0.35	0.46	0.63	0.69	1.50	0.10–2.90	0.54	3	0.00005[a]
PCB 167	293	390	412	470	766	59.0–840	170	0	0.02[a]	0.65	0.84	0.99	1.10	2.20	0.17–3.40	3.07	0	0.00007[a]
PCB 169	4.68	7.05	9.00	11.0	20.6	1.40–25.0	5.88	0	0.60[a]								100	0.003[a]
PCB 189	86.3	110	110	140	166	26.0–220	42.3	0	0.005[a]	0.10	0.15	0.26	0.29	0.82	0.10–1.30	1.28	30	0.00003[a]
PCB 77	4.93	6.80	8.76	9.93	20.9	1.90–35.0	6.51	0	0.002[a]	0.10	0.15	0.48	0.50	1.98	0.10–2.50	0.65	33	0.0002[a]
PCB 81	0.10	0.42	0.60	0.98	1.61	0.10–1.90	0.55	28	0.0005[a]								91	0.00005[a]
PCB 118	2300	2700	3361	3575	8395	470–14000	2316	0	0.25[a]	8.30	9.80	9.63	11.0	13.4	4.30–20.0	1.84	0	0.0004[a]
BDE 100	94.0	130	160	178	290	46.0–860	141	0	300	0.52	0.63	0.83	0.97	1.86	0.10–2.40	0.54	3	2.00
BDE 153	190	265	371	378	779	8.00–2400	448	0	800	0.10	0.25	0.42	0.41	1.68	0.05–1.80	0.47	21	1.70
BDE 154	6.65	12.0	19.7	16.8	50.0	3.20–160	29.3	0	50								82	
BDE 183	11.3	21.0	23.2	31.0	52.6	0.10–72.0	18.0	12	55								70	
BDE 28	43.3	54.5	74.2	69.5	174	19.0–470	79.3	0	180	0.15	0.28	0.48	0.55	1.58	0.10–2.50	0.53	18	1.60
BDE 47	383	505	660	688	1155	191–6600	891	0	1200	4.70	6.00	7.25	8.50	15.5	2.00–20.8	2.94	0	16.0
BDE 99	86.3	116	166	160	417	30.0–1100	182	0	450	0.86	1.40	1.91	2.20	5.04	0.41–7.40	2.56	0	5.00
ΣPBDE	800	1076	1234	1492	2667	470–3750	679	0	2700	6.80	9.20	11.2	13.0	25.6	2.90–32.5	2.76	0	26.0
	Individual samples maternal milk (ng/g fat)									Individual samples men's serum (ng/g)								
PCB 138	10	10	10	10	30	10–200	10	57	30								99	
PCB 153	10	10	20	20	50	10–200	200	52	50								98	
PCB 180	10	10	10	10	20	10–90	10	49	20								100	
PCB 28								100									100	
PCB 52								100									100	
PCB 101								100									100	
ΣPCB	5	20	40	50	130	0–510	70	5	130	0.30	0.30	0.31	0.30	0.30	0.15–1.70	0.11	32	0.30
HCB	5	5	6	5	10	5–20	3	78	10								100	
p,p' - DDT								99									100	
o,p' - DDT								100									100	
o,p' - DDE								100									100	
p.p'-DDE	30	50	60	70	120	20–500	40	2	120	0.10	0.25	0.28	0.33	0.61	0.10–1.30	0.17	21	0.60

(continued on next page)

Table 2 (*continued*)

	Pooled samples maternal milk (pg/g fat)									Pooled samples men's plasma (pg/g)							
	P25	Median	A. mean	P75	P95	range	SD	< LOD %	RV	P25	Median	A. mean	P75	P95	Range	SD	< LOD %	RV
p,p' - DDD								100									100	
o,p' - DDD								100									100	
ΣDDT	40	60	80	90	190	20–500	60	0	190									
Aldrin								100									100	
Endrin								100									100	
Dieldrin								99									100	
Isodrin																	100	
α HCH								100									100	
β HCH								97									100	
δ HCH								100										
γ HCH								100									99	
Heptachlor								100									100	
cis-HCE								100									100	
trans-HCE								100									100	
cis Chlordane								100									100	
trans chlordane								100									100	
α Endosulfan								100										
β endosulfan								100										

[a] pg/g TEQ.

3.4. Correlations among analytes

3.4.1. Intra- and interclass associations in samples of maternal milk (PMM + MM)

The results for correlations among analytes within the same class are presented in the supplementary Tables A.8.1 – A.10. In MM samples, the strongest correlations were observed between ΣDDT and p,p'–DDE (rho = 1, p-value < 0.0001), and between ΣPCBs and PCB 153 (rho = 0.98, p-value < 0.0001).

In PMM, we observed strong correlations within PCBs and within PBDE congeners, whereas PCDD/Fs had a weaker association with one another. 2,3,4,7,8 – PeCDF and 1,2,3,6,7,8 – H6CDD were associated with the most PCDD/Fs and 2,3,7,8 – TCDF with the least. Among PCBs, PCB 77 was not correlated with any other, whereas all other PCBs seemed strongly related. All PBDE congeners were correlated with at least one of the others, except for BDE 154, which did not appear to have any relationship with other analytes.

The strongest interclass correlations were observed between PBDE congeners and PCBs, whereas PCDD/Fs exhibited much weaker correlations with other contaminants (supplementary Tables A.8.1, A.8.2, and A.10). BDE 183 and 153 were correlated with almost all PCB analytes in this study. Among PCDD/Fs, only 1,2,3,4,6,7,8,9-OCDD was correlated with almost all PCBs and PBDEs, whereas correlations among other analytes were sporadic. As Fig. 2 shows, PCA results support the correlation outcomes. PBDEs were grouped closely together as were PCBs, whereas PCDD/Fs were more scattered. Some interclass associations were suggested, such as between 1,2,3,4,6,7,8,9 – OCDD and BDE 183. Principal component 1 (PC1) accounts for only 17% of the variation, however.

Cluster analysis (Fig. 2) indicates the presence of five clusters (determined by the elbow method) containing (1) PCDD/Fs, (2) PCB 77, 126, and 168, (3) 1,2,3,4,6,7,8,9- OCDD and BDE 183, (4) BDE 100, 99, 28, and PCB 189, and (5) PCB 167, 114, and 157.

In MM samples, all analytes showed positive correlations among each other. Only PCB 180 and HCB did not seem to have a significant relationship.

3.4.2. Associations in pooled men's plasma (PP)

In PP samples, PCBs and PBDE congeners were strongly correlated within their respective groups (Table A.9), and strong correlations were observed between PCB 114, 123, and 156 and most PBDE congeners (supplementary Table A.9). The two PCDD/Fs detected in men's plasma were significantly correlated with each other, but not with any of the other analytes.

Cluster analysis resulted in two clusters, as determined by the elbow method (Fig. 2) indicating a cluster containing PCB 118, BDE 47, and ΣPBDE and a second group containing other contaminants. In the PCA plot, PCB 118 and 105 are separated from the other compounds on the right side of the graph, whereas other analytes seemed more closely related to one another. PC1 accounted for 24% of the variation.

3.5. Age trends

Age trends investigated using linear regression showed significant positive trends for p,p'-DDE, ΣDDT, PCB 153, PCB 180, PCB 138, and HCB in MM (p-values < 0.0001, 0.01, <0.0001, 0.007, 0.05, and <0.0001, respectively). P,p'–DDE levels in men's S samples were significantly correlated with age as well (p-value < 0.0001). Furthermore, we observed decreasing p,p'-DDT/p,p'-DDE ratios with age in MM samples (p-values < 0.0001). Importantly, levels of p,p'-DDT were mostly below LOQ (LOQ/2); therefore this trend should be taken as indicatory.

3.6. BMI

The geometric mean of BMI in this population was 24.3 with a

Table 3
Presentation of PCDD/Fs and dl-PCBs TEQ (pg/g), PBDE (ng/g), ndl-PCB (PCB 138, 153, 180, ng/g), and selected OCP (ng/g) levels as reported in the literature (P = primiparae).

Reference	Country	Sample	n	Sampling period	TEF year	ΣPCDD/Fs	ΣPCBs	ΣTEQ	ΣPBDE	Σndl-PCBs	HCB	p,p'-DDE	ΣDDT
Present study	**Slovenia – All study areas**	**pooled, P**		**2008–2014**	**2005**	**1.57a**	**1.47a**	**3.04a**	**1.08a**				
	Bela krajina					**1.77a**	**2.99a**	**4.76a**					
	Celje					**2.07a**	**1.30a**	**3.37a**					
	Posočje and Idrija					**1.80a**	**1.20a**	**2.99a**					
	Jesenice					**1.52a**	**1.28a**	**2.80a**					
	Kočevje and Cerknica					**1.31a**	**1.67a**	**2.99a**					
	Koper					**1.80a**	**1.96a**	**3.75a**					
	Ljubljana					**2.23a**	**2.61a**	**4.84a**					
	Maribor					**0.72a**	**1.14a**	**1.86a**					
	Pomurje					**2.15a**	**1.46a**	**3.61a**					
	Mežica Valley					**1.22a**	**1.16a**	**2.37a**					
	Savinjsko - Posavska					**2.89a**	**1.01a**	**3.9a**					
	Zasavje					**0.29a**	**1.25a**	**1.54a**					
Abballe et al. (2008)	Italy	pooled, P		1998–2001		12.4	15.7	28.2					
Bake et al. (2007)	Latvia	pooled		2002/2004	1998	7.69b	14.3b	22.0b		142b			
						7.63b	5.84b	13.5b		111b			
Croes et al. (2013)	Belgium	pooled		2009–2010	2005	6.90b	3.70b	10.6b					
Fängström et al. (2005)	Faroe Islands	pooled, P		1987					1.95				
				1994/95					1.80				
				1999					2.55				
Harden et al. (2007)	Australia	pooled, P		2002/2003	1998	5.60	2.60	8.90					
Ingelido et al. (2007)	Italy	pooled		2000/2001	2005				2.75				
Li et al. (2009)	China	pooled		2007	2005	3.12	1.46	4.58					
Polder et al. (2008a)	Russia	pooled, P		2000–2002	1998	9.00	17.0	26.0	1.29		51.3a	782a	884a
Pratt et al. (2012)	Ireland	pooled, P		2010	2008	6.32	3.34	9.66					
Ryan and Rawn (2014)	Canada	pooled		2005	2005	6.6a	2.2a	8,8a					
Wong et al. (2013)	Hong Kong	pooled, P		2009	2005	7.48b	3.79b	11.3b					
Zhang et al. (2011)	China	pooled		2007					1.49a				
Zhang et al. (2017)	China	pooled, P		2011					1.47b				
Thomsen et al. (2010)	Norway	pooled		2003–2005					2.10a				
Toms et al. (2007)	Australia	pooled, P		2002–2003					11.0a				
Wasser et al. (2015)	Israel	pooled, P		2011–2012					6.77	6.87		1.47	168
De Felip et al. (2014)	Italy (Campania)	pooled, P		2008–2009		6.82a	5.55a	12.4a	2.53				
Fång et al. (2013)	Sweden	pooled, P		2008	2005	2.95	1.60	4.55					
				2009		2.90	2.00	4.95					
				2010		3.15	2.60	5.70					
				2011		2.90	2.15	5.05					
Pacheco Ferreira and Rabello Alves (2015)	Brazil	pooled, P		2012–2014	2005	15.4	6.96	22.3					
Present study	**Slovenia**	**Individual, P**	448	**2008–2014**						**30a**	**5a**	**50a**	**60a**
Alivernini et al. (2011)	Italy (Rome)	Individual, P	13	2005–2007						118b			
Colles et al. (2008)	Belgium	Individual, P	197	2006						98.4b	15.5b	95.9b	
Raab et al. (2008)	Germany	Individual, P	85	2005						200a	21a	87a	99a
Polder et al. (2008b)	Norway	Individual, P	29	2000–2001						37a	19a	99a	109a
Lignell et al. (2009)	Sweden	Individual, P	335	1996–2006						34.3a			
Kalantzi et al. (2004)	UK	Individual	54	2001–2003						111a	20.0b	220b	
Çok et al. (2009)	Turkey	Individual	51	2007						14.9b			
	South Africa	Individual	28	2004						8.40	1.80	3550a	4920a

(*continued on next page*)

Table 3 (*continued*)

Reference	Country	Sample	n	Sampling period	TEF year	ΣPCDD/Fs	ΣPCBs	ΣTEQ	ΣPBDE	Σndl-PCBs	HCB	p,p'-DDE	ΣDDT
Darnerud et al. (2011)													
Kim et al. (2013)	Korea	Individual, P	50							18.0 (PCB 138 only)	20.6a	150a	187a
Zietz et al. (2008)	Germany	Individual	523	2006						183a	23a		81a
Chao et al. (2006)	Taiwan	Individual	36	2000–2001								310b	333b
Kunisue et al. (2006)	Japan	Individual, P	38	2001–2004						140b	14.0b	330b	340b
Rodas-Ortíz et al. (2008)	Mexico	Individual	38	2006						1541b	92.0b	3041b	3065b
Ennaceur et al. (2008)	Tunisia	Individual	237	2003–2005						196b	85.0b	676b	1931b
Mannetje et al. (2013)	New Zealand	Individual, P	39	2007–2010			1.54b			13.3b		378b	
Polder et al. (2009)	Norway	Individual	423	2002–2006							11.0a	41.0a	
Rawn et al. (2017)	Canada	Individual	298	2008–2011						5.67a			
She et al. (2007)	Pacific Northwest (USA, Canada)	Individual, P	40	2003						40.2a			

*a = median, b = mean.

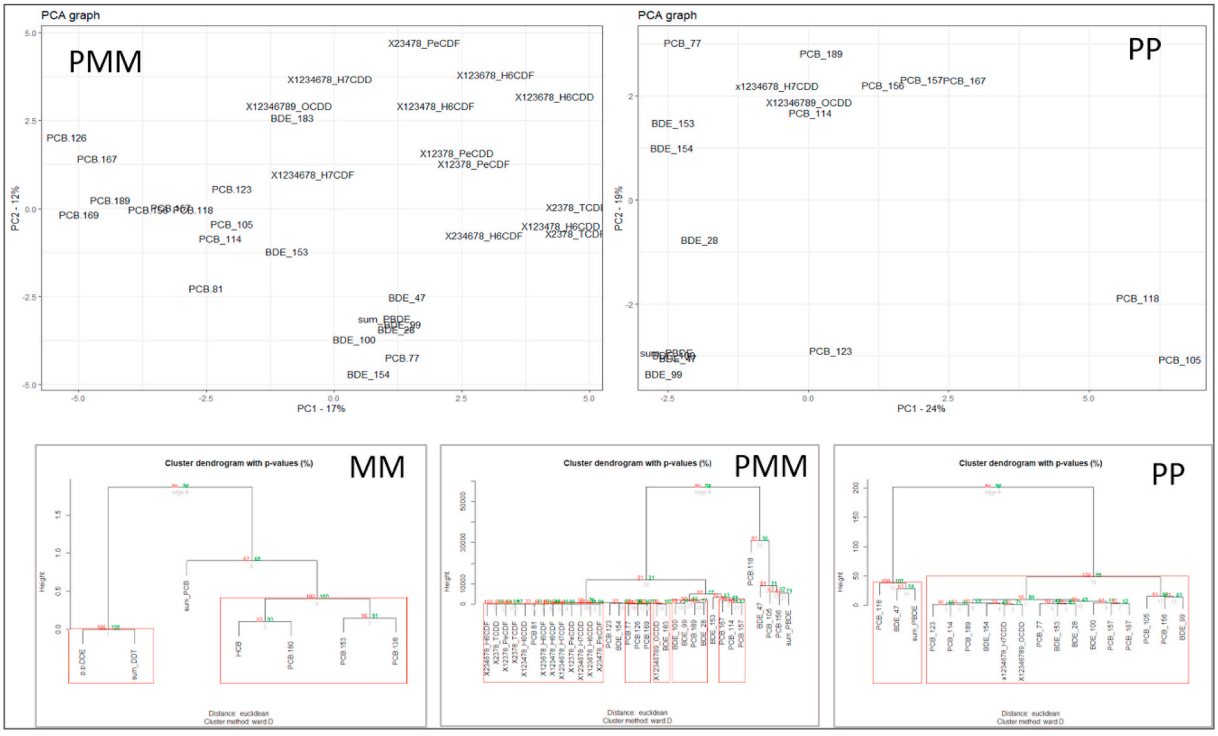

Fig. 2. Results of principal component analysis and cluster analysis in pooled samples of maternal milk (PMM), pooled samples of men's plasma (PP), and individual samples of maternal milk (MM).

standard deviation of 3.8 (supplementary Table A.1). Contaminant concentrations in MM samples were significantly inversely correlated for PCB 153 and PCB 180, as well as for p,p'-DDE in S samples after age correction.

3.7. Smoking

Non-smokers had significantly higher concentrations of p,p'-DDE (15–500 ng/g fat), ΣDDT (20–500 ng/g fat), and (marginally) significantly higher concentrations of HCB (5–20 ng/g fat) in MM samples (p-values = 0.03, 0.02, and 0.06, respectively).

3.8. Diet and food origin

A full overview of obtained data and answer frequencies is provided in the supplementary Table A.6. We observed significantly higher concentrations of p,p'–DDE, PCB 153, and PCB 180 (p-values = 0.01, 0.002, 0.0001, respectively) in MM of participants who reported higher consumption of seafood (>1x/month) and higher concentrations of p,p'–DDE in men's S samples in the same consumption group (p-value = 0.07). Regular intake of freshwater fish was significantly associated with higher concentrations of ΣPCBs in MM. The frequent consumption of eggs (>5x/week) was positively associated with elevated levels of ΣDDT

metabolites in MM. Domestic poultry was positively associated with elevated levels of p,p'-DDE in men's S as well as consumption of domestic (undefined) meat. Significant positive associations were observed between vegetable intake and p,p'-DDE in MM and men's S. In general, analyte concentrations in both matrices did not differ between vegetarians and nonvegetarians. Participants who reported frequent alcohol consumption (>1/week) had significantly higher concentrations of p, p'–DDE, ΣDDT, and PCB 153 in MM. The significance of this relationship disappeared when the source of alcohol (homemade or bought) was introduced into the model. P,p'-DDE in men's S was significantly correlated with homemade alcohol.

3.9. Sociodemographic characteristics

Concentrations of p,p'-DDE, HCB, PCB 153, PCB 180, and PCB 138 in MM samples were positively associated with the age of the building. Proximity to local roads was associated with elevated concentrations of PCB 180 in MM. Participants working in industrial production had significantly higher concentrations of PCB 153, PCB 138, and ΣPCBs in milk (p-values = 0.004, 0.001, and 0.0003, respectively). ΣPCBs in MM were significantly (p-value < 0.0001) associated with private water supplies. The percentage of participants using private water supplies in different regions was between 0% and 14%.

3.10. Regional differences

We observed significant differences among the 12 regions in Slovenia. The largest variations could be observed among PBDEs. Elevated concentrations were detected in PMM samples from Kočevje and Cerknica (BDE 154, 28, p-values = 0.02, 0.04), Bela krajina (BDE 153, p-values < 0.0001), and Zasavje (BDE 154 (PMM), 153, 154, 28, 47, ΣPBDE (PP), p-values < 0.0001, 0.01, <0.0001, 0.02, 0.003, 0.004). Significantly lower levels of BDE 183 were present in PMM from Maribor (p-value < 0.0001). The highest concentrations of p,p' – DDE in MM were detected in Ljubljana (p-value < 0.0001), and those of PCB 153 in Ljubljana and Bela krajina (p-value < 0.0001). Significantly elevated levels of p,p' – DDE were observed in men's S samples from Ljubljana (p-value = 0.0009).

ΣPCDD/Fs + dl-PCBs in PMM was 3.04 pg/gTEQ with regional differences. The highest TEQ values were obtained in the polluted region of Bela krajina (4.76 pg/g) and Ljubljana (4.84 pg/g) and the lowest in Zasavje (1.54 pg/g). ΣPCDD/FsTEQ was highest in Savinjsko-Posavska (2.89 pg/g) and lowest in Zasavje (0.29 pg/g). Σdl-PCBsTEQ was highest in Bela krajina (2.99 pg/g) and lowest in Savinjsko-Posavska (1.01 pg/g). Presenting individual compounds, 1,2,3,7,8,9 – H6CDD was significantly higher in Pomurje (PMM), and TEQ-levels of 2,3,4,7,8 – PeCDF were significantly higher in Ljubljana and Celje (PMM). TEQs of 2,3,4,7,8 – PeCDF were significantly lower in PMM and higher in PP samples from Zasavje. Concentrations of 1,2,3,6,7,8 – H6CDF, 1,2,3,7,8 – PeCDF, 1,2,3,4,7,8,9 – H7CDF, and 1,2,3,4,6,7,8 – H7CDF were significantly higher in PP samples from Zasavje, but none of these trends could be confirmed in PMM samples. Bela krajina had significantly higher TEQ values for PCB 105, 114, 123, 126, 156, 157, 167, 169, 81, and 118 in PMM. TEQs were significantly higher also in Ljubljana for PCB 126 and 169 (PMM), in Kočevje and Cerknica for PCB 169 (PMM), and in Zasavje for PCB 169 (PMM), 114, 156, 157, 189, and 77 (PP). TEQs of PCB 105 were significantly lower for PP samples from Zasavje, and PCB 126 TEQs were significantly elevated in Pomurje (PP). The impact of dl-PCBs on ΣTEQ values differed between the regions and between the sample matrices. In PMM samples, the contribution of PCBs to ΣPCDD/Fs + PCBs TEQ ranged from 26% (Savinjsko-Posavska) to 81% (Zasavje), whereas the range of percentages in PP samples was 5% (Zasavje) to 20% (Pomurje).

3.11. Results for POP (PCB, PCDD/Fs, HCB) air emissions for Slovenia between 1990 (base year) and 2014

For Slovenia, the trend of POP emissions declined from 1990 to 2014 as follows: for PCB (−75.4%), PCDD/Fs (−26.1%), and HCB (−98.9%) (Logar et al., 2016). The main sources for PCB emissions are industrial process and product use with a share of more than 99% that have been reduced due to best available techniques (BAT), industrial use of high temperature fuel combustion, and reductions in the solvent and product use subsector. A temporary increase of PCDD/Fs emissions between 2009 and 2014 could be attributed to larger consumptions of wood biomass in the residential sector as a result of the global economic crisis. Small combustion and industrial processes contribute a share of 70% and 17% to the total emissions, respectively. Emissions of HCB in Slovenia have dropped considerably in 2002 due to abatement of hexachloroethane (HCE) tablets as degassing agents in aluminium production (Rode et al., 2010).

3.12. Literature comparison

We compared the PMM and MM concentrations observed in the present study with those found in the literature for similar time periods and populations (2000–2014) (Fig. 3, Table 3). Comparable time periods and populations are essential for reliable comparisons of POP body burdens, as POPs are known to increase with age group and decrease over time (Li et al., 2019). As information on POP exposure of specific populations is limited, not many studies were available that fit the study population as well as the time period. Population matched comparisons are especially important in our population, as parity and lactation increase the elimination of POPs from the body as compared to child-free women of the same age (Dennis et al., 2017; Nøst et al., 2019). The highest TEQ values obtained in PMM samples were from Italy (Abballe et al., 2008; Ingelido et al., 2007), followed by Russia (Polder et al., 2008a), Brazil (Pacheco Ferreira and Rabello Alves, 2015), and Latvia (Bake et al., 2007), whereas Slovenia ranked among the lowest, with similar numbers being reported from China (Li et al., 2009) and Sweden (Fång et al., 2013). ΣTEQ levels from Bela krajina and Ljubljana were higher than the Slovenian average, but still among the lowest values reported. The highest levels of ΣPBDE were reported from Australia (Toms et al., 2007) and Israel (Wasser et al., 2015), whereas other countries reported values between 1 and 2 ng/g. Concentrations in Slovenian samples were among the lowest.

4. Discussion

4.1. Internal exposure to persistent organic pollutants

As described in Section 3, compared to the RVs for PCDD/Fs set for unpolluted regions (24 pg TEQ/g PMM [Solomon and Weiss, 2002], 7.4 pg TEQ/g PP [Umweltbundesamt, 2002], the levels determined in the Slovenian population are notably low (3.04 pg TEQ/g PMM, 0.09 pg TEQ/g PP), however it should be noted that the values obtained for lactating women are not representative of the general population. The large contribution of 1,2,3,4,6,7,8,9 – OCDD, 1,2,3,4,6,7,8 – H7CDD, and 2,3,4,7,8 – PeCDF to ΣPCDD/Fs (pg/g) has been reported in many studies, as have high concentrations of PCB 156 and 118 (Fromme et al., 2015). These results may be due to the half-lives of individual contaminants. This explanation finds support in the low number of correlations among PCDD/Fs (Section 3.5) as well as the large standard deviation among samples (Table 2). Among PCBs, the weakest correlations with other compounds were observed for analytes with the shortest half-life (PCB 77 and 81), whereas the pentachlorinated congeners PCB 105 and 118 were measured at high levels and were associated with many other analytes. A previous study examining the PCB burden in sediments and cave salamanders from the polluted Krupa River reported high concentrations of PCB 118 in the environment (Pezdirc et al.,

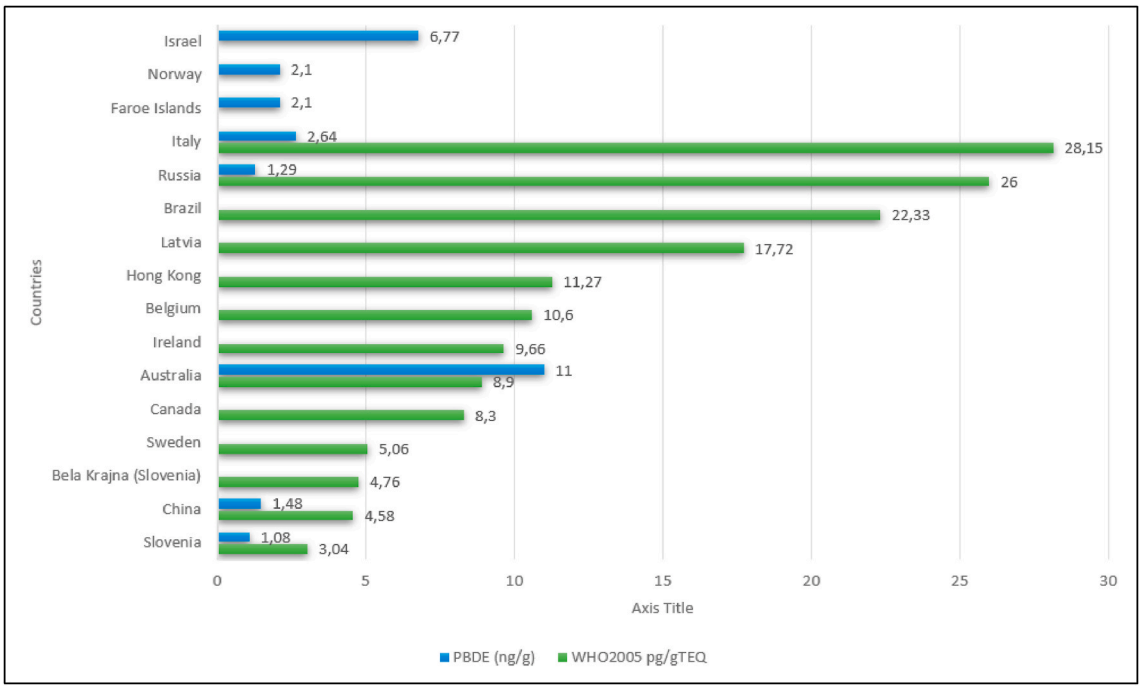

Fig. 3. Presentation of WHO 2005 TEQ and PBDE levels obtained from the literature presented in Table 3. If multiple studies on comparable populations were available for the same country, the average of values obtained from the literature was used.

2011). BDE 153, 100, and 47 have been observed to be dominant contributors to the PBDE burden of humans (Fromme et al., 2015), but exposure exceeded the RVs set for PBDE in PMM and men's PP (3210 pg/g [Main et al., 2007] and 2100 pg/g [EPA, 2008], respectively) in only one sample of PMM. The weak correlation of BDE 28 with other analytes might be due to its faster degradation in the environment. However, PCA analysis does not support any differences among analytes depending on degree of halogenation (Fig. 2). We therefore urge researchers to conduct more studies on differences in metabolism, enzyme activity, and/or genetic predisposition with respect to the elimination of pollutants from the body.

In individual samples, as described in detail in Section 3.3, p,p'- DDE could be measured above the LOQ in both matrices, but not above the RV of 6000 ng/g for ΣDDT (Solomon and Weiss, 2002) in MM and with 3% of samples above the RV in men's S (0.7 ng/g) (Linhardt, 2005; Wilhelm et al., 2003). The low ratio (0.1, Section 3.3) between p,p'-DDT and p,p'-DDE observed in our study indicates legacy exposure from historical applications of DDT, as described by Fång et al. (2015), whereas a ratio $>$ 0.5 would hint at recent release of DDT into the environment. The decreasing p,p'-DDT:p,p'-DDE ratio with age indicates higher exposure of p,p'-DDE in the younger participants compared to the older ones. The RVs of 2.2, 3.3, and 2.4 ng/g in S (PCB 138, 153, 180) (Wilhelm et al., 2003), 1430 ng/g for ΣPCB in MM (Solomon and Weiss, 2002), 0.3 ng/g HCB in S (Wilhelm et al., 2003), and 10 ng/g HCB in MM (Solomon and Weiss, 2002) have not been reached in most cases. In MM samples, 12% were above the reference limit for HCB. The dominant contribution of the ndl-PCB congeners 138, 153, and 180 in human samples has been reported widely in the literature (Glynn et al., 2011; Rawn et al., 2012).

Among our study regions, the contribution of dl-PCBs to ΣPCDD/Fs + PCB TEQ varies, making the hypothesis of larger PCDD/Fs contribution highly geographically dependent, as previously reported in the literature (Bake et al., 2007; Croes et al., 2013; Harden et al., 2007; Polder et al., 2008a; Rawn et al., 2012). Concentrations of POPs reported from different countries reveal large differences in the chemical burden of these chemicals (Aylward et al., 2014; Fromme et al., 2015; Glynn et al., 2011; Rawn et al., 2012). Our results indicate much lower exposure in Slovenia by comparison, although regional differences still apply. The highest values were obtained in samples from Bela krajina and Ljubljana and are comparable with values from other countries that report low exposure. ΣPBDE exposure is equally low in Slovenia and comparable with Norway, the Faroe Islands, Russia, and China. In the absence of immediate sources, the spread of POPs in the environment is driven mainly by environmental factors such as wind, ocean currents, and atmospheric pressure cells. We propose that Slovenia's location between the Julian Alps and the Adriatic Sea provides shelter from the long-range transport of POPs via westerly winds, which is discussed in the following section.

4.2. Geographical and environmental determinants of exposure

In Slovenia, industrial regions are found in Zasavje (thermal power plant [1966–2014], cement industry [1876–2015], waste incineration), Jesenice (iron and steel industry), and Celje (steel industry and chemical companies). The Zasavje region is located in deep valleys with frequently occurring meteorological inversions. Indeed, we observed significantly elevated (TEQ) concentrations of some PCBs (PP), PBDEs (PP, MM), and PCDD/Fs (PP) in this region. Jesenice is home to iron and steel manufacturing companies located in a narrow valley, and it is polluted mainly with sulphur oxides and solid particles (Smrekar et al., 2020). We did not observe higher levels of POPs in these regions, though, which could be explained by the type of industry and the application of modern filter systems. It should be emphasized that POP emissions in Slovenia have been decreasing since 1990 (Section 3.12). In Celje, we observed higher concentrations of PCBs and p,p'-DDE.

It is commonly assumed that urban areas have higher air concentrations of POPs due to the presence of older buildings in immediate proximity to one another and meteorological conditions that limit air exchange. Studies investigating POP concentrations in aerosol samples have confirmed a high burden of these pollutants associated with fine particulate matter because of its higher organic matter content (Odabasi et al., 2015). The urban regions included in this study are Ljubljana, Maribor, and Koper, as well as Celje and Jesenice which are located in industrial areas. Indeed, we observed significantly higher

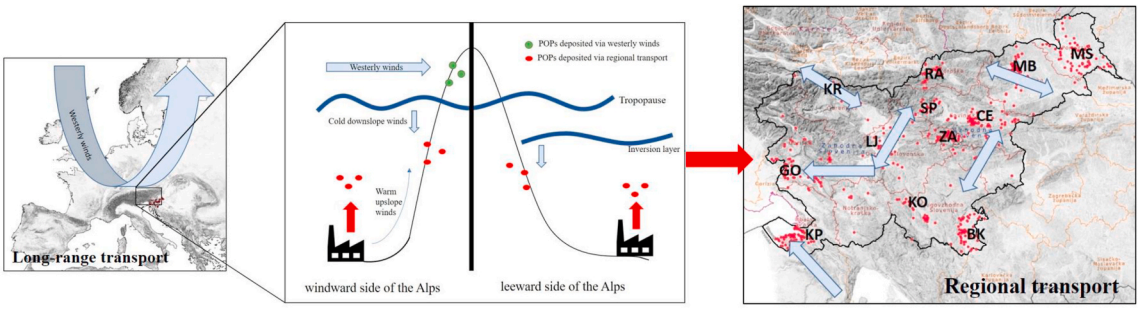

Fig. 4. Sources of POPs in the Alps. Figure adapted from Hageman et al. (2015). The map displaying regional transport contains the averaged wind directions between 2008 and 2014 according to the Slovenian Environment Agency (Republika Slovenije, 2008, 2009, 2010, 2011, 2012, 2013, 2014).

concentrations of some POPs (PCBs, p,p'-DDE) in Ljubljana. Participants from Maribor seemed less exposed (Section 3.11), which could be explained by the presence of fresh air channels, less dense construction, and multiple green areas as well as by the absence of any active emitters. Other urban locations did not reveal any significant trends.

The regions Kočevje and Cerknica, Pomurje, and Savinjsko-Posavska were chosen as unpolluted rural areas. Interestingly, PMM samples from Kočevje and Cerknica contained significantly higher concentrations of two PBDE congeners (28, 154) compared to the other regions. Its location in the wind channel from the nearby city Novo Mesto (Fig. 4) is a possible explanation, but reports of environmental monitoring of water quality have stated that the area exhibits no chemical contamination (Ambrožič et al., 2008). Besides environmental background contamination, PBDEs are present in consumer products and indoor air, although at lower concentrations than, for instance, in North America (Frederiksen et al., 2009).

The regions Posočje and Idrija, Mežica valley, and Bela krajina were chosen as areas polluted with different contaminants. Idrija is the location of a former mercury mine. Mežica valley is traditionally a lead mining and steel manufacturing region. None of the POPs included in our study has been observed in these locations in elevated concentrations. The area Bela krajina, on the other hand, stood out since 1983, when the dimensions of PCB pollution caused by illegal waste deposition were revealed. Between 1962 and 1983, a capacitor manufacturer had been disposing an assumed total of 60 t of PCB-contaminated waste. In hollow spaces underground, elevated levels of PCBs have been identified above the groundwater level, and they are assumed to be the cause of increasing concentrations of PCBs in river water after longer precipitation events (Polič et al., 2000). All PCB congeners (except PCB 77) were identified at significantly higher concentrations (TEQ) in PMM as was BDE 153. The contribution of PCBs to ΣTEQ is higher than in most other study regions. Interestingly, the addition of homemade alcohol as a confounder eliminates the significance of PCBs in MM samples, but we cannot confirm this for other matrices. Environmental data (soil and water) support elevated PCB levels (Hrvatin et al., 2020; Zupan et al., 2008). This confirms the hypothesis that – on a national level – the legacy of POPs contamination is still visible in Slovenia.

Geographical differences in POP burden do not follow a comparable trend in milk and blood samples. We attribute these results to two main factors. Firstly, maternal milk is an excretion matrix that is known to have higher fat and POP contents than blood. Secondly, POPs in PMM and MM were determined per gram fat while concentrations in blood samples are unadjusted for lipid content.

As mentioned in Section 4.1, the concentrations observed in this study are notably low. In women, the temporary physiological state is known to enhance metabolism of drugs and pollutants (Koh et al., 2014) and is, thus, a potential explanation. However, this study lacks the data to conclusively evaluate this and the low concentrations observed in men cannot be explained by our dataset. We hypothesise that the underlying cause might be Slovenia's geographical location. As a result of their low temperatures, high precipitation, and barrier effects, mountain ecosystems hinder atmospheric transport of POPs (Belis et al., 2009). The general principle is presented in Fig. 4. Studies of Central Europe have suggested that pollutants are subject to atmospheric transport via westerly winds (Weiss and Moche, 2015). Thus, as reported by the MONAPROP study, they accumulate in needles of *Picea abies* L. and in forest soils on the northern side of the Alps, but transport over the Alps is limited (Belis et al., 2009; Hageman et al., 2015; Offenthaler et al., 2009). According to this hypothesis, local sources and interchanging wind directions (Republika Slovenije, 2008, 2009, 2010, 2011, 2012, 2013, 2014) would have a larger impact on the POP burden of the country, as illustrated in Fig. 4. This finds further support in the up to seven times lower concentrations of polyaromatic hydrocarbons (PAHs) in Slovenian moss compared with neighbouring countries (Milojković, 2013) and low (<4 ng/g) PCB concentrations in sediments of the Sava River (Heath et al., 2010). Additionally, the Slovenian Environment Agency (ARSO) confirms low average annual emissions of PCDD/Fs, PCBs, and PBDEs in Slovenia (European Environment Agency, 2016). According to this report, Slovenia is emitting an average of 162 kg PCB/year and 15 kg PCDD/Fs/year (Supplementary, Figure A.1) which is below the reported international median for PCDD/Fs (36 kg PCDD/Fs/year) but above the median for PCBs (37 kg PCB/year).

4.3. Socioeconomic characteristics and lifestyle as determinants of exposure

We observed significant differences among regions that can be attributed only partially to environmental background levels. Naturally, socioeconomic characteristics and individual lifestyles determine the degree to which an individual comes into contact with pollutants. The observed correlations with age have been widely reported in the literature and have been found to be the consequence of long-term exposure to persistent, lipophilic compounds (Arrebola et al., 2010). Additionally, it has been reported that P450 enzyme activity decreases with age (Grandjean et al., 2008), slowing down the elimination of these compounds. The decreasing ratio between p,p'-DDT and p,p'-DDE with age additionally supports the hypothesis of decreasing exposure to the parent compound DDT, while exposure to the metabolite DDE increases. The same trend has been observed in other studies (Porta et al, 2010, 2012).

The inverse relationship between BMI and the levels of two ndl-PCBs observed in this study has been observed in other studies as well (Ingelido et al., 2017), but the results throughout the literature are highly inconsistent (Arrebola et al., 2010; Tsukino et al., 2006). It has been proposed that a larger lipid compartment size could cause a dilution effect, leading to participants with a higher BMI seemingly having lower lipid-based concentrations (Ingelido et al., 2017). Other studies suggest, longer half-lives in the human body of higher chlorinated PCBs compared to lesser chlorinated congeners (Bjerregaard-Olesen et al., 2017). Henríquez-Hernández et al. (2021) point out that elevated concentrations of PCB 153 and 180 could be expected in the adipose tissue rather than in blood and milk.

We observed an inverse relationship between smoking and contaminant concentrations that has previously been reported resulting in higher POP concentrations in non-smokers (Flesch-Janys, 1996; Ingelido et al., 2017; Miyashita et al., 2015). Smoking was found to induce P450 enzymes, which are known to be responsible for compound degradation (Flesch-Janys, 1996; Miyashita et al., 2015). Especially, CYP1B1, CYP1A1, CYP1A2, CYP2B6, CYP2C9, CYP2C19, and CYP3A4 that have been reported to metabolize chlorinated pollutants (Abass et al., 2012; Docea et al., 2017), are known to be induced by smoking, leading to faster elimination of POPs from the body (Klomp et al., 2020). Oliveira et al. (2017) advice in their extensive review to personalize drug treatment of smokers, due to pharmacokinetic interactions that influence treatment efficiency. However, associations with smoking are not consisting throughout the literature as studies report positive associations or no associations as well (Arrebola et al., 2010; Deutch et al, 2003, 2007). Alcohol consumption, on the other hand, seemed to be positively correlated with POP concentrations as other studies have shown (Miyashita et al., 2015). A plausible cause is the potential effect of alcohol intake on hepatic drug-metabolising enzymes that would decrease the elimination rate of POPs within the body (Miyashita et al., 2015). It should be noted that we observed an additional positive association between POP concentrations and the source of alcohol, namely domestic, as well as a significant correlation between alcohol-intake frequency and homemade alcohol, suggesting that the source plays a more important role than consumption frequency itself. The contribution of domestic alcohol to total alcohol consumption is the highest in Bela krajina (50%), which may contribute to the higher POP burden in this region.

It has repeatedly been reported that meat, fish, and seafood are sources of POP exposure (Bjerregaard-Olesen et al., 2017). Miklavčič et al. (2011) measured PCB levels in fresh and canned fish available in Slovenia and found levels ranging from < LOD to 0.039 μg/g dw. Compared to the safety level for fish set by the U.S. Food and Drug Administration (2 μg/g ww = ~10 μg/g dw), these values are very low, which could add to the explanation of generally low levels in the Slovenian population. The reason we did not observe any significant difference between vegetarians and nonvegetarians is most likely the difference in sample size (3% vegetarians). Observed associations with egg intake might be the result of the chicken's feeding behaviour (DiGangi and Petrlík, 2005).

Products present in buildings can be sources of industrial POPs (Flores-Ramírez et al., 2017). Our findings point to old building materials, roads/traffic, and industrial production as potential sources of exposure. Furthermore, we did observe an association between POP levels and private water supplies. Because water from private supplies generally lacks both the treatment applied to tap or bottled water and the monitoring of potential contamination, it represents a potential source of POPs.

5. Study limitations and lessons learned

This is the first national human biomonitoring study in Slovenia to determine regional differences in population exposure. This study has overcome several challenges. The variety of sample matrices and different sample treatments (individual and pooled) provided opportunities, but also limitations in terms of making comparisons between sexes. Differences in sample matrix characteristics between milk and blood samples might be the underlying driver of differences in concentration, detection rates, and associations. Such characteristics include milk as a pathway of excretion and a higher fat content compared to human blood. Furthermore, the pooling method needs optimization to achieve an equal number of samples per pool for each region. Furthermore, the obtained results are not completely representative for Slovenia. Lactating women represent merely a subpopulation especially vulnerable to harmful chemicals, whereas the included men represent the general population. As such, all drawn conclusions are in need of verification via follow-up studies.

6. Conclusions

Despite strict regulations, the general population is still exposed to a wide range of POPs. In this study, we detected almost all analytes in PMM samples, whereas concentrations were mostly below the LOQ in men's PP samples. In individual samples of MM and men's S, only certain PCBs, DDT derivatives, and HCB could be detected. We observed geographical differences in POP distribution among the 12 regions that reveal histories of pollution. Even though levels in the PCB-polluted region of Bela krajina were higher than the national average, exposure was low on an international level. Using individual samples, we were able to confirm some known sources (diet, private water supply, proximity to roads, old building materials, etc.) of POPs even at low levels of exposure. We conclude that the low POP concentrations in the population are a result of decreasing local emissions of POPs and of the Alpine barrier effect, which hinders long-range transport of POPs to Slovenia. Further, the study represents the POP burden in Slovenia between 2008 and 2014, which will be useful for future biomonitoring studies. For future work, in addition to human samples, environmental samples of air, water, soil, and sediment should be included to estimate the effect of Slovenia's geography on POP distribution in the environment.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.111224.

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Credit author statement

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References

Abass, K., Turpeinen, M., Rautio, A., Hakkola, J., Pelkone, O., 2012. Metabolism of pesticides by human cytochrome P450 enzymes in vitro – a survey. In: Insecticides - Advances in Integrated Pest Management. InTech. https://doi.org/10.5772/28088.

Abballe, A., Ballard, T.J., Dellatte, E., Domenico, A., di, Ferri F., Fulgenzi, A.R., Grisanti, G., Iacovella, N., Ingelido, A.M., Malisch, R., Miniero, R., Porpora, M.G., Risica, S., Ziemacki, G., Felip, E. De, 2008. Persistent environmental contaminants in human milk: concentrations and time trends in Italy. Chemosphere 73, S220–S227. https://doi.org/10.1016/j.chemosphere.2007.12.036.

Alivernini, S., Battistelli, C.L., Turrio-Baldassarri, L., 2011. Human milk as a vector and an indicator of exposure to PCBs and PBDEs: temporal trend of samples collected in Rome. Bull. Environ. Contam. Toxicol. 87, 21–25. https://doi.org/10.1007/s00128-011-0262-7.

Allende, D., Ruggeri, M.F., Lana, B., Garro, K., Altamirano, J., Puliafito, E., 2016. Inventory of primary emissions of selected persistent organic pollutants to the atmosphere in the area of Great Mendoza. Emerg. Contam. 2, 14–25. https://doi.org/10.1016/j.emcon.2015.12.001.

Ambrožič, Š., Cvitanič, I., Dobnikar Tehovnik, M., Gacin, M., Grbović, J., Jesenovec, B., Kozak Legiša, Š., Krajnc, M., Mihorko, P., Poje, M., Remec Rekar, Š., Rotar, B., Sodja, E., 2008. Water Quality in Slovenia. Ljubljana.

Angerer, J., Ewers, U., Wilhelm, M., 2007. Human biomonitoring: state of the art. Int. J. Hyg Environ. Health 210, 201–228. https://doi.org/10.1016/j.ijheh.2007.01.024.

Arrebola, J.P., Fernandez, M.F., Porta, M., Rosell, J., de la Ossa, R.M., Olea, N., Martin-Olmedo, P., 2010. Multivariate models to predict human adipose tissue PCB concentrations in Southern Spain. Environ. Bar Int. 36, 705–713. https://doi.org/10.1016/j.envint.2010.05.004.

Aylward, L.L., Green, E., Porta, M., Toms, L.-M., Den Hond, E., Schulz, C., Gasull, M., Pumarega, J., Conrad, A., Kolossa-Gehring, M., Schoeters, G., Mueller, J.F., 2014. Population variation in biomonitoring data for persistent organic pollutants (POPs): an examination of multiple population-based datasets for application to Australian pooled biomonitoring data. Environ. Int. 68, 127–138. https://doi.org/10.1016/j.envint.2014.03.026.

Bake, M.A., Linnika, Z., Sudmalis, P., Kočan, A., Jursa, S., Pike, A., Ruce, M., 2007. Assessment of the exposure of breast milk to persistent organic pollutants in Latvia. Int. J. Hyg Environ. Health 210, 483–489. https://doi.org/10.1016/j.ijheh.2007.01.016.

Belis, C.A., Offenthaler, I., Uhl, M., Nurmi-Legat, J., Bassan, R., Jakobi, G., Kirchner, M., Knoth, W., Kräuchi, N., Levy, W., Magnani, T., Moche, W., Schramm, K.-W., Simončič, P., Weiss, P., 2009. A comparison of Alpine emissions to forest soil and spruce needle loads for persistent organic pollutants (POPs). Environ. Pollut. 157, 3185–3191. https://doi.org/10.1016/j.envpol.2009.05.035.

Bjerregaard-Olesen, C., Long, M., Ghisari, M., Bech, B.H., Nohr, E.A., Uldbjerg, N., Henriksen, T.B., Olsen, J., Bonefeld-Jørgensen, E.C., 2017. Temporal trends of lipophilic persistent organic pollutants in serum from Danish nulliparous pregnant women 2011–2013. Environ. Sci. Pollut. Res. 24, 16592–16603. https://doi.org/10.1007/s11356-017-8992-7.

Buekers, J., David, M., Koppen, G., Bessems, J., Scheringer, M., Lebret, E., Sarigiannis, D., Kolossa-Gehring, M., Berglund, M., Schoeters, G., Trier, X., 2018. Development of policy relevant human biomonitoring indicators for chemical exposure in the European population. Int. J. Environ. Res. Public Health 15 (2085). https://doi.org/10.3390/ijerph15102085.

Chao, H.-R., Wang, S.-L., Lin, T.-C., Chung, X.-H., 2006. Levels of organochlorine pesticides in human milk from central Taiwan. Chemosphere 62, 1774–1785. https://doi.org/10.1016/j.chemosphere.2005.07.036.

Çok, I., Donmez, M.K., Uner, M., Demirkaya, E., Henkelmann, B., Shen, H., Kotalik, J., Schramm, K.-W., 2009. Polychlorinated dibenzo-p-dioxins, dibenzofurans and polychlorinated biphenyls levels in human breast milk from different regions of Turkey. Chemosphere 76, 1563–1571. https://doi.org/10.1016/j.chemosphere.2009.05.032.

Colles, A., Koppen, G., Hanot, V., Nelen, V., Dewolf, M.-C., Noël, E., Malisch, R., Kotz, A., Kypke, K., Biot, P., Vinkx, C., Schoeters, G., 2008. Fourth WHO-coordinated survey of human milk for persistent organic pollutants (POPs): Belgian results. Chemosphere 73, 907–914. https://doi.org/10.1016/j.chemosphere.2008.07.002.

Croes, K., Colles, A., Koppen, G., De Galan, S., Vandermarken, T., Govarts, E., Bruckers, L., Nelen, V., Schoeters, G., Van Larebeke, N., Denison, M.S., Mampaey, M., Baeyens, W., 2013. Determination of PCDD/Fs, PBDD/Fs and dioxin-like PCBs in human milk from mothers residing in the rural areas in Flanders, using the CALUX bioassay and GC-HRMS. Talanta 113, 99–105. https://doi.org/10.1016/j.talanta.2013.03.086.

Curtean-Bănăduc, A., Burcea, A., Mihuţ, C.-M., Berg, V., Lyche, J.L., Bănăduc, D., 2020. Bioaccumulation of persistent organic pollutants in the gonads of Barbus barbus (Linnaeus, 1758). Ecotoxicol. Environ. Saf. 201 (110852) https://doi.org/10.1016/j.ecoenv.2020.110852.

Darnerud, P.O., Aune, M., Larsson, L., Lignell, S., Mutshatshi, T., Okonkwo, J., Botha, B., Agyei, N., 2011. Levels of brominated flame retardants and other pesistent organic pollutants in breast milk samples from Limpopo province, South Africa. Sci. Total Environ. 409, 4048–4053. https://doi.org/10.1016/j.scitotenv.2011.05.054.

De Felip, E., Bianchi, F., Bove, C., Cori, L., D'Argenzio, A., D'Orsi, G., Fusco, M., Miniero, R., Ortolani, R., Palombino, R., Parlato, A., Pelliccia, M.G., Peluso, F., Piscopo, G., Pizzuti, R., Porpora, M.G., Protano, D., Senofonte, O., Spena, S.R., Simonetti, A., di Domenico, A., 2014. Priority persistent contaminants in people dwelling in critical areas of Campania Region, Italy (SEBIOREC biomonitoring study). Sci. Total Environ. 487, 420–435. https://doi.org/10.1016/j.scitotenv.2014.04.016.

Dennis, K.K., Marder, E., Balshaw, D.M., Cui, Y., Lynes, M.A., Patti, G.J., Rappaport, S. M., Shaughnessy, D.T., Vrijheid, M., Barr, D.B., 2017. Biomonitoring in the era of the exposome. Environ. Health Perspect. 125, 502–510. https://doi.org/10.1289/EHP474.

Deutch, B., Edersen, H.S., Jøsrgensen, E.C.B., Hansen, J.C., 2003. Smoking as a determinant of high organochlorine levels in Greenland. Arch. Environ. Heal. An Int. J. 58, 30–36. https://doi.org/10.3200/AEOH.58.1.30-36.

Deutch, B., Pedersen, H., Asmund, G., Hansen, J., 2007. Contaminants, diet, plasma fatty acids and smoking in Greenland 1999–2005. Sci. Total Environ. 372, 486–496. https://doi.org/10.1016/j.scitotenv.2006.10.043.

DiGangi, J., Petrlik, J., 2005. The Egg Report. https://doi.org/10.13140/RG.2.2.19316.7.

Docea, A.O., Vassilopoulou, L., Fragou, D., Arsene, A.L., Fenga, C., Kovatsi, L., Petrakis, D., Rakitskii, V.N., Nosyrev, A.E., Izotov, B.N., Golokhvast, K.S., Zakharenko, A.M., Vakis, A., Tsitsimpikou, C., Drakoulis, N., 2017. CYP polymorphisms and pathological conditions related to chronic exposure to organochlorine pesticides. Toxicol. Rep. 4, 335–341. https://doi.org/10.1016/j.toxrep.2017.05.007.

Ennaceur, S., Gandoura, N., Driss, M.R., 2008. Distribution of polychlorinated biphenyls and organochlorine pesticides in human breast milk from various locations in Tunisia: levels of contamination, influencing factors, and infant risk assessment. Environ. Res. 108, 86–93. https://doi.org/10.1016/j.envres.2008.05.005.

EPA, 2008. Toxicological review of 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) (CAS No. 5436-43-1). In: Support of Summary Information on the Integrated Risk Information System (IRIS).

European Environment Agency, 2016. European Union Emission Inventory Report 1990–2014 under the UNECE Convention on Long-Range Transboundary Air Pollution (LRTAP). https://doi.org/10.2800/628267.

Ewers, U., Krause, C., Schulz, C., Wilhelm, M., 1999. Reference values and human biological monitoring values for environmental toxins. Int. Arch. Occup. Environ. Health 72, 255–260. https://doi.org/10.1007/s004200050369.

Fång, J., Nyberg, E., Bignert, A., Bergman, Å., 2013. Temporal trends of polychlorinated dibenzo-p-dioxins and dibenzofurans and dioxin-like polychlorinated biphenyls in mothers' milk from Sweden, 1972–2011. Environ. Int. 60, 224–231. https://doi.org/10.1016/j.envint.2013.08.019.

Fång, J., Nyberg, E., Winnberg, U., Bignert, A., Bergman, Å., 2015. Spatial and temporal trends of the Stockholm Convention POPs in mothers' milk — a global review. Environ. Sci. Pollut. Res. 22, 8989–9041. https://doi.org/10.1007/s11356-015-4080-z.

Fängström, B., Strid, A., Grandjean, P., Weihe, P., Bergman, Å., 2005. A retrospective study of PBDEs and PCBs in human milk from the Faroe Islands. Environ. Heal. 4 (12) https://doi.org/10.1186/1476-069X-4-12.

Flesch-Janys, D., 1996. ELIMINATION OF POLYCHLORINATED DIBENZO-p-DIOXINS AND DIBENZOFURANS IN OCCUPATIONALLY EXPOSED PERSONS. J. Toxicol. Environ. Health 47, 363–378. https://doi.org/10.1080/009841096161708.

Flores-Ramírez, R., Pérez-Vázquez, F., Rodríguez-Aguilar, M., Medellín-Garibay, S., Van Brussel, E., Cubillas-Tejeda, A., Carrizales-Yáñez, L., Díaz-Barriga, F., 2017. Biomonitoring of persistent organic pollutants (POPs) in child populations living near contaminated sites in Mexico. Sci. Total Environ. 579, 1120–1126. https://doi.org/10.1016/j.scitotenv.2016.11.087.

Frederiksen, M., Vorkamp, K., Thomsen, M., Knudsen, L.E., 2009. Human internal and external exposure to PBDEs – a review of levels and sources. Int. J. Hyg Environ. Health 212, 109–134. https://doi.org/10.1016/j.ijheh.2008.04.005.

Fromme, H., Albrecht, M., Appel, M., Hilger, B., Völkel, W., Liebl, B., Roscher, E., 2015. PCBs, PCDD/Fs, and PBDEs in blood samples of a rural population in South Germany. Int. J. Hyg Environ. Health 218, 41–46. https://doi.org/10.1016/j.ijheh.2014.07.004.

Glynn, A., Lignell, S., Darnerud, P.O., Aune, M., Halldin Ankarberg, E., Bergdahl, I.A., Barregård, L., Bensryd, I., 2011. Regional differences in levels of chlorinated and brominated pollutants in mother's milk from primiparous women in Sweden. Environ. Int. 37, 71–79. https://doi.org/10.1016/j.envint.2010.07.003.

Govaerts, A., Verhaert, V., Covaci, A., Jaspers, V.L.B., Berg, O.K., Addo-Bediako, A., Jooste, A., Bervoets, L., 2018. Distribution and bioaccumulation of POPs and mercury in the Ga-Selati river (South Africa) and the rivers Gudbrandsdalslågen and rena (Norway). Environ. Int. 121, 1319–1330. https://doi.org/10.1016/j.envint.2018.10.058.

Govarts, E., 2018. A06_Calculation of European Reference Values [WWW Document]. URL. https://www.hbm4eu.eu/mdocs-posts/a06_calculation-of-european-reference-values/.

Grandjean, P., Budtz-Jørgensen, E., Barr, D.B., Needham, L.L., Weihe, P., Heinzow, B., 2008. Elimination half-lives of polychlorinated biphenyl congeners in children. Environ. Sci. Technol. 42, 6991–6996. https://doi.org/10.1021/es800778q.

Hageman, K.J., Bogdal, C., Scheringer, M., 2015. Long-Range and Regional Atmospheric Transport of POPs and Implications for Global Cycling, pp. 363–387. https://doi.org/10.1016/B978-0-444-63299-9.00011-9.

Harden, F.A., Toms, L.M.L., Symons, R., Fürst, P., Berry, Y., Müller, J.F., 2007. Evaluation of dioxin-like chemicals in pooled human milk samples collected in Australia. Chemosphere 67, S325–S333. https://doi.org/10.1016/j.chemosphere.2006.05.126.

Heath, E., Ščančar, J., Zuliani, T., Milačič, R., 2010. A complex investigation of the extent of pollution in sediments of the Sava River: part 2: persistent organic pollutants. Environ. Monit. Assess. 163, 277–293. https://doi.org/10.1007/s10661-009-0833-9.

Hebert, C.E., Keenleyside, K.A., 1995. To normalize or not to normalize? Fat is the question. Environ. Toxicol. Chem. 14, 801–807. https://doi.org/10.1002/etc.5620140509.

Henríquez-Hernández, L.A., Ortiz-Andrelluchi, A., Álvarez-Pérez, J., Acosta-Dacal, A., Zumbado, M., Martínez-González, M.A., Boada, L.D., Salas-Salvadó, J., Luzardo, O. P., Serra-Majem, L., 2021. Human biomonitoring of persistent organic pollutants in elderly people from the Canary Islands (Spain): a temporal trend analysis from the PREDIMED and PREDIMED-Plus cohorts. Sci. Total Environ. 758 (143637) https://doi.org/10.1016/j.scitotenv.2020.143637.

Horvat, M., Mazej, D., Snoj Tratnik, J., Osredkar, J., Krsnik, M., Lapanje, V., Harlander, D., Miljavec, B., Kobal, A.B., 2010. Monitoring kemikalij v organizmih 2007 – 2009. Ljubljana.

Horvat, M., Baskar, M., Cenčič Kodba, Z., Fajon, V., Jagodic, M., Križanec, B., Krsnik, M., Levačič, Z., Mazej, D., Pavlin, M., Prezelj, M., Skitek, M., Snoj Tratnik, J., Stajnko, A., Šlejkovec, Z., Vončina, E., Žerjal, E., 2015. Monitoring kemikalij in njihovih ostankov v ljudeh za leto 2011-2014. Ljubljana.

Hrvatin, M., Komac, B., Zorn, M., 2020. Water Resources in Slovenia, pp. 47–79. https://doi.org/10.1007/978-3-030-22468-4_3.

Ingelido, A.M., Ballard, T., Dellatte, E., di Domenico, A., Ferri, F., Fulgenzi, A.R., Herrmann, T., Iacovella, N., Miniero, R., Päpke, O., Porpora, M.G., Felip, E. De, 2007. Polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in milk from Italian women living in Rome and Venice. Chemosphere 67, S301–S306. https://doi.org/10.1016/j.chemosphere.2006.05.111.

Ingelido, A.M., Abate, V., Abballe, A., Albano, F.L., Battista, T., Carraro, V., Conversano, M., Corvetti, R., De Luca, S., Franchini, S., Fulgenzi, A.R., Giambanco, L., Iacovella, N., Iamiceli, A.L., Maiorana, A., Maneschi, F., Marra, V., Pirola, F., Porpora, M.G., Procopio, E., Suma, N., Valentini, S., Valsenti, L., Vecchiè, V., De Felip, E., 2017. Concentrations of polychlorinated dibenzodioxins, polychlorodibenzofurans, and polychlorobiphenyls in women of reproductive age in Italy: a human biomonitoring study. Int. J. Hyg. Environ. Health 220, 378–386. https://doi.org/10.1016/j.ijheh.2016.11.009.

Islam, R., Kumar, S., Karmoker, J., Kamruzzaman, M., Rahman, M.A., Biswas, N., Tran, T. K.A., Rahman, M.M., 2018. Bioaccumulation and adverse effects of persistent organic pollutants (POPs) on ecosystems and human exposure: a review study on Bangladesh perspectives. Environ. Technol. Innov 12, 115–131. https://doi.org/10.1016/j.eti.2018.08.002.

Jan, J., Tratnik, M., 1988. Polychlorinated biphenyls in residents around the river Krupa, Slovenia, Yugoslavia. Bull. Environ. Contam. Toxicol. 41, 809–814. https://doi.org/10.1007/BF02021038.

Kalantzi, O.I., Martin, F.L., Thomas, G.O., Alcock, R.E., Tang, H.R., Drury, S.C., Carmichael, P.L., Nicholson, J.K., Jones, K.C., 2004. Different levels of polybrominated diphenyl ethers (PBDEs) and chlorinated compounds in breast milk from two U.K. Regions. Environ. Health Perspect. 112, 1085–1091. https://doi.org/10.1289/ehp.6991.

Kim, D., Ryu, H.-Y., Lee, Jun H., Lee, Jin H., Lee, Y.J., Kim, H.-K., Jang, D.D., Kim, H.S., Yoon, H.-S., 2013. Organochlorine pesticides and polychlorinated biphenyls in Korean human milk: contamination levels and infant risk assessment. J. Environ. Sci. Heal. Part B 48, 243–250. https://doi.org/10.1080/03601234.2013.742413.

Klomp, S.D., Manson, M.L., Guchelaar, H.-J., Swen, J.J., 2020. Phenoconversion of cytochrome P450 metabolism: a systematic review. J. Clin. Med. 9 (2890) https://doi.org/10.3390/jcm9092890.

Koh, K.H., Pan, X., Zhang, W., McLachlan, A., Urrutia, R., Jeong, H., 2014. Krüppel-like factor 9 promotes hepatic cytochrome P450 2D6 expression during pregnancy in CYP2D6-humanized mice. Mol. Pharmacol. 86, 727–735. https://doi.org/10.1124/mol.114.093666.

Kunisue, T., Muraoka, M., Ohtake, M., Sudaryanto, A., Minh, N.H., Ueno, D., Higaki, Y., Ochi, M., Tsydenova, O., Kamikawa, S., Tonegi, T., Nakamura, Y., Shimomura, H., Nagayama, J., Tanabe, S., 2006. Contamination status of persistent organochlorines in human breast milk from Japan: recent levels and temporal trend. Chemosphere 64, 1601–1608. https://doi.org/10.1016/j.chemosphere.2005.11.010.

Li, J., Zhang, L., Wu, Y., Liu, Y., Zhou, P., Wen, S., Liu, J., Zhao, Y., Li, X., 2009. A national survey of polychlorinated dioxins, furans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in human milk in China. Chemosphere 75, 1236–1242. https://doi.org/10.1016/j.chemosphere.2009.01.073.

Li, L., Hoang, C., Arnot, J.A., Wania, F., 2019. Clarifying temporal trend variability in human biomonitoring of polybrominated diphenyl ethers through mechanistic modeling. Environ. Sci. Technol. acs.est.9b04130. https://doi.org/10.1021/acs.est.9b04130.

Lignell, S., Aune, M., Darnerud, P.O., Cnattingius, S., Glynn, A., 2009. Persistent organochlorine and organobromine compounds in mother's milk from Sweden 1996–2006: compound-specific temporal trends. Environ. Res. 109, 760–767. https://doi.org/10.1016/j.envres.2009.04.011.

Linhardt, D.L., 2005. Recalculation of U.S. Background Dioxin Blood Serum Levels. North Caroline, Cary.

Logar, M., Rode, B., Verbič, J., Makinda Majaron, T., 2016. Informative Inventory Report for Slovenia, Submission under the UNECE Convention on Long-Range Transboundary Air Pollution.

Main, K.M., Kiviranta, H., Virtanen, H.E., Sundqvist, E., Tuomisto, J.T., Tuomisto, J., Vartiainen, T., Skakkebæk, N.E., Toppari, J., 2007. Flame retardants in placenta and breast milk and cryptorchidism in newborn boys. Environ. Health Perspect. 115, 1519–1526. https://doi.org/10.1289/ehp.9924.

Mannetje, A., t Coakley, J., Bridgen, P., Brooks, C., Harrad, S., Smith, A.H., Pearce, N., Douwes, J., 2013. Current concentrations, temporal trends and determinants of persistent organic pollutants in breast milk of New Zealand women. Sci. Total Environ. 458–460, 399–407. https://doi.org/10.1016/j.scitotenv.2013.04.055.

Miklavčič, A., Stibilj, V., Heath, E., Polak, T., Tratnik, J.S., Klavž, J., Mazej, D., Horvat, M., 2011. Mercury, selenium, PCBs and fatty acids in fresh and canned fish available on the Slovenian market. Food Chem. 124, 711–720. https://doi.org/10.1016/j.foodchem.2010.06.040.

Milojković, V., 2013. Mahovi Kot bioindikatorji Onesnaženosti zraka z Organskimi Onesnažili. University of Ljubljana.

Miyashita, C., Sasaki, S., Saijo, Y., Okada, E., Kobayashi, S., Baba, T., Kajiwara, J., Todaka, T., Iwasaki, Y., Nakazawa, H., Hachiya, N., Yasutake, A., Murata, K., Kishi, R., 2015. Demographic, behavioral, dietary, and socioeconomic characteristics related to persistent organic pollutants and mercury levels in pregnant women in Japan. Chemosphere 133, 13–21. https://doi.org/10.1016/j.chemosphere.2015.02.062.

Nawab, J., Wang, X., Khan, S., Tang, Y.-T., Rahman, Z., Ali, A., Dotel, J., Li, G., 2020. New insights into the bioaccumulation of persistent organic pollutants in remote alpine lakes located in Himalayas. Pakistan. Environ. Pollut 114952. https://doi.org/10.1016/j.envpol.2020.114952.

Nøst, T.H., Berg, V., Hanssen, L., Rylander, C., Gaudreau, E., Dumas, P., Breivik, K., Sandanger, T.M., 2019. Time trends of persistent organic pollutants in 30 year olds sampled in 1986, 1994, 2001 and 2007 in Northern Norway: measurements, mechanistic modeling and a comparison of study designs. Environ. Res. 172, 684–692. https://doi.org/10.1016/j.envres.2019.02.047.

Odabasi, M., Cetin, B., Bayram, A., 2015. Persistent organic pollutants (POPs) on fine and coarse atmospheric particles measured at two (urban and industrial) sites. Aerosol Air Qual. Res. 15, 1894–1905. https://doi.org/10.4209/aaqr.2015.02.0118.

Offenthaler, I., Bassan, R., Belis, C., Garo-Stach, I., Ganz, S., Iozza, S., Jakobi, G., Kaiser, A., Kirchner, M., Knoth, W., Kräuchi, N., Levy, W., Moche, W., Nurmi-Legat, J., Raccanelli, S., Schramm, K.-W., Schröder, P., Sedivy, I., Simončič, P., Staudinger, M., Thanner, G., Uhl, M., Vilhar, U., Weiss, P., 2009. MONARPOP Technical Report.

Oliveira, P., Ribeiro, J., Donato, H., Madeira, N., 2017. Smoking and antidepressants pharmacokinetics: a systematic review. Ann. Gen. Psychiatr. 16 (17) https://doi.org/10.1186/s12991-017-0140-8.

Pacheco Ferreira, A., Rabello Alves, S., 2015. Investigation of polychlorinated dioxins, furans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in human milk. J. Chem. Heal. Risks 5, 73–80.

Patil, I., 2018. Ggstatsplot: "Ggplot2" Based Plots with Statistical Details.

Pezdirc, M., Heath, E., Bizjak Mali, L., Bulog, B., 2011. PCB accumulation and tissue distribution in cave salamander (Proteus anguinus anguinus, Amphibia, Urodela) in the polluted karstic hinterland of the Krupa River, Slovenia. Chemosphere 84, 987–993. https://doi.org/10.1016/j.chemosphere.2011.05.026.

Polder, A., Gabrielsen, G.W., Odland, J.Ø., Savinova, T.N., Tkachev✠, A., Løken, K.B., Skaare, J.U., 2008a. Spatial and temporal changes of chlorinated pesticides, PCBs, dioxins (PCDDs/PCDFs) and brominated flame retardants in human breast milk from Northern Russia. Sci. Total Environ. 391, 41–54. https://doi.org/10.1016/j.scitotenv.2007.10.045.

Polder, A., Thomsen, C., Lindström, G., Løken, K.B., Skaare, J.U., 2008b. Levels and temporal trends of chlorinated pesticides, polychlorinated biphenyls and brominated flame retardants in individual human breast milk samples from Northern and Southern Norway. Chemosphere 73, 14–23. https://doi.org/10.1016/j.chemosphere.2008.06.002.

Polder, A., Skaare, J.U., Skjerve, E., Løken, K.B., Eggesbø, M., 2009. Levels of chlorinated pesticides and polychlorinated biphenyls in Norwegian breast milk (2002–2006), and factors that may predict the level of contamination. Sci. Total Environ. 407, 4584–4590. https://doi.org/10.1016/j.scitotenv.2009.04.032.

Polič, S., Leskovšek, H., Horvat, M., 2000. PCB pollution of the karstic environment (Krupa River, Slovenia). Acta Carsol. 29, 141–152.

Porta, M., Puigdomènech, E., Ballester, F., Selva, J., Ribas-Fitó, N., Llop, S., López, T., 2008. Monitoring concentrations of persistent organic pollutants in the general population: the international experience. Environ. Bar Int. 34, 546–561. https://doi.org/10.1016/j.envint.2007.10.004.

Porta, M., López, T., Gasull, M., Rodríguez-Sanz, M., Garí, M., Pumarega, J., Borrell, C., Grimalt, J.O., 2012. Distribution of blood concentrations of persistent organic pollutants in a representative sample of the population of Barcelona in 2006, and comparison with levels in 2002. Sci. Total Environ. 423, 151–161. https://doi.org/10.1016/j.scitotenv.2012.02.001.

Pratt, I.S., Anderson, W.A., Crowley, D., Daly, S.F., Evans, R.I., Fernandes, A.R., Fitzgerald, M., Geary, M.P., Keane, D.P., Malisch, R., McBride, J., Morrison, J.J., Reilly, A., Tlustos, C., 2012. Polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in breast milk of first-time Irish mothers: impact of the 2008 dioxin incident in Ireland. Chemosphere 88, 865–872. https://doi.org/10.1016/j.chemosphere.2012.03.095.

Raab, U., Preiss, U., Albrecht, M., Shahin, N., Parlar, H., Fromme, H., 2008. Concentrations of polybrominated diphenyl ethers, organochlorine compounds and nitro musks in mother's milk from Germany (Bavaria). Chemosphere 72, 87–94. https://doi.org/10.1016/j.chemosphere.2008.01.053.

Rawn, D.F.K., Ryan, J.J., Sadler, A.R., Sun, W.-F., Haines, D., Macey, K., Van Oostdam, J., 2012. PCDD/F and PCB concentrations in sera from the Canadian health measures survey (CHMS) from 2007 to 2009. Environ. Int. 47, 48–55. https://doi.org/10.1016/j.envint.2012.05.008.

Rawn, D.F.K., Sadler, A.R., Casey, V.A., Breton, F., Sun, W.-F., Arbuckle, T.E., Fraser, W. D., 2017. Dioxins/furans and PCBs in Canadian human milk: 2008–2011. Sci. Total Environ. 595, 269–278. https://doi.org/10.1016/j.scitotenv.2017.03.157.

Rodas-Ortíz, J.P., Ceja-Moreno, V., González-Navarrete, R.L., Alvarado-Mejía, J., Rodríguez-Hernández, M.E., Gold-Bouchot, G., 2008. Organochlorine pesticides and polychlorinated biphenyls levels in human milk from chelem, Yucatán, México. Bull. Environ. Contam. Toxicol. 80, 255–259. https://doi.org/10.1007/s00128-007-9356-7.

Rode, B., Gartner, D., Logar, M., Kanduč, T., 2010. Informative Inventory Report 2010 for Slovenia : Submission under the UNECE Convention on Longe-Range Transboundary Air Pollution. Ljubljana.

Ryan, J.J., Rawn, D.F.K., 2014. Polychlorinated dioxins, furans (PCDD/Fs), and polychlorinated biphenyls (PCBs) and their trends in Canadian human milk from 1992 to 2005. Chemosphere 102, 76–86. https://doi.org/10.1016/j.chemosphere.2013.12.065.

Schulz, C., Wilhelm, M., Heudorf, U., Kolossa-Gehring, M., 2011. Update of the reference and HBM values derived by the German human biomonitoring commission. Int. J. Hyg Environ. Health 215, 26–35. https://doi.org/10.1016/j.ijheh.2011.06.007.

Schwarzenbach, R.P., Egli, T., Hofstetter, T.B., von Gunten, U., Wehrli, B., 2010. Global water pollution and human health. Annu. Rev. Environ. Resour. 35, 109–136. https://doi.org/10.1146/annurev-environ-100809-125342.

She, J., Holden, A., Sharp, M., Tanner, M., Williams-Derry, C., Hooper, K., 2007. Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in breast milk from the Pacific Northwest. Chemosphere 67, S307–S317. https://doi.org/10.1016/j.chemosphere.2006.05.154.

Republika Slovenije, 2008. Naše Okolje. Letnik XV. Številka 1-12, Ljubljana.

Republika Slovenije, 2009. Naše Okolje. Letnik XVI. Številka 1-12, Ljubljana.

Republika Slovenije, 2011. Naše Okolje. Letnik XVIII. Številka 1-12, Ljubljana.

Republika Slovenije, 2012. Naše Okolje. Letnik XIX. Številka 1-12, Ljubljana.

Republika Slovenije, 2013. Naše Okolje. Letnik XX. Številka 1-12, Ljubljana.

Republika Slovenije, 2014. Naše Okolje. Letnik XXI. Številka 1-12, Ljubljana.

Smrekar, A., Breg Valjavec, M., Polajnar Horvat, K., 2020. Human-induced degradation in Slovenia. In: The Geography of Slovenia. Springer, Cham.

Snoj Tratnik, J., Falnoga, I., Mazej, D., Kocman, D., Fajon, V., Jagodic, M., Stajnko, A., Trdin, A., Šlejkovec, Z., Jeran, Z., Osredkar, J., Sešek-Briški, A., Krsnik, M., Kobal, A. B., Kononenko, L., Horvat, M., 2019. Results of the first national human biomonitoring in Slovenia: trace elements in men and lactating women, predictors of exposure and reference values. Int. J. Hyg Environ. Health 222, 563–582. https://doi.org/10.1016/j.ijheh.2019.02.008.

Solberg, H.E., 1987a. Approved recommendation (1986) on the theory of reference values. Part 1. The concept of reference values. Clin. Chim. Acta 165, 111–118. https://doi.org/10.1016/0009-8981(87)90224-5.

Solberg, H.E., 1987b. Approved recommendation (1987) on the theory of reference values. Part 5. Statistical treatment of collected reference values. Determination of reference limits. Clin. Chim. Acta 170, S13–S32. https://doi.org/10.1016/0009-8981(87)90151-3.

Solomon, G.M., Weiss, P.M., 2002. Chemical contaminants in breast milk: time trends and regional variability. Environ. Health Perspect. 110 https://doi.org/10.1289/ehp.021100339.

Thomsen, C., Stigum, H., Frøshaug, M., Broadwell, S.L., Becher, G., Eggesbø, M., 2010. Determinants of brominated flame retardants in breast milk from a large scale Norwegian study. Environ. Int. 36, 68–74. https://doi.org/10.1016/j.envint.2009.10.002.

Toms, L.-M.L., Harden, F.A., Symons, R.K., Burniston, D., Fürst, P., Müller, J.F., 2007. Polybrominated diphenyl ethers (PBDEs) in human milk from Australia. Chemosphere 68, 797–803. https://doi.org/10.1016/j.chemosphere.2007.02.059.

Tsukino, H., Hanaoka, T., Sasaki, H., Motoyama, H., Hiroshima, M., Tanaka, T., Kabuto, M., Turner, W., Patterson, D.G., Needham, L., Tsugane, S., 2006. Fish intake and serum levels of organochlorines among Japanese women. Sci. Total Environ. 359, 90–100. https://doi.org/10.1016/j.scitotenv.2005.04.014.

Umweltbundesamt, 2002. Dioxin-Referenzmessprogramm. 4. Bericht der Bund/Länder-Arbeitsgruppe DIOXINE, Bonn.

Van den Berg, M., Birnbaum, L.S., Denison, M., De Vito, M., Farland, W., Feeley, M., Fiedler, H., Hakansson, H., Hanberg, A., Haws, L., Rose, M., Safe, S., Schrenk, D., Tohyama, C., Tritscher, A., Tuomisto, J., Tysklind, M., Walker, N., Peterson, R.E., 2006. The 2005 world health organization reevaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds. Toxicol. Sci. 93, 223–241. https://doi.org/10.1093/toxsci/kfl055.

Warenik-Bany, M., Maszewski, S., Mikolajczyk, S., Piskorska-Pliszczynska, J., 2019. Impact of environmental pollution on PCDD/F and PCB bioaccumulation in game animals. Environ. Pollut. 255 (113159) https://doi.org/10.1016/j.envpol.2019.113159.

Wasser, J., Berman, T., Lerner-Geva, L., Grotto, I., Rubin, L., 2015. Biological monitoring of persistent organic pollutants in human milk in Israel. Chemosphere 137, 185–191. https://doi.org/10.1016/j.chemosphere.2015.07.038.

Weiss, P., Moche, W., 2015. MONARPOP – ERGEBNISSE DER DIOXIN- UND PCB-MESSUNGEN IN LUFT. UND DEPOSITION, Wien.

WHO, 2007. Fourth WHO-coordinated survey of human milk for persistent organic pollutants in cooperation with UNEP. Guidelines for Developing a National Protocol.

Wilhelm, M., Ewers, U., Schulz, C., 2003. Revised and new reference values for some persistent organic pollutants (POPs) in blood for human biomonitoring in environmental medicine. Int. J. Hyg Environ. Health 206, 223–229. https://doi.org/10.1078/1438-4639-00208.

Wong, T.W., Wong, A.H.S., Nelson, E.A.S., Qiu, H., Ku, S.Y.K., 2013. Levels of PCDDs, PCDFs, and dioxin-like PCBs in human milk among Hong Kong mothers. Sci. Total Environ. 463–464, 1230–1238. https://doi.org/10.1016/j.scitotenv.2012.07.097.

Zhang, L., Li, J., Zhao, Y., Li, X., Yang, X., Wen, S., Cai, Z., Wu, Y., 2011. A national survey of polybrominated diphenyl ethers (PBDEs) and indicator polychlorinated biphenyls (PCBs) in Chinese mothers' milk. Chemosphere 84, 625–633. https://doi.org/10.1016/j.chemosphere.2011.03.041.

Zhang, L., Yin, S., Zhao, Y., Shi, Z., Li, J., Wu, Y., 2017. Polybrominated diphenyl ethers and indicator polychlorinated biphenyls in human milk from China under the Stockholm Convention. Chemosphere 189, 32–38. https://doi.org/10.1016/j.chemosphere.2017.09.014.

Zietz, B.P., Hoopmann, M., Funcke, M., Huppmann, R., Suchenwirth, R., Gierden, E., 2008. Long-term biomonitoring of polychlorinated biphenyls and organochlorine pesticides in human milk from mothers living in northern Germany. Int. J. Hyg Environ. Health 211, 624–638. https://doi.org/10.1016/j.ijheh.2008.04.001.

Zupan, M., Grčman, H., Lobnik, F., 2008. (ARSO), A.R.S. za O. Raziskave Onesnaženosti tal Slovenije, Ljubljana.