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Levels of persistent halogenated organic pollutants (POP's) in human milk from first-time mothers in Uppsala, Sweden: results from year 2023-2024, and temporal trends for the time period 1996-2024

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Sammanfattning
Sedan 1996 har Livsmedelsverket regelbundet samlat in modersmjölk från förstföderskor i Uppsala för analys av persistenta halogenerade organiska miljöföroreningar (POP). I följande rapport redovisas halterna av industrikemikalien PCB (mono-, di- och non-*orto* PCB), oavsiktligt bildade dioxiner och furaner (PCDD/F) och bromerade flamskyddsmedel (PBDE och HBCDD) i 30 modersmjölksprover insamlade 2023-2024. Nya data har också använts för att uppdatera tidstrenderna för dessa ämnen. Bland PCBerna var medelkoncentrationen i modersmjölk (2023-2024) högst för CB 153 (15 ng/g fett). Medelhalten för PCDD TEQ och PCDF TEQ var 0,75 respektive 0,76 pg/g fett beräknade med de nya toxiska ekvivalensfaktorerna, 2022 WHO TEF. Bland de polybromerade difenyletrarna (PBDE) hade BDE 153 (0,52 ng/g fett) högst medelhalt.

Utvärdering av tidstrender för perioden 1996-2024 visade att halterna av di-*orto* PCBer, mono-*orto* PCB TEQ och non-*orto* PCB TEQ har minskat med i medeltal 5-6 % per år. Halterna av PCDD TEQ har minskat fortare än halterna av PCDF TEQ (7 % respektive 3 % per år). När olika tidperioder studerades visade resultaten att minskningen skett snabbare i början av studien 1996-2006/2007 jämfört med den senare delen fram till 2024 förutom för CB 28 som minskar snabbare under den sista delen (2014-2024). Även om modersmjölknivåerna av total TEQ minskar, hade fortfarande 4 av de 30 kvinnor som provtagits under 2023-2024 nivåer över Efsas modellerade kritiska halt för modersmjölk (beräknat utifrån de tidigare TEFarna från 2005).

Resultaten visade att summahalterna av dioxinlika PCB, PCDF och PCDD var lägre om TEFarna från 2022 användes i jämförelse med de från 2005, i medel 44 % för summa PCB/PCDD/F TEQ.

Halterna av BDE 47, BDE 99, BDE 100, sumPBDE och HBCDD har minskat med 6-12% per år 1996-2024. När studieperioden delades upp i flera delar visar resultaten att halterna sjunker snabbare mot slutet av perioden. BDE 209 har bara analyserats kontinuerligt i modersmjölk sedan 2009 och den minskning som för första gången sågs i föregående rapport har nu bekräftats, med en minskning omkring 7% per år. För BDE 153, BDE 209 och HBCDD ökade halterna signifikant i bröstmjölk 1996-2002/2007/2012 och därefter minskade halterna med i medeltal 3, 12 respektive 10 %.

Resultaten stämmer överens med det som rapporterats tidigare inom POPUP. Fortsatta undersökningar av POPar i modersmjölk kan ge svar på om halterna av PCBer och PCDD/F håller på att stabiliseras på nuvarande nivåer eller om nivåerna fortsätter att minska.

INTRODUCTION

With funding from the Swedish Environmental Protection Agency (EPA), the Swedish Food Agency (SFA) has made recurrent measurements of persistent halogenated organic pollutants (POP) in human milk from primiparous women in Uppsala since 1996. The study is called POPUP (Persistent Organic Pollutants in Uppsala Primiparas), and the aim is to estimate the body burdens of POP among pregnant and nursing women and to estimate temporal trends of the exposure of fetuses and breast-fed infants. Temporal trends of polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), poly-chlorinated dibenzofurans (PCDFs), brominated flame retardants (e.g. polybrominated diphenylethers (PBDE)), and hexabromocyclododecane (HBCDD) between 1996 and 2024 have been published earlier (Glynn et al. 2007a, Lignell et al. 2008, Lignell et al. 2009a, Lignell et al. 2009b, Lignell et al. 2012, Lignell et al. 2014, Lignell et al. 2015, Gyllenhammar et al 2017, Gyllenhammar et al. 2021, Hedvall Kallerman et al. 2021, Hedvall Kallerman et al. 2023, Hedvall Kallerman et al. 2024a), and this is a follow-up.

The following report presents results of analysis of di-*ortho* PCBs, mono-*ortho* PCBs, non-*ortho* PCBs, PCDD/Fs, PBDEs, and HBCDD in human milk sampled in 2023-2024 (according to agreement 215-24-005). The new data is used to establish updated temporal trends for the period 1996-2024. The temporal trends in human milk are also used as one of the indicators for the environmental quality objectives "A non-toxic environment" (sverigesmiljomal.se).

New TEFs from WHO

The toxicity of the individual congeners of dioxins, furans, and dioxin-like PCBs are expressed as toxic equivalency factors (TEFs) and are set in relation to the compound considered the most toxic, 2,3,7,8-TCDD, which is given the TEF 1. The TEF is multiplied by the concentration of each compound to generate toxic equivalents (TEQs). In 2024 new TEFs were published and the new are referred to as 2022 WHO TEFs (DeVito et al. 2024) compared to the older TEFs from 2005, 2005 WHO TEFs (Van den Berg et al. 2006). Several compounds were given lower TEFs in the revised version of WHO TEFs (DeVito et al. 2024). This is in part due to an updated database, and a different method to evaluate the data, than for the 2005 WHO TEFs. The 2005 WHO TEFs were used by the European Food Safety Authority (EFSA), in 2018, when publishing a scientific opinion on health risks of PCDD/Fs and dioxin-like PCBs in food (EFSA 2018). EFSA established a tolerable weekly intake (TWI) of 2 pg TEQ_{2005}/kg body

weight/week. When establishing the TWI, a modelling of a safe lifetime maternal body burden before pregnancy was performed to protect children from negative health effects (taking into account pregnancy and 12 months of breastfeeding). As a result, an estimated safe human milk level was determined to 5.9 pg TEQ_{2005}/g lipid based on 2005 WHO TEF (Van den Berg et al. 2006). As the EFSA estimated "safe human milk level" is based on 2005 WHO TEFs, comparisons with data from the POPUP-study in the present report are made on data calculated with the 2005 WHO TEFs. EFSA is currently re-evaluating the scientific opinion on health risks of PCDD/Fs and dioxin-like PCBs in food that is estimated to be finished during spring 2026.

MATERIALS AND METHODS

Recruitment and sampling

Mothers were randomly recruited among primiparas who were Swedish by birth and delivered at Uppsala University Hospital from January 2023 to November 2024 (n=60). The participating rate was 50% for the entire study period and 30% in 2023-2024.

The participating mothers sampled milk at home during the third week after delivery (day 14-21 post-partum). Milk was sampled during nursing using a manual human milk pump and/or a passive human milk sampler. The women were instructed to sample milk both at the beginning and at the end of the breast-feeding sessions. The goal was to sample 500 mL from each mother during 7 days of sampling. During the sampling week, the milk was stored in the home freezer in acetone-washed bottles. Newly sampled milk was poured on top of the frozen milk. At the end of the sampling week, a midwife visited the mother to collect the bottles. Data on age, weight, length etc. of the mothers were obtained from questionnaires (Table 1). The recruitment procedure has been described earlier (Glynn et al. 2007a, Lignell et al. 2009a). Human milk was sampled from a total of 969 women between 1996 and 2024 (60 women in 2023-2024). From the participants in 2023-2024, 30 women were randomly selected for analysis.

Table 1. Characteristics of the mothers in the study in 2023-2024 (n=30).

Variable		**N**	**Mean**	**Median**	**Range**
Age of the mother (yr)		30	31.2	29.9	24.2-44.0
Pre-pregnancy body mass index (BMI, kg/m^2)		30	23.8	22.7	16.9-39.2
Weight gain during pregnancy (% of initial weight)		30	19.9	20.8	0.0-35.6
Weight reduction from delivery to sampling (%)[a]		30	7.3	8.0	1.5-14.0
Variable		**N**	**%**		
Education	max 3-4 yr high school	5	17		
	1-3 yr higher education	8	27		
	>3 yr higher education	17	57		

[a]Weight reduction minus birth weight of the child in % of the mothers weight just before delivery.

Analysis

The compounds that were analysed in the human milk samples from 2023 to 2024 were 6 non-dioxin like PCBs (CB 28, 52, 101, 138, 153, 180), 8 mono-*ortho* substituted PCBs (CB 105, 114, 118, 123, 156, 157, 167, 189), 4 non-*ortho* PCBs (CB 77, 81, 126, 169), 7 tetra- to octa-chlorinated PCDD congeners, 10 tetra- to octa-chlorinated PCDF congeners, 10 tri- to deca-brominated PBDE-congeners (BDE 28, 47, 66, 99, 100, 153, 154, 183, 209), and hexabromocyclododecane (HBCDD).

All analyses of samples from 2023 to 2024 were performed at the SFA. PCBs and PCDD/Fs were analysed using a method based on Aune et al. 2012 with modifications. Briefly the determination was performed with gas chromatography coupled to high resolution mass spectrometry (GC-HRMS) using isotopic dilution technique and single ion monitoring (SIM) at the resolution of 10 000. The clean-up and fractionation of PCBs and PCDD/Fs was performed with a Miura GO-2HT from Miura Co (Japan). PBDEs and HBCDD were analysed by gas chromatography/mass spectroscopy/electron-capture negative ionization (GC/MS/ECNI) using SIM technique (Lignell et al. 2009a).

In all analyses, internal standards were added to samples prior to extraction to correct for analytical losses and to ensure quality control. A number of control samples were analysed together with the samples to verify the accuracy and precision of the measurements. The laboratory is accredited according to ISO/ICE 17025 for analysis of PCDD/F, PCBs, and brominated flame retardants in human milk.

Calculations and statistics

A few mothers recruited in the beginning of the study were not Swedish by birth, and mothers who were born in non-Nordic countries (n=13) were excluded before the statistical analysis of temporal trends 1996-2024. After this exclusion, a total of 655 women were included in the data set. Human milk concentrations of POPs were lipid-adjusted and when the concentrations were below the limit of quantification (LOQ), half of LOQ (medium bound, MB) was taken as an estimated value in the calculations. PBDEs and HBCDD concentrations were adjusted for concentrations in blank samples. PBDE-levels below LOQ were available for human milk samples from 2009-2024 (and in some samples 2002-2008) and these reported levels below LOQ (adjusted for levels in blank samples) were used instead of half of LOQ. Levels estimated to be zero or negative after blank reduction were in the statistical analyses set to the lowest estimated level found above zero for each compound.

Before the evaluation of temporal trends, POPs were grouped into di-*ortho* PCBs (sum of CB 153, 138, and 180), mono-*ortho* PCB toxic equivalents (TEQ) (sum of CB 105, 118, 156, and 167 TEQs), non-*ortho* PCB TEQ (sum of CB 77, 126, and 169 TEQs), PCDD TEQ, PCDF TEQ and sumPBDE (sum of BDE 47, 99, 100, and 153) (Table 2 and 3). In addition, temporal trends were evaluated for the single compounds CB 28, CB 153, BDE 47, BDE 99, BDE 100, BDE 153, BDE 209, and HBCDD. BDE 209 was included in the analytical method in year 2009 and has so far only been quantified in samples collected in 2009-2024, and in some samples 1999, and 2002-2007. However, in the statistical analyses only data from 2009-2024 for BDE 209 were used. Calculated TEQs were based on 2022 WHO TEFs for PCB/PCDD/F (DeVito et al. 2024) but calculations based on the 2005 WHO TEFs (Van den Berg et al. 2006) were also presented in Table 2 and Figure 1 for comparison. The temporal trends were based on 2022 WHO TEFs (Table 4).

Temporal trends were investigated for the whole study period (1996-2024) using multiple linear regressions to analyse associations between concentrations of POPs in human milk and sampling year. Logarithmically transformed POP-levels were used to present the association between sampling year and POP concentrations as percent change of concentrations per year. In addition, linear regression models with sampling year modeled with restricted cubic splines (henceforth called cubic spline models) were used to analyse associations between log-transformed concentrations and sampling year (shown as a red line in trend graphs, Figure 2-3 and Appendix). Multiple linear regressions and cubic spline models were adjusted for independent variables (life-style factors) that have been shown to influence POP levels in serum and human milk (Glynn et al. 2007b, Lignell et al. 2011). The variables considered were age of the mother (years), pre-pregnancy body mass index (BMI) (kg/m^2), body weight gain during pregnancy (%), body weight change during the period from delivery to sampling (%), and educational level (Table 1 and 4-5). The number of knots for the cubic spline bases were determined by fitting models with 3 to 7 knots and the model that provided the lowest Akaike information criterion (AIC) was preferred. The temporal trends expressed as mean percentage change per year in Table 4-5 were assessed using linear regression models with sampling year modeled with linear splines (henceforth called linear spline models), where the specified knots were placed to approximate the cubic spline models. The linear spline models were adjusted for the same covariates as for the cubic spline models.

The specified knots in the linear spline models were placed at the year after the year with the highest geometric mean levels compared to 1996 (when two or more years had the same level the last year of the two were chosen). For BDE 209, the year 2009 was used for

comparison of geometric mean instead of 1996, since data was available only from 2009. If the geometric mean was decreasing throughout the time period, a change in size of the decrease between years were considered to set the specified knots, together with how the trend line in the trend graph was outlined. Statistical analyses were performed using the software package STATA version 19.0.

RESULTS AND DISCUSSION

PCB, dioxin and furan concentrations in human milk

Levels of PCBs, PCDDs, and PCDFs in milk samples collected in 2023-2024 are shown in Table 2. In Table 2 concentrations of dioxin-like PCBs, PCDDs, and PCDFs were calculated with the 2022 WHO TEFs with the 2005 WHO TEFs in parentheses. Among the PCBs, the di-*ortho* congener CB 153 showed the highest mean concentration (15 ng/g lipid) followed by CB 180 (8.8 ng/g lipid) and CB 138 (6.9 ng/g lipid) (Table 2). All PCB-congeners could be quantified in all samples, except of four samples for CB 52 and 12 samples for CB 123, although the levels of most congeners were very low (e.g. CB 28, 52, 101, 105, 114, 123, 157, 167, 189). CB 126 was the non-*ortho* congener with the highest concentration followed by CB 169, and these two contributed most to the non-*ortho* PCB TEQ_{2022}. Among the PCDD/Fs in Table 2, 1,2,3,4,7,8-HxCDF, 2,3,4,7,8-PeCDF, and 1,2,3,7,8-PeCDD contributed most to the total PCDD/F TEQ_{2022} concentration (19%, 18% and 18% respectively), followed by 2,3,7,8-TCDD (15%) (data not shown). The mean total-TEQ_{2022} level was 2.4 pg/g lipid and PCDFs, PCDDs, and non-*ortho* PCBs contributed almost equally to this level (mean 0.76, 0.75, and 0.74 pg TEQ/g lipid respectively) followed by mono-*ortho* PCBs (0.15 pg TEQ/g lipid) (Table 2).

In year 2023-2024, 13% of the women (4 out of 30 women) had human milk levels above the EFSA estimated safe level of 5.9 pg TEQ_{2005}/g lipid (calculated with 2005 WHO TEFs). Whereas for the entire study period, 1996-2024 it was estimated that 62% of the women had levels above the safe level.

Comparison of PCB/PCDD/F concentrations between 2005 and 2022 WHO TEFs

In Figure 1, mean concentrations of PCB TEQ, PCDD TEQ, and PCDF TEQ (1996-2024) are presented as TEQ_{2005} and TEQ_{2022}. The new 2022 TEFs, results in lower sum TEQs with the largest decrease for PCB TEQ, in mean 50%, followed by PCDD TEQ (41%) and PCDF TEQ (37%). For the total TEQ, the 2022 TEFs results in mean 44% lower human milk levels compared to the 2005 TEFs. This is in line with the 40-42% lower total TEQ_{2022} in human milk compared to total TEQ_{2005} presented by DeVito at al. (DeVito et al. 2024).

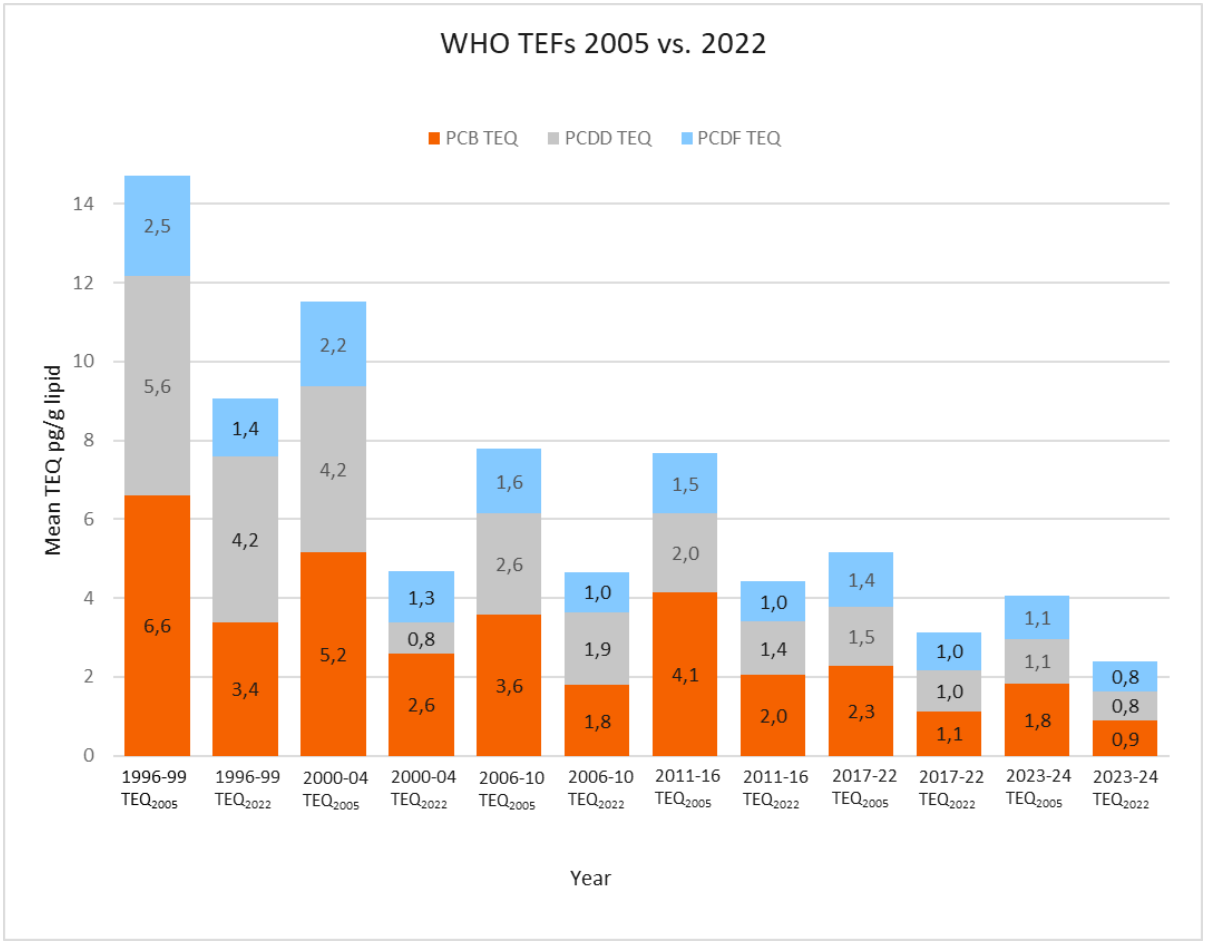


Figure 1. Comparison of mean concentrations of PCB TEQ, PCDD TEQ, and PCDF TEQ using WHO TEFs from 2005 and 2022, from the study period 1996-2024.

Table 2. Concentrations of PCBs and PCDD/Fs in human milk sampled from primiparous women in Uppsala in 2023-2024 (n=30). Values <LOQ were set to ½LOQ in the calculations of means, medians and TEQs.

Compound	**Mean**	**Median**	**Min**	**Max**	**n<LOQ**
PCBs (ng/g lipid)					
CB 28	0.64	0.47	0.25	2.0	0
CB 52	0.13	0.10	<0.004	0.58	4
CB 101	0.20	0.19	0.06	0.77	0
CB 138	6.9	6.2	1.8	13	0
CB 153	15	14	4.7	30	0
CB 180	8.8	7.8	1.8	24	0
di-*ortho* PCB[a]	31	28	9.3	63	-
CB 105	0.46	0.41	0.067	1.1	0
CB 114	0.12	0.11	0.042	0.24	0
CB 118	2.3	2.2	0.43	4.6	0
CB 123	0.02	0.02	<0.006	0.06	12
CB 156	1.8	1.6	0.46	4.1	0
CB 157	0.29	0.26	0.087	0.60	0
CB 167	0.38	0.35	0.10	0.88	0
CB 189	0.16	0.14	0.031	0.43	0
mono-*ortho* PCB TEQ_{2022}[b] (pg/g lipid)	0.15	0.14	0.047	0.28	-
non-*ortho* PCBs (pg/g lipid)					
CB 77	1.2	1.1	<0.5	2.8	4
CB 81	0.54	0.47	0.19	1.8	0
CB 126	14	12	1.0	47	0
CB 169	10	9.4	2.7	22	0
non-*ortho* PCB $TEQ_{2022\ (2005)}$[c]	0.74 (1.7)	0.66 (1.5)	0.09 (0.30)	2.4 (5.1)	-
PCDDs (pg/g lipid)					
2,3,7,8-TCDD	0.23	0.23	<0.01	0.52	2
1,2,3,7,8-PeCDD	0.68	0.68	<0.1	1.4	2
1,2,3,4,7,8-HxCDD	0.29	0.27	0.11	0.55	0
1,2,3,6,7,8-HxCDD	1.4	1.3	0.62	2.6	0
1,2,3,7,8,9-HxCDD	0.32	0.30	<0.05	0.81	2
1,2,3,4,6,7,8-HpCDD	2.1	2.0	0.67	7.2	0
OctaCDD	10	8.8	4.0	29	0
PCDD $TEQ_{2022\ (2005)}$	0.75 (1.1)	0.75 (1.0)	0.28 (0.32)	1.6 (2.3)	-
PCDFs (pg/g lipid)					
2,3,7,8-TCDF	0.23	0.18	<0.06	0.78	3
1,2,3,7,8-PeCDF	0.17	0.07	<0.09	0.87	16
2,3,4,7,8-PeCDF	2.7	2.3	0.91	5.2	0
1,2,3,4,7,8-HxCDF	1.0	0.88	0.29	2.6	0
1,2,3,6,7,8-HxCDF	0.97	0.78	0.34	2.6	0
1,2,3,7,8,9-HxCDF	0.09	0.09	<0.1	0.17	29
2,3,4,6,7,8-HxCDF	0.52	0.40	0.17	1.7	0
1,2,3,4,6,7,8-HpCDF	0.66	0.47	0.17	2.5	0
1,2,3,4,7,8,9-HpCDF	0.05	0.03	<0.03	0.27	26
OctaCDF	0.02	0.02	<0.01	0.09	21
PCDF $TEQ_{2022\ (2005)}$	0.76 (1.1)	0.67 (0.93)	0.25 (0.37)	1.8 (2.3)	-
PCDD/F $TEQ_{2022\ (2005)}$[d] (pg/g lipid)	1.5 (2.2)	1.5 (2.1)	0.53 (0.85)	3.4 (4.6)	-
TOTAL-$TEQ_{2022\ (2005)}$[e] (pg/g lipid)	2.4 (4.1)	2.4 (4.2)	0.67 (1.2)	4.9 (7.6)	-

[a]The sum of CB 153, 138 and 180. [b]The sum of CB 105, 118, 156, 167 TEQs (TEF_{2005} and TEF_{2022} have the same toxic equivalency factors). [c]The sum of CB 77, 126, 169 TEQs. [d]The sum of PCDD TEQ and PCDF TEQ. [e]The sum of mono-*ortho* PCB TEQ, non-*ortho* PCB TEQ, PCDD TEQ and PCDF TEQ.

PBDE and HBCDD concentrations in human milk

Levels of PBDEs and HBCDD in milk samples collected in 2023-2024 are shown in Table 3. Among the PBDEs, BDE 153 showed the highest mean concentration (0.52 ng/g lipids) followed by BDE 209 (0.43 ng/g lipids), BDE 47 (0.39 ng/g lipids), and BDE 99 (0.17 ng/g lipids) (Table 3). However, the levels of BDE 100 and BDE 154 and HBCDD were below LOQ in 22, 16, and 24 of the analysed samples, respectively. The level of BDE 28, BDE 47, BDE 66, BDE 99, BDE 183, and BDE 209 were also below LOQ in most samples (90-97%). Estimated PBDEs and HBCDD concentrations below LOQ, adjusted for concentrations in blank samples, are presented in brackets in Table 3 and were used in the analyses of temporal trends.

Table 3. Concentrations of PBDEs and HBCDD (ng/g lipid) in human milk sampled from primiparous women in Uppsala in 2023-2024 (n=30). Values below the LOQ were set to ½LOQ in the calculations of means, medians and sumPBDE. Levels below LOQ were also reported and calculated results using these levels (adjusted for levels in blank samples) are presented in brackets ([ ]).

Compound	Mean	Median	Min	Max	n<LOQ[b] [n=0][c]
BDE 28	0.03 [0.02]	0.02 [0.01]	<0.024 [0]	0.13	28 [1]
BDE 47	0.39 [0.32]	0.17 [0.06]	<0.18 [0]	6.0	27 [2]
BDE 66	0.02 [0.01]	0.02 [0.007]	<0.024 [0]	0.07	29 [2]
BDE 99	0.17 [0.09]	0.12 [0.01]	<0.13 [0]	1.7	28 [8]
BDE 100	0.08 [0.12]	0.03 [0.03]	<0.006 [0]	1.4	22 [2]
BDE 153	0.52	0.34	0.12	1.7	0 [0]
BDE 154	0.04 [0.05]	0.03 [0.04]	<0.024	0.14	16 [0]
BDE 183	0.03 [0.01]	0.02 [0.005]	<0.024 [0]	0.25	29 [5]
BDE 209	0.43 [0.14]	0.33 [0.01]	<0.36 [0]	3.5	29 [13]
sumPBDE(4)[a]	1.2 [1.01]	0.61 [0.53]	0.29 [0.13]	10.8	-
HBCDD	0.06 [0.05]	0.05 [0.03]	<0.046 [0.003]	0.17	24 [0]

[a]The sum of BDE 47, 99, 100, and 153. [b]Number of samples with levels below LOQ. [c]Number of samples with levels estimated to be zero or negative after adjustment for blank levels.

Temporal trends

Multiple linear regressions showed that the adjusted mean decrease in concentrations of PCBs were around 5-6% per year during 1996-2024, (Table 4, Figure 2, and Appendix). The mean decrease in levels of PCDD TEQ and PCDF TEQ were 6.8% and 2.6% respectively, showing a faster declining rate for PCDD TEQ than for PCDF TEQ (Table 4, Appendix). These results are in agreement with previous observed declining trends between 1996 and 2022 within the POPUP study (Hedvall Kallerman et al. 2024a).

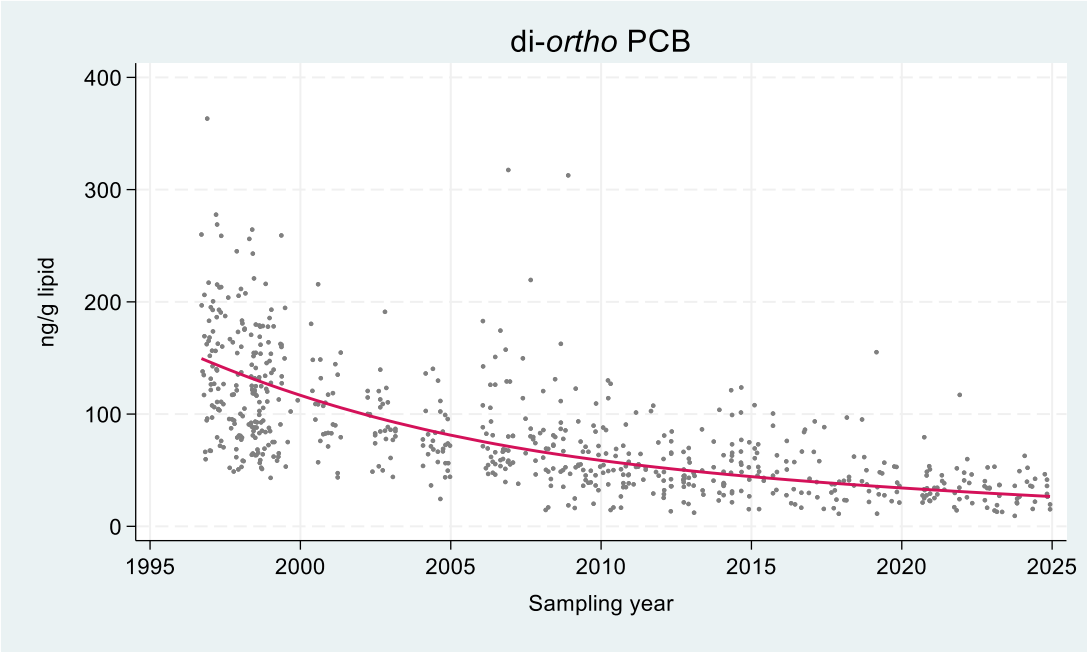
When PCBs and PCDD/Fs were analysed before and after specified years using linear spline models, slower decreasing rates were observed towards the end of the study period

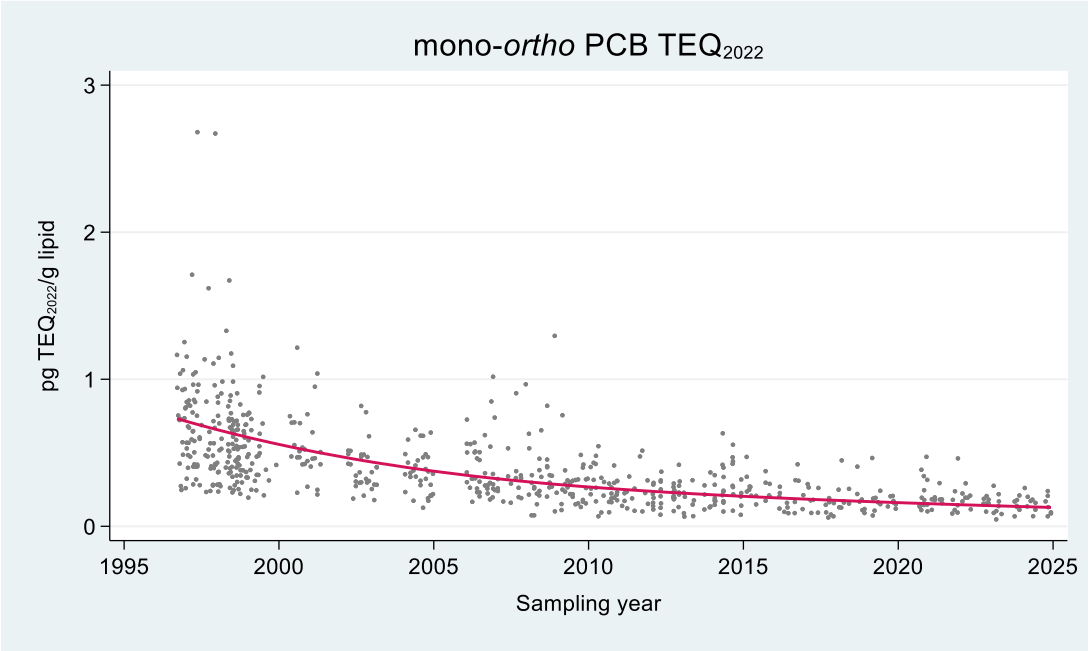
for all compounds, except of CB 28.The temporal trend for CB 28 were divided into three time periods showing a slower decrease in levels during 2003-2013 compared to the time period before and after that (Table 4). The decline in human milk levels of PCBs and total-TEQ between 1996 and 2024 is in agreement with results from five Swedish market basket studies performed 1999, 2005, 2010, 2015, and 2022 showing an annual decline of 6% in the calculated per capita intake of CB 153 and around 4% for total-TEQ_{2005} from food (Livsmedelsverket. 2024). However, the annual change of total-TEQ in the Swedish market basket studies was calculated with the 2005 TEFs (Van den Berg et al. 2006), but in the POPUP-study (Table 4) with the 2022 TEFs (DeVito et al. 2024). It is important to continue with the temporal trend studies of POPs in human milk to investigate whether concentrations continue to decrease or are stabilizing at current levels.

Table 4. Percent change in concentrations of PCBs and PCDD/Fs per year in human milk from primiparous women in Uppsala 1996-2024 using linear regression models. The change in concentration per year is presented before and after specified years using linear spline models. Both models are adjusted for age of the mother, pre-pregnancy BMI, weight gain during pregnancy, weight loss after delivery and educational level. Concentrations <LOQ was recalculated to ½LOQ.

Compound	n	Years	Mean change per year %	95% CI	p	Years	Mean change per year %	95% CI	p	Years	Mean change per year %	95% CI	p	R^{2a}
CB 28	655	1996-2024	-4.8	-5.4/-4.1	<0.001									25
		1996-2002	-6.2	-9.4/-2.8	<0.001	2003-2013	-2.7	-4.7/-0.7	<0.01	2014-2024	-7.8	-9.9/-5.7	<0.001	26
CB 153	664	1996-2024	-6.2	-6.5/-5.8	<0.001									70
		1996-2007	-7.4	-8.1/-6.7	<0.001	2008-2024	-4.9	-5.7/-4.0	<0.001					71
di-*ortho*	665	1996-2024	-6.0	-6.4/-5.7	<0.001									71
PCB[b]		1996-2008	-6.9	-7.6/-6.3	<0.001	2009-2024	-5.1	-5.9/-4.3	<0.001					72
mono-*ortho*	662	1996-2024	-6.2	-6.5/-5.8	<0.001									69
PCB TEQ[c]		1996-2008	-7.4	-8.1/-6.7	<0.001	2009-2024	-4.8	-5.6/-4.0	<0.001					70
non-*ortho*	522	1996-2024	-5.5	-5.9/-5.1	<0.001									59
PCB TEQ[d]		1996-2008	-7.1	-7.9/-6.2	<0.001	2009-2024	-4.0	-5.0/-2.9	<0.001					61
PCDD TEQ	487	1996-2024	-6.8	-7.2/-6.5	<0.001									80
		1996-2007	-8.5	-9.2/-7.9	<0.001	2008-2024	-5.6	-6.2/-4.9	<0.001					81
PCDF TEQ	488	1996-2024	-2.6	-3.0/-2.2	<0.001									35
		1996-2006	-4.2	-5.1/-3.3	<0.001	2007-2024	-1.6	-2.4/-0.9	<0.001					37
PCDD/F	487	1996-2024	-5.3	-5.6/-4.9	<0.001									69
TEQ[e]		1996-2007	-7.2	-7.9/-6.5	<0.001	2008-2024	-3.8	-4.5/-3.2	<0.001					71
Total-TEQ[f]	486	1996-2024	-5.3	-5.7/-5.0	<0.001									71
		1996-2007	-7.2	-7.8/-6.5	<0.001	2008-2024	-4.0	-4.7/-3.3	<0.001					73

[a]Coefficient of determination for the regression model. [b]sum of CB 153, 138, 180. [c]sum of CB 105, 118, 156, 167 TEQs based on 2022 WHO TEFs (DeVito et al. 2024). [d]sum of CB 77, 126, 169 TEQs based on 2022 WHO TEFs (DeVito et al. 2024). [e]sum of PCDD TEQ and PCDF TEQ. [f]sum of mono-*ortho* PCB TEQ, non-*ortho* PCB TEQ, PCDD TEQ and PCDF TEQ


di-*ortho* PCB
ng/g lipid
400
300
200
100
0
1995
2000
2005
2010
2015
2020
2025
Sampling year


mono-*ortho* PCB TEQ$_{2022}$
pg TEQ$_{2022}$/g lipid
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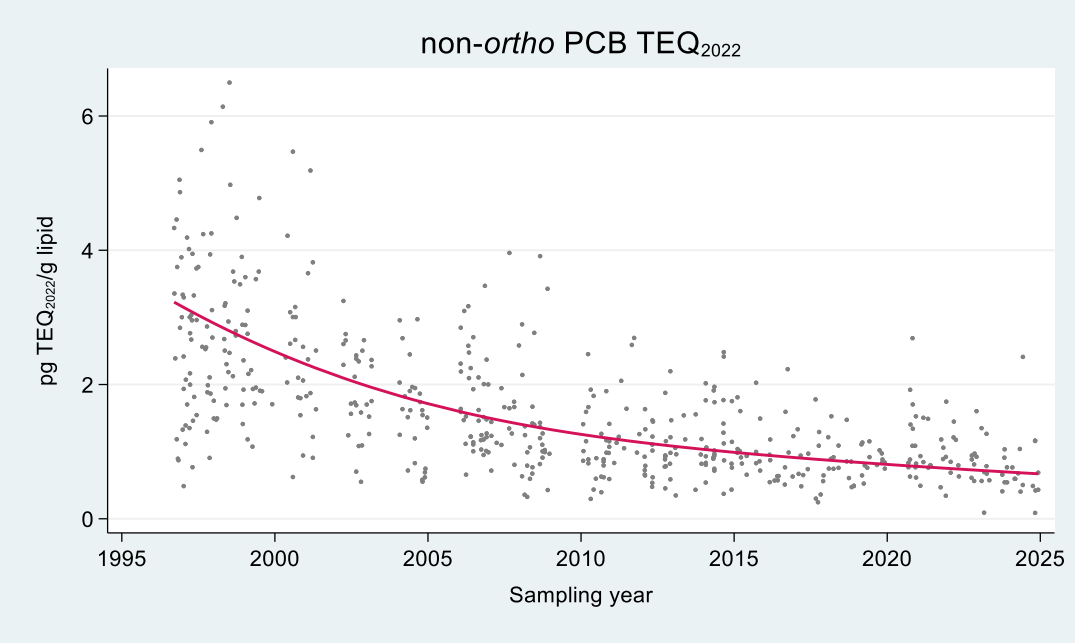
2
1
0
1995
2000
2005
2010
2015
2020
2025
Sampling year


non-*ortho* PCB TEQ$_{2022}$
pg TEQ$_{2022}$/g lipid
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2
4
6
1995
2000
2005
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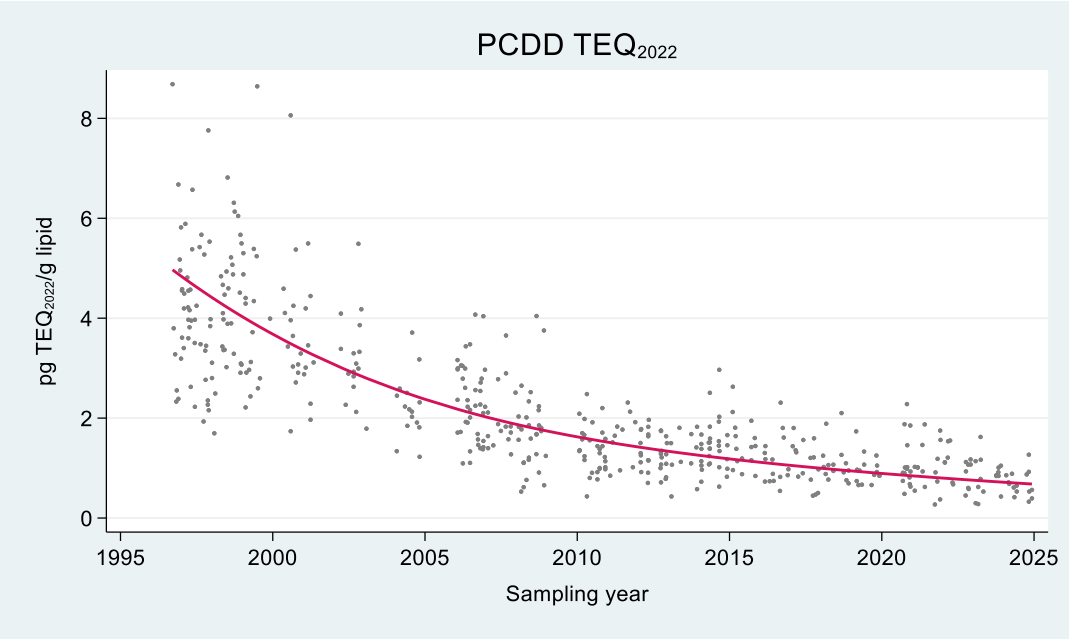
2015
2020
2025
Sampling year


PCDD TEQ$_{2022}$
pg TEQ$_{2022}$/g lipid
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2
4
6
8
1995
2000
2005
2010
2015
2020
2025
Sampling year

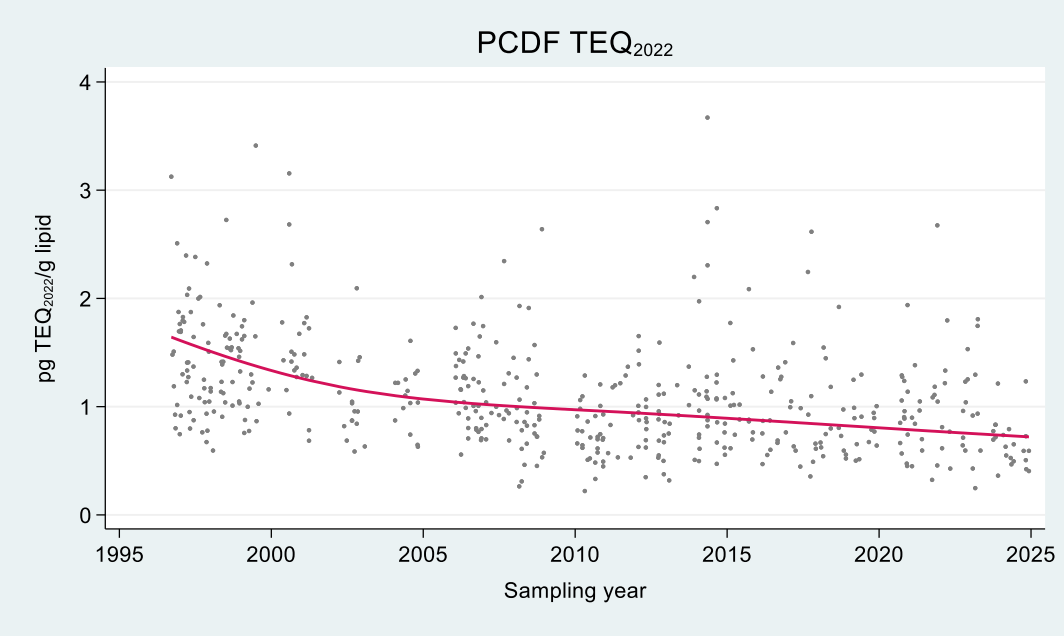


Figure 2. Levels of di-*ortho* PCBs (n=665), mono-*ortho* PCB TEQ_{2022} (n=662), non-*ortho* PCB TEQ_{2022} (n=522), PCDD TEQ_{2022} (n=487), and PCDF TEQ_{2022} (n=488) in human milk from first-time mothers in Uppsala, Sweden sampled in 1996-2024. Each point corresponds to the concentration in a milk sample from an individual woman. Concentrations <LOQ were recalculated to LOQ/2. The red lines show the temporal trend from the cubic spline models adjusted for maternal age, pre-pregnancy BMI, body weight gain during pregnancy, body weight change during the period from delivery to sampling, and educational level.

The levels of BDE 47, BDE 99, BDE 100, sumPBDE, and HBCDD have decreased with similar rates, in mean 6-12 % per year during 1996-2024, as in the latest report of the POPUP-study (Hedvall Kallerman et al. 2024a) (Table 5). As previously reported in human milk, BDE 209 continues to show a significant decreasing temporal trend, around 7% per year (2009-2024). The decreasing rate was higher compared to the decrease of BDE 209 in pooled blood serum samples from women in the POPUP-study, that was around 3% between 1996 and 2023 (Hedvall Kallerman et al. 2024b).

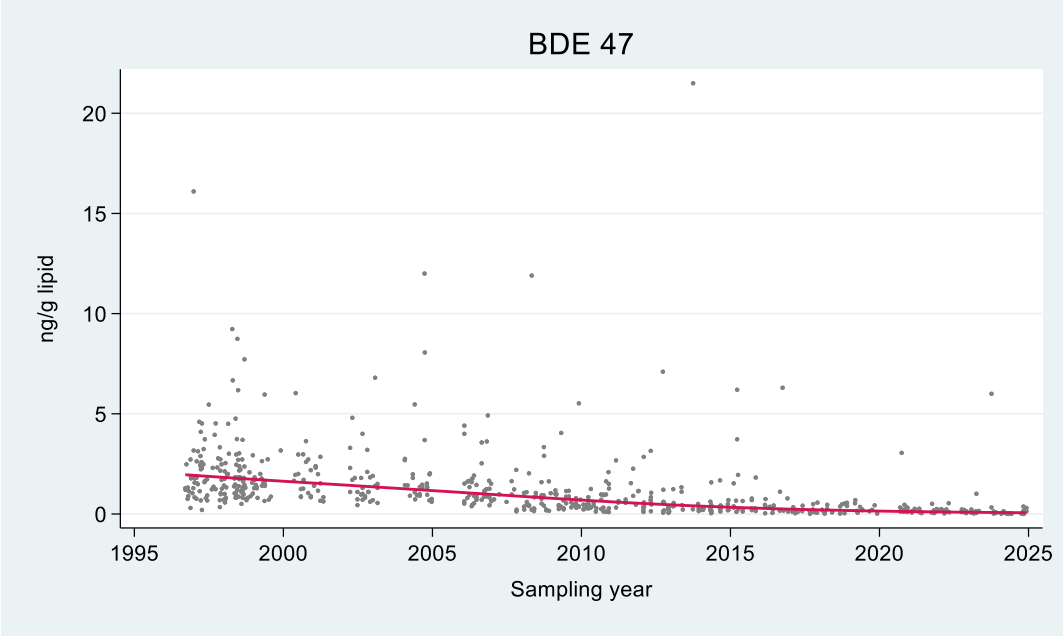
In addition, when PBDEs were studied before and after specified years using linear spline models, faster declining trends were observed towards the end of the study period compared with the entire study period and the beginning of the study (Table 5, Figure 3, and Appendix). A decrease in concentrations of BDE 47, BDE 99, and BDE 100 is now seen in the beginning of the study (1996-2003/2008/2010) which were non-significant in the previous report (Hedvall Kallerman et al. 2024a). The specified years used in the linear spline models were different between the previous and the present report. Hence, different years were included in the regressions presented in table 5 which in turn might have affected the difference in significance between the two reports. A significant increase during the first years of the study (1996-2002/2007) was still seen for BDE 153 and HBCDD compared with the previous report, however for BDE 209 the previous non-significant increase is now significant (2009-2012). This might, as for BDE 47, BDE 99, and BDE 100, have been affected by differences in specified years used in the linear spline model for BDE 209. In the last part of the study there was a decrease of about 12-16% for BDE 47, BDE 99, BDE 100, and BDE 209 (2004/2009/2011-2024, and 2009-2024) whereas for BDE 153, and HBCDD (2003/2008-2024) the decrease was 3 and 10% respectively. Overall, the decreases seen in the last part of the study were slightly higher than those reported previously (Hedvall Kallerman et al. 2024a).

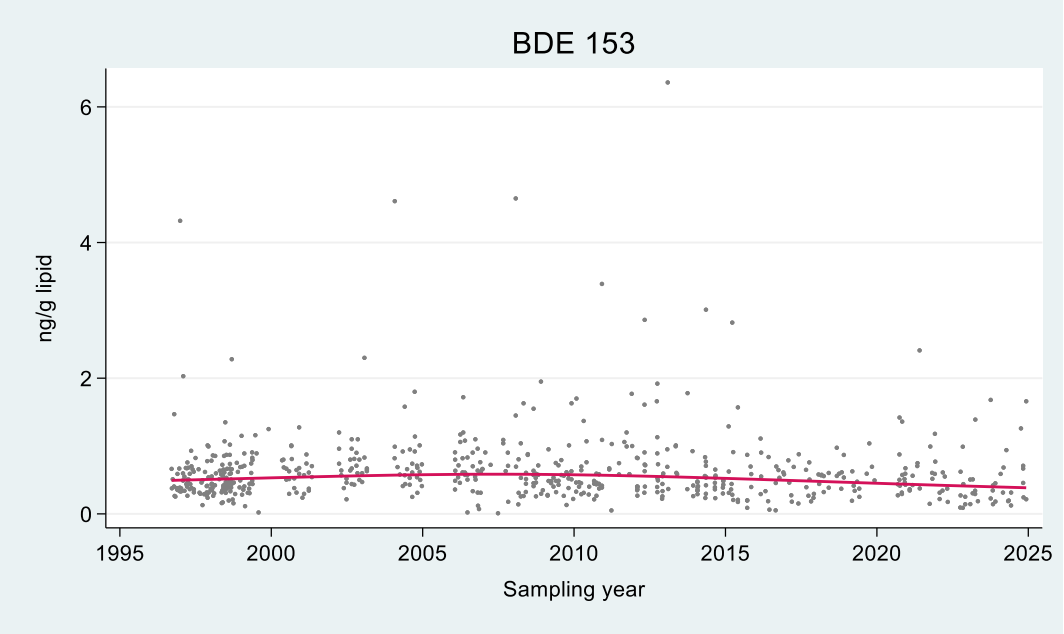
Decreasing levels of PBDEs in humans and faster declining rates during the latter part of the study are expected since the use of lower brominated congeners has been voluntarily reduced since the 1990s and the use of PBDEs in electric and electronic products has been restricted by law since 2008 (European Parliament 2011). In agreement with our results, Swedish market basket studies performed between 1999 and 2022, showed that the mean per capita intake of BDE 47, BDE 99, BDE 100, and HBCDD has decreased around 3-10% per year during the study period (Livsmedelsverket. 2024). The mean per capita intake for BDE 209 was uncertain in the Market basket 2022.

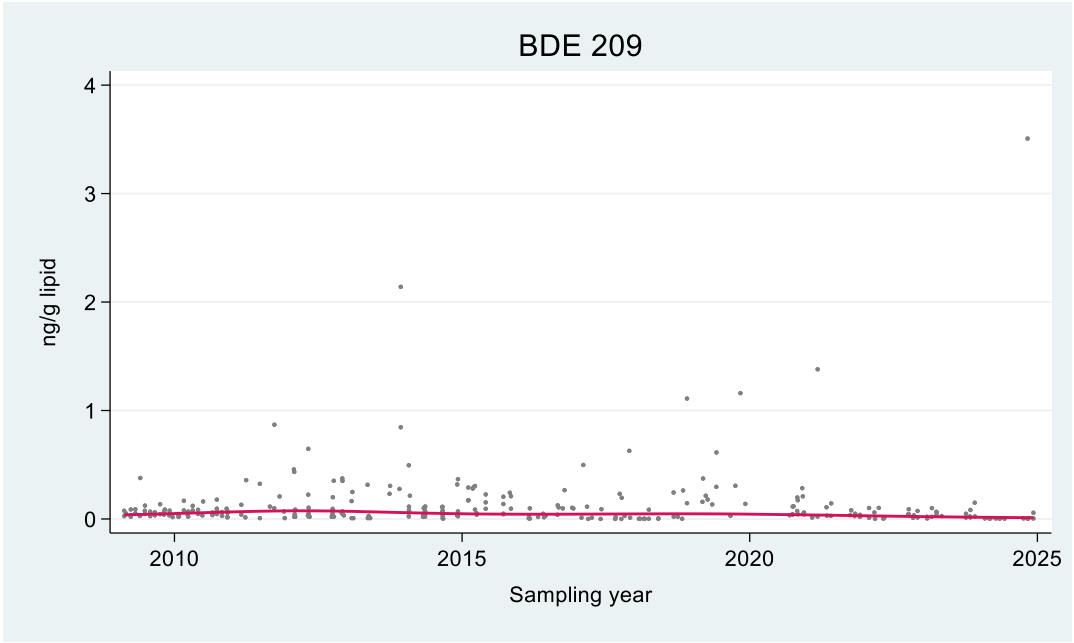
Table 5. Percent change in concentrations of PBDEs and HBCDD per year in human milk from primiparous women in Uppsala 1996-2024 using linear regression models. Thereafter the change in concentration per year is presented before and after specified years using linear spline models. Adjusted for age of the mother, pre-pregnancy BMI, weight gain during pregnancy, weight loss after delivery, and educational level. Reported PBDE and HBCDD concentrations, adjusted for concentrations in blank samples, were used instead of LOQ/2 when available.

Compound	n	Years	Mean change per year %	95% CI	p	Years	Mean change per year %	95% CI	p	R^{2a}
BDE 47	607	1996-2024	-11.0	-11.9/-10.2	<0.001					52
		1996-2010	-8.0	-9.4/-6.6	<0.001	2011-2024	-15.7	-18.2/-13.1	<0.001	54
BDE 99	607	1996-2024	-11.6	-12.6/-10.5	<0.001					44
		1996-2003	-8.5	-11.4/-5.4	<0.001	2004-2024	-12.7	-14.3/-11.1	<0.001	45
BDE 100	607	1996-2024	-8.0	-8.9/-7.2	<0.001					36
		1996-2008	-3.9	-5.5/-2.3	<0.001	2009-2024	-12.3	-14.4/-10.0	<0.001	40
BDE 153	607	*1996-2024*	*-0.6*	*-1.3/0.0*	*0.052*					8
		1996-2007	1.5	0.1/3.0	<0.01	2008-2024	-2.5	-3.8/-1.1	0.001	10
BDE 209	292	2009-2024	-7.0	-10.4/-3.4	<0.001					3
		2009-2012	11.9	0.2/25.0	<0.05	2013-2024	-12.4	-17.0/-7.5	<0.001	8
sumPBDE[b]	607	1996-2024	-6.1	-6.8/-5.5	<0.001					65
		1996-2008	-4.9	-6.2/-3.7	<0.001	2009-2024	-7.4	-8.8/-6.0	<0.001	40
HBCDD	511	1996-2024	-6.4	-7.3/-5.5	<0.001					25
		1996-2002	10.5	6.5/14.6	<0.001	2003-2024	-9.5	-10.9/-8.1	<0.001	33

[a]Coefficient of determination for the regression model. [b]Sum of BDE 47, 99, 100, 153.


BDE 47
ng/g lipid
0
5
10
15
20
1995
2000
2005
2010
2015
2020
2025
Sampling year


BDE 153
ng/g lipid
0
2
4
6
1995
2000
2005
2010
2015
2020
2025
Sampling year



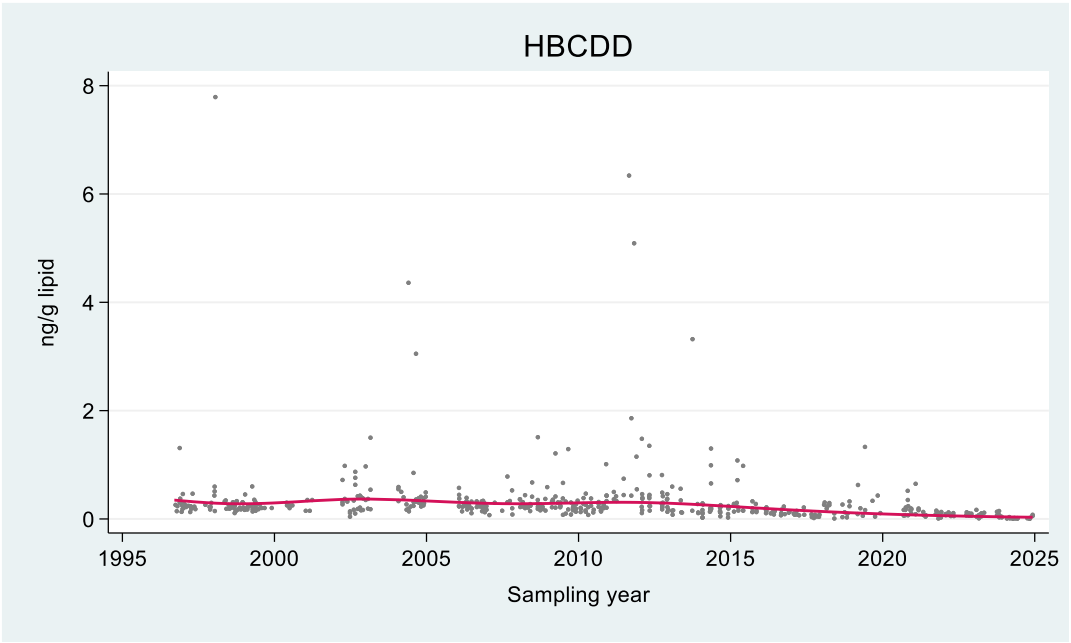


Figure 3. Levels of BDE 47 (n=607), BDE 153 (n=607), BDE 209 (n=292), and HBCDD (n=511) in human milk from first-time mothers in Uppsala, Sweden 1996-2024 (2009-2024 for BDE 209). Each point corresponds to the concentration in a milk sample from an individual woman. Reported PBDE and HBCDD concentrations, adjusted for concentrations in blank samples, were used instead of LOQ/2 when available. The red lines show the temporal trend from the cubic spline models adjusted for maternal age, pre-pregnancy BMI, body weight gain during pregnancy, body weight change during the period from delivery to sampling, and educational level.

CONCLUSION

The levels of PCBs and PCDD/Fs in human milk from the POPUP-cohort showed over all decreasing temporal trends between 1996 and 2024. The levels of PCDD TEQ have decreased faster than the levels of PCDF TEQ (mean 7% and 3% per year, respectively). When different time periods were evaluated, the results showed that the decrease in levels occurred faster at the beginning of the study 1996-2006/2007 compared to the latter part until 2024. Although human milk concentrations of total TEQ is decreasing, still 4 out of 30 women (13%), sampled 2023-2024, had levels above the EFSA estimated safe level (using 2005 WHO TEFs as EFSA is currently revising its Scientific Opinion on dioxin-like PCBs and dioxins). A comparison between TEQs calculated with the new and old TEFs showed that total TEQs in human milk samples from 1996-2024 were in mean 44% lower when calculated with the new 2022 WHO TEFs, due to the decreased TEF-values for several congeners. However, the lower TEQ does not mean that the risk has decreased for dioxin-like PCBs and dioxins as the TWI from EFSA needs to be revised. Further, all PBDEs and HBCDD except BDE 153 showed decreasing trends 1996-2024. When the study period was divided into two parts, the results show that the levels decreased faster during the second part of the period compared to the first part. In the last report of the POPUP-study the temporal trend of BDE 209 was for the first time significantly decreasing. In the present report this finding has been confirmed with a decrease of 7% per year for the whole time period 2009-2024 and with a faster decrease of about 12% during 2013-2024. For BDE 153 and HBCDD the levels in human milk increased significantly during 1996-2002/2007 and after that the levels decreased on average with 3 and 10% respectively. It is important to continue monitoring concentrations of POPs in human milk from Swedish mothers in order to follow and further investigate if the concentrations of PCBs and PCDD/Fs are stabilizing at current levels or continue to decrease.

ACKNOWLEDGEMENT

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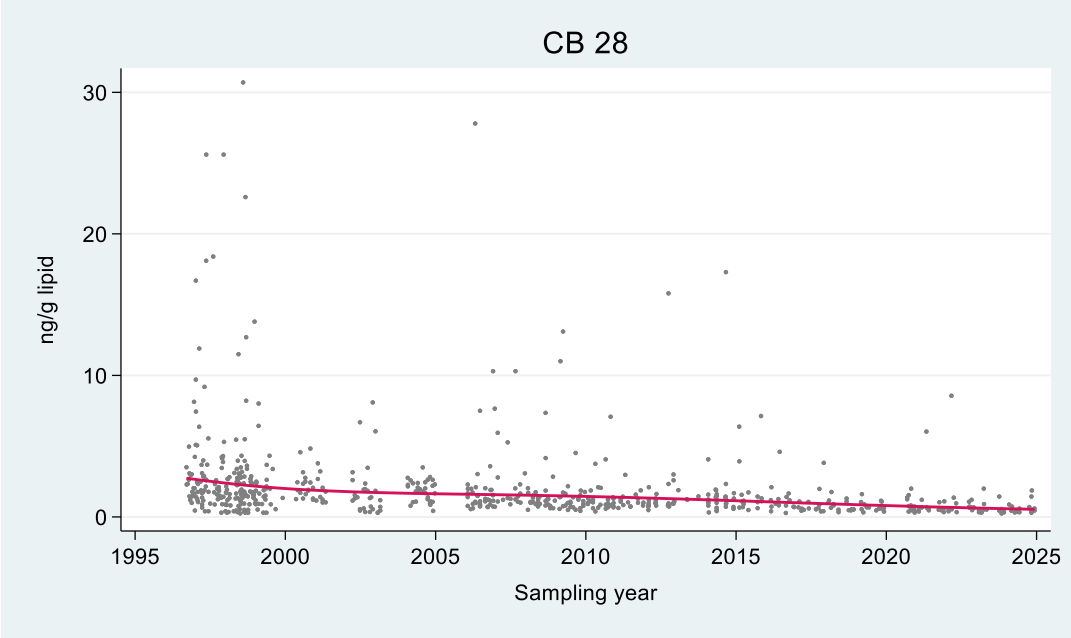
APPENDIX

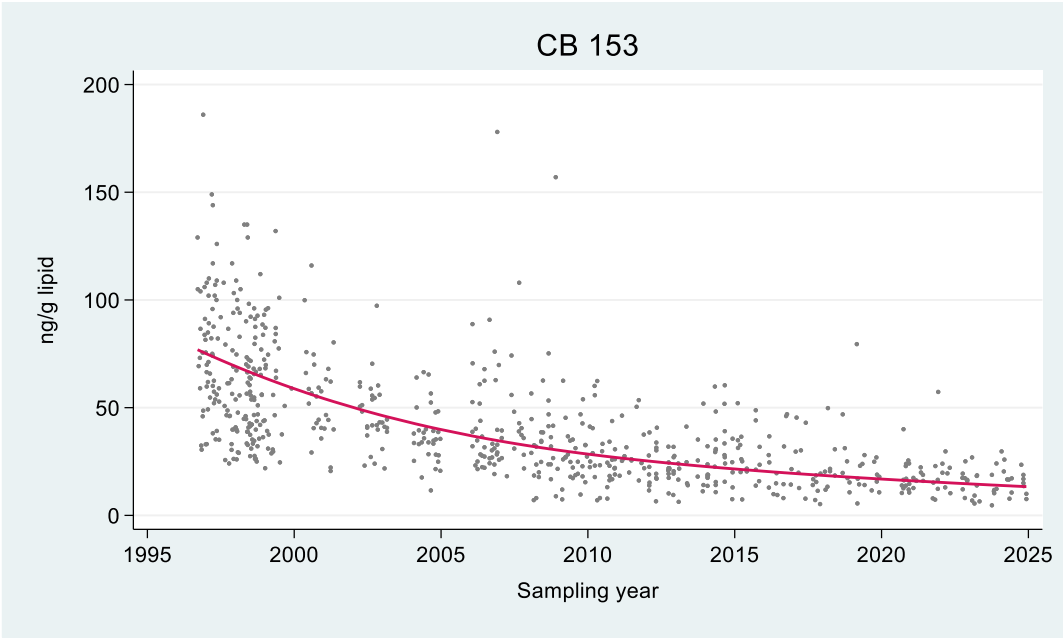
Additional figures

The figures below are not included in the report.

Levels of PCB 28 (n=655), PCB 153 (n=664), PCDD/F TEQ_{2022} (n=487), total TEQ_{2022} (n=486), BDE 99 (n=607), BDE 100 (n=607) and sumPBDE (the sum of BDE 47, 99, 100 and 153) (n=607) in human milk from first-time mothers in Uppsala, Sweden in 1996-2024. Each point corresponds to the concentration in a milk sample from an individual woman.

Concentrations <LOQ was recalculated to LOQ/2. PBDE-levels were adjusted for levels in blank samples. Concentrations below LOQ were available for human milk samples from 2009-2024 (and in some samples 2002-2008) and these reported levels below LOQ (adjusted for levels in blank samples) were used instead of half of LOQ. Levels estimated to be zero or negative after blank reduction were in the statistical analyses set to the lowest estimated level found above zero. The red lines show the temporal trend from the cubic spline models adjusted for maternal age, pre-pregnancy BMI, body weight gain during pregnancy, body weight change during the period from delivery to sampling, and educational level.

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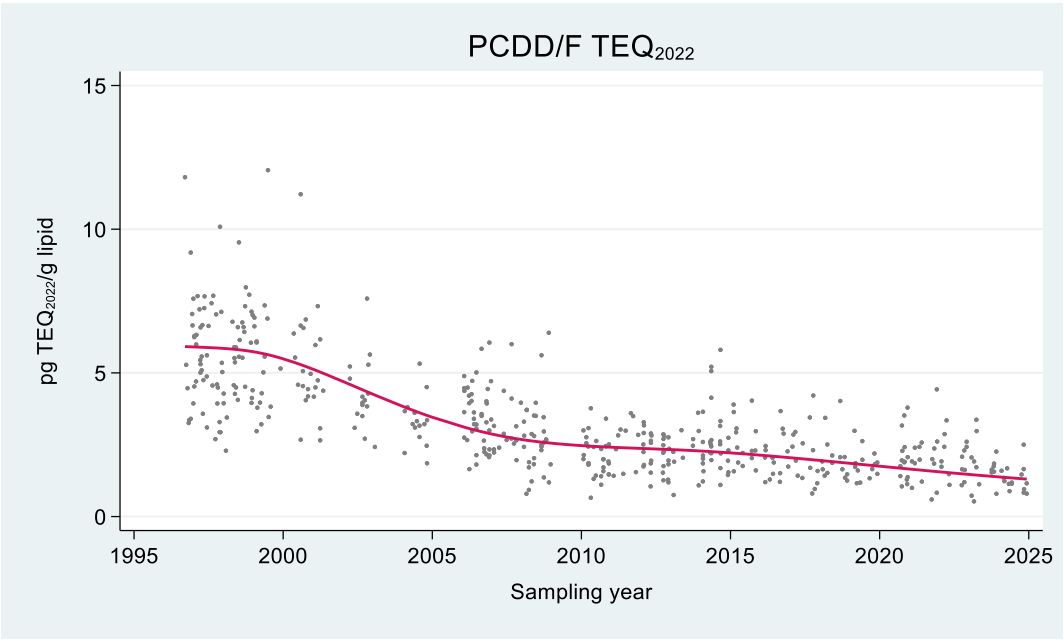
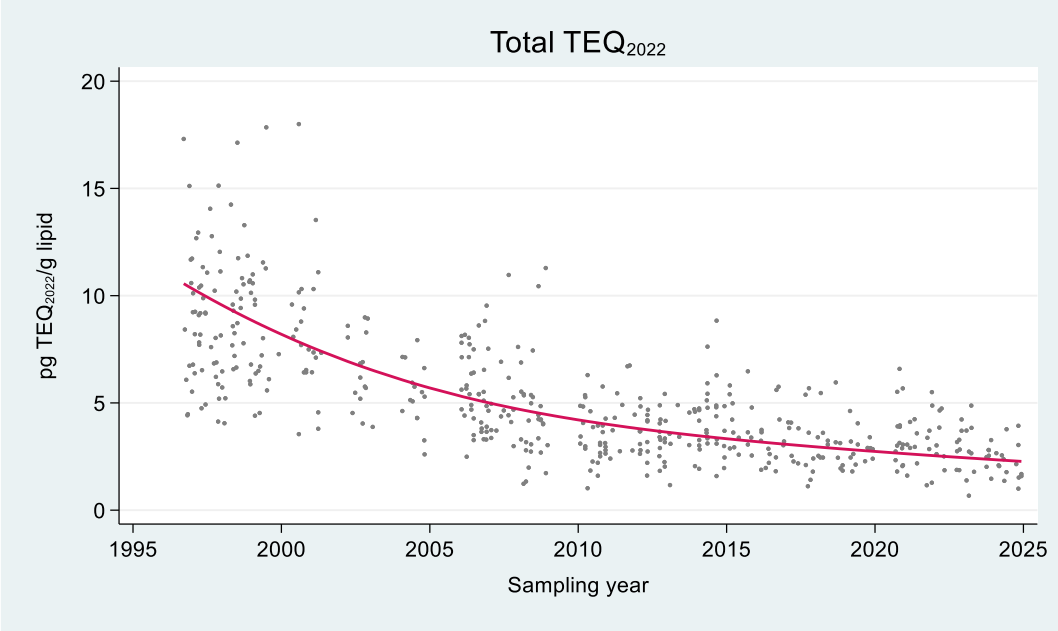
ng/g lipid
200
150
100
50
0
1995
2000
2005
2010
2015
2020
2025
Sampling year


PCDD/F TEQ2022
pg TEQ2022/g lipid
15
10
5
0
1995
2000
2005
2010
2015
2020
2025
Sampling year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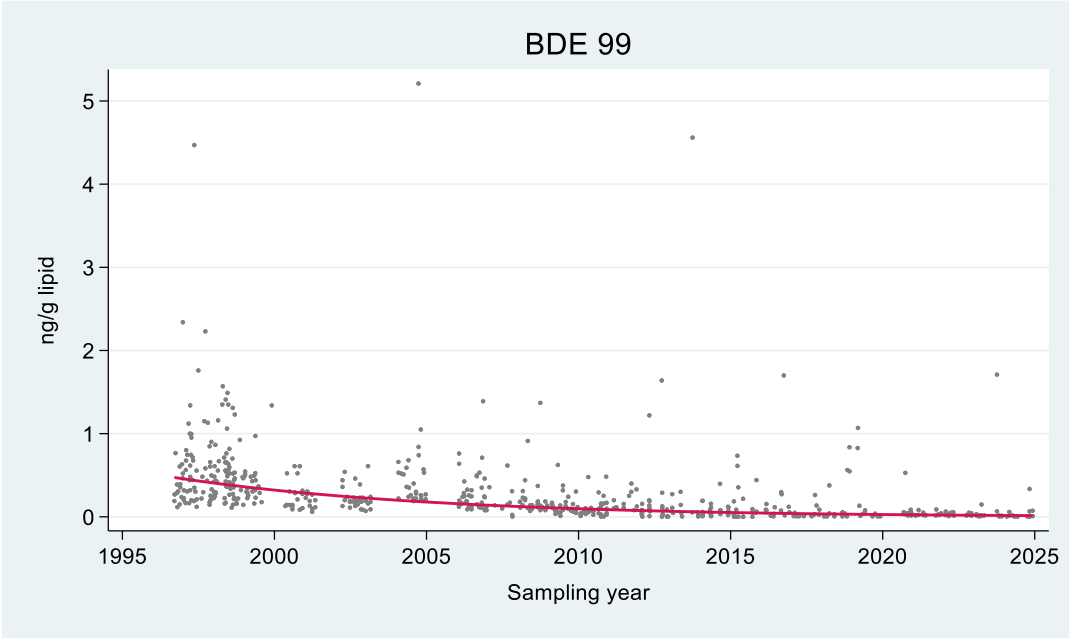
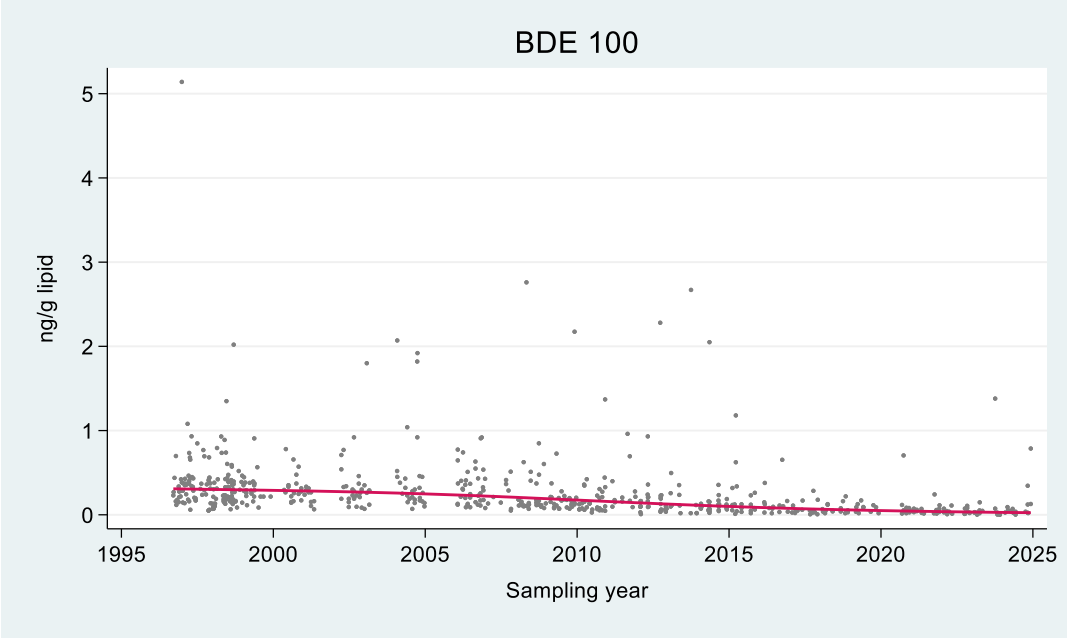
5
10
15
20
1995
2000
2005
2010
2015
2020
2025
Sampling year


BDE 99
ng/g lipid
0
1
2
3
4
5
1995
2000
2005
2010
2015
2020
2025
Sampling year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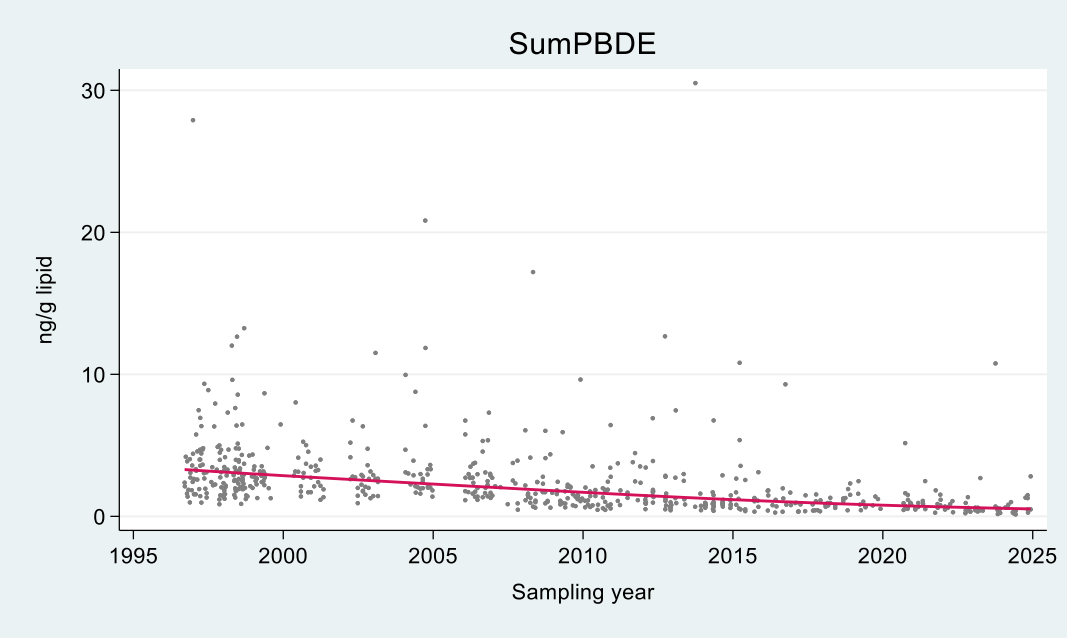
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